Herbals: Therapeutic and Adverse Effects
A bibliography with abstracts
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The purpose of this bibliography is to provide a brief survey of the literature covering the publication years 1997-1999. This bibliography includes citations from published articles, books, books chapters, and technical reports. Citations to articles in non-English languages are indicated with [ ] around the title. The language is also indicated. Citations are organized under subject categories; General, Adverse Effects, Mechanisms/Pharmacology, Therapeutic Use. Citations have been selected from the TOXLINE database of the National Library of Medicine, National Institutes of Health. The search strategy included terms for the general concept of herbals as well as many specifics.

General

Naturals, botanicals and minerals. Cosmet Toiletries 1998 Oct;113:81-2, 84, 86, 88, 90-1
IPA COPYRIGHT: ASHP A list of new natural, botanical, and mineral materials for the cosmetic industry, including trade names, properties, claims, applications, and sources, is presented.

Adamolekun B, Hakim JG. **Opsoclonus-myoclonus associated with traditional medicine ingestion: case report.** East Afr Med J 1998;75(2):120-1.
A case of Opsoclonus-Myoclonus occurring in a young man, in association with traditional herbal medicine consumption is presented. Clinical and laboratory investigations did not reveal any of the known aetiological associations of the Opsoclonus-Myoclonus syndrome, raising the possibility that the traditional herbal medicine may be aetiologically implicated. This report highlights the need for proper identification and documentation of the contents of common herbal remedies and their possible side effects amongst Africans.

Ali M. **Herbal pharmacy.** Indian J Pharm Educ 1997;31(1):13-7.
IPA COPYRIGHT: ASHP The history of Ayurvedic, Unani, and Chinese herbal pharmacy, herbal drugs in western countries, and the place of herbal drugs in modern medicine and pharmacy are discussed.

Baek NI, Kim JM, Park JH, Ryu JH, Kim SI, et al . **Ginsenoside Rs3, a genuine dammarane-glycoside from Korean red ginseng.** Arch Pharmacal Res 1997;20(3):280-2.

Balcerska I, Wedzisz A, Uramowski J. **[Nitrates and nitrites in selected herbs and herbal preparations].** Bromatol Chem Toksykol 1997;30(2):119-23. (Pol)
BIOSIS COPYRIGHT: BIOL ABS. Several single herbs, herbal blends and granulates were tested for their nitrate and nitrite content. Griess colorimetry was used. All test herbs and preparations were found to contain nitrates and nitrites.

Bao K. **Traditional Chinese materia medica (TCMM).** Altern Ther Health Med 1997;3(1):18.

Barton BE, Tagat JR. **Current status of interleukin-6 inhibitors.** Drugs Future 1997 Apr;22:391-5.
IPA COPYRIGHT: ASHP A review of interleukin inhibitors is presented, including biopharmaceuticals such as antibodies, toxic fusion proteins, and peptide antagonists; synthetic chemicals; and miscellaneous compounds such as botanical extracts, marine extract, and tretinoin (retinoic acid).

Borkowski B. **[Herbal drugs used in atherosclerosis--antisclerotica].** Farm Pol 1998;54(10):435-47. (Pol)

Bull SS, Melian M. **Contraception and culture: the use of yuyos in Paraguay.** Health Care Women Int 1998;19(1):49-60.
The use of herbs (yuyos) as contraception is common practice in Paraguay. This report analyzes data from the 1995-1996 Paraguayan Reproductive Health Survey. The analysis reveals that women are more familiar with yuyos (88%) than any other method of family planning. Modeling the determinants of ever having relied on yuyos as contraception demonstrates that older women (OR = 1.043) and women with more children (OR = 2.283) are significantly more likely to have used yuyos, but an interaction between older women with more children shows they are less likely to have used this method (OR = .982). Women living in rural areas (OR = .664) and those with more education (OR = .883) are less likely to have used the method. These findings show widespread acceptance and use of yuyos for contraception in Paraguay. More research into the chemical properties of yuyos is needed to determine their contraceptive efficacy and to prevent harmful effects from their misuse.

Chan TY. **Monitoring the safety of herbal medicines.** Drug Saf 1997;17(4):209-15.
Extremely limited knowledge about the ingredients in herbal medicines and their effects in humans, the lack of stringent quality control and the heterogenous nature of herbal medicines all necessitate the continuous monitoring of the safety of these products. In Hong Kong, safety information on herbal medicines has come from the enquiries and reports received by our Drug

and Poisons Information Service, on-going surveillance of patients treated in a large general teaching hospital and review of reports from the medical literature. Circumstances under which poisonings have occurred are also analysed in order to devise preventive measures. Once collected, this information is then distributed to health professionals in Hong Kong and abroad. WHO projects and pilot studies in Europe are also under way to promote and facilitate reporting of adverse reactions to herbal medicines.

Chandler F, Osborne F. **Burdock.** Can Pharm J 1997 Jun;130:46-9.
IPA COPYRIGHT: ASHP The botanical features, traditional and modern medicinal uses, constituents, pharmacology, toxicity, contraindications, precautions, and dosage of burdock (Arctium lappa; Arctium minus) are discussed.

Chavez ML, Chavez PI. **Saint John's Wort.** Hosp Pharm 1997 Dec;32:1621-8, 1631-2.
IPA COPYRIGHT: ASHP An overview of the chemistry, history, use, pharmacokinetics, and clinical pharmacology of St. John's Wort, a shrubby, perennial weed that has been used as an antidepressant, is presented, including a summary of clinical trials of St. John's Wort for depression as well as for antiviral effects, dosage and administration, and side effects and contraindications.

Chen DF, Zhang SX, Wang HK, Zhang SY, Sun QZ, Cosentino LM, Lee KH. **Novel anti-HIV lancilactone C and related triterpenes from Kadsura lancilimba.** J Nat Prod 1999;62(1):94-7.
Three new triterpene lactones, lancilactones A (1), B (2), and C (3), together with the known kadsulactone A (4), were isolated from the stems and roots of Kadsura lancilimba. Their structures and stereochemistries were determined primarily from mass and NMR spectral data. Compound 3 inhibited HIV replication with an EC50 value of 1.4 microg/mL and a therapeutic index of greater than 71.4.

Chung KT, Wong TY, Wei CI, Huang YW, Lin Y. **Tannins and human health: a review.** Crit Rev Food Sci Nutr 1998;38(6):421-64.
Tannins (commonly referred to as tannic acid) are water-soluble polyphenols that are present in many plant foods. They have been reported to be responsible for decreases in feed intake, growth rate, feed efficiency, net metabolizable energy, and protein digestibility in experimental animals. Therefore, foods rich in tannins are considered to be of low nutritional value. However, recent findings indicate that the major effect of tannins was not due to their inhibition on food consumption or digestion but rather the decreased efficiency in converting the absorbed nutrients to new body substances. Incidences of certain cancers, such as esophageal cancer, have been reported to be related to consumption of tannins-rich foods such as betel nuts and herbal teas, suggesting that tannins might be carcinogenic. However, other reports indicated that the carcinogenic activity of tannins might be related to components associated with tannins rather than tannins themselves. Interestingly, many reports indicated negative association between tea consumption and incidences of cancers. Tea polyphenols and many tannin components were suggested to be anticarcinogenic. Many tannin molecules have also been shown to reduce the mutagenic activity of a number of mutagens. Many carcinogens and/or mutagens produce oxygen-free radicals for interaction with cellular macromolecules. The anticarcinogenic and antimutagenic potentials of tannins may be related to their antioxidative property, which is

important in protecting cellular oxidative damage, including lipid peroxidation. The generation of superoxide radicals was reported to be inhibited by tannins and related compounds. The antimicrobial activities of tannins are well documented. The growth of many fungi, yeasts, bacteria, and viruses was inhibited by tannins. We have also found that tannic acid and propyl gallate, but not gallic acid, were inhibitory to foodborne bacteria, aquatic bacteria, and off-flavor-producing microorganisms. Their antimicrobial properties seemed to be associated with the hydrolysis of ester linkage between gallic acid and polyols hydrolyzed after ripening of many edible fruits. Tannins in these fruits thus serve as a natural defense mechanism against microbial infections. The antimicrobial property of tannic acid can also be used in food processing to increase the shelf-life of certain foods, such as catfish fillets. Tannins have also been reported to exert other physiological effects, such as to accelerate blood clotting, reduce blood pressure, decrease the serum lipid level, produce liver necrosis, and modulate immunoresponses. The dosage and kind of tannins are critical to these effects. The aim of this review is to summarize and analyze the vast and sometimes conflicting literature on tannins and to provide as accurately as possible the needed information for assessment of the overall effects of tannins on human health.

Chyau CC, Mau JL. **Release of volatile compounds from microwave heating of garlic juice with 2,4-decadienals.** Food Chem 1999;64(4):531-5.
BIOSIS COPYRIGHT: BIOL ABS. Garlic (Allium sativum L.) juice and 2,4-decadienals were heated in a microwave oven at the full power of 700 W. The volatile compounds of heated samples were isolated using diethyl ether solvent extraction and analysed using gas chromatography and gas chromatography-mass spectrometry. A total of 23 compounds were identified from these samples, among which 14 sulfide compounds, five aldehydes, two alcohols, one acid and one furan were identified. Three tentatively identified compounds, dithio(1-propenyl)propionate, dihydro-2(3H)-thiophenthione and n-hexanethiol were newly found in deep-fried garlic flavor. During microwave heating, levels of most volatiles decreased as the heating time continued. 2-Pentylfuran, isopropyl alcohol, hexanal and (E)-2-octenal were formed from the degradation of 2,4-decadienals. Sulfur dioxide was generated predominantly from the degradation and oxidation of sulfide compounds.

Cicero LA, Pareddy SR, Rosenberg JM. **Can depression patients be treated with worts?** Drug Top 1997 Sep 1;141:24.
IPA COPYRIGHT: ASHP The use of Hypericum perforatum (St. John's Wort) for depression therapy, including results of studies, possible mechanisms of action, toxicity, and dosage, is presented.

Combest WL. **Ginger.** US Pharm 1998 Feb;23:74, 79, 83-4, 86.
IPA COPYRIGHT: ASHP An overview of the medicinal uses of Zingiber officinale (ginger) is presented, including a discussion of the chemical composition and active constituents of ginger, pharmacology, side effects, and toxicity.

Combest WL. **Valerian.** US Pharm 1997 Dec;22:62, 64, 66, 68.
IPA COPYRIGHT: ASHP The uses, chemical composition, active constituents, results of

clinical studies, toxicity, dosage forms and recommendations of Valerian for insomnia are discussed.

Combest WL, Nemecz G. **Echinacea.** US Pharm 1997 Oct;22:126, 129-30, 132.
IPA COPYRIGHT: ASHP An overview of the medicinal uses of Echinacea species, which is also called purple coneflower, is presented, and components of active fractions of the plant, various types of Echinacea preparations, and the toxicity of Echinacea are considered.

Cornell S. **Alternatives to hormone replacement therapy. Do they measure up to estrogen?** Adv Nurse Pract 1997;5(7):45-6, 49, 72.

Crone CC, Wise TN. **Use of herbal medicines among consultation-liaison populations. A review of current information regarding risks, interactions, and efficacy.** Psychosomatics 1998;39(1):3-13. Consultation-liaison psychiatrists evaluate a wide variety of patients who are often disillusioned with conventional medical care and are seeking to gain some measure of control over their illness. With the growing popularity of alternative health care practices, consultation-liaison psychiatrists must learn more about the implications of herbal medicine usage. This review provides an overview of herbal medicines, a vital component of the alternative medicine movement.

Dasgupta P, Fowler CJ. **Chillies: from antiquity to urology.** Br J Urol 1997;80(6):845-52.

Davis WM. **Most frequently asked questions regarding depression.** Drug Top 1997 Oct 6;141:98-107.
IPA COPYRIGHT: ASHP Types of depression, risk factors, symptoms, causes, suicidal risk, genetic role, and therapy of clinical depression with antidepressants, including their side effects, effects on sex life, types of drugs used during pregnancy, herbal drugs, ethyl alcohol interactions, and electroconvulsive therapy, are discussed. This article qualifies for 2 hours U.S. CE credit by the ACPE.

De Smet PA. **The role of plant-derived drugs and herbal medicines in healthcare.** Drugs 1997;54(6):801-40.
Many of our present medicines are derived directly or indirectly from higher plants. While several classic plant drugs have lost much ground to synthetic competitors, others have gained a new investigational or therapeutical status in recent years. In addition, a number of novel plant-derived substances have entered into Western drug markets. Clinical plant-based research has made particularly rewarding progress in the important fields of anticancer (e.g. taxoids and camptothecins) and antimalarial (e.g. artemisinin compounds) therapies. In addition to purified plant-derived drugs, there is an enormous market for crude herbal medicines. Natural product research can often be guided by ethnopharmacological knowledge, and it can make substantial contributions to drug innovation by providing novel chemical structures and/or mechanisms of action. In the end, however, both plant-derived drugs and crude herbal medicines have to take the same pharmacoeconomic hurdle that has become important for new synthetic pharmaceuticals.

De Smet PA, Brouwers JR. **Pharmacokinetic evaluation of herbal remedies. Basic introduction, applicability, current status and regulatory needs.** Clin Pharmacokinet 1997;32(6):427-36.

De Vincenzi M, Mancini E. **Monographs on botanical flavouring substances used in foods. Part VI.** Fitoterapia 19997;68(1):49-61.
BIOSIS COPYRIGHT: BIOL ABS. RRM LITERATURE REVIEW ORIGANUM-MAJORANA ORIGANUM-CRETICUM MELITTIS-MELISSOPHYLLUM STACHYS-OFFICINALIS AJUGA-CHAMAEPITYS GALEOPSIS-SEGETUM POGOSTEMON-CABLIN VERBASCUM-DENSIFLORUM VERONICA-ALLIONII VERONICA-OFFICINALIS BALLOTA-NIGRA SALVIA-OFFICINALIS SATUREJA-MONTANA MARJORAM WOOD BETONY AJUGA PATCHOULI MULLEIN SPEEDWELL BLACK HOREHOUND SAGE WINTER SAVORY BIOCHEMISTRY AND BIOPHYSICS FOODS BOTANICAL FLAVORING SUBSTANCES CHEMICAL COMPONENTS TOXIC PROPERTIES.

Debrunner B, Meier B. **Petasites hybridus: a tool for interdisciplinary research in phytotherapy.** Pharm Acta Helv 1998;72(6):359-62.
The 3rd Petasites gathering took place in Romanshorn, Switzerland on March 29, 1996 and gave 16 European scientists the opportunity to transmit their latest considerable discoveries to interested researchers working in different scientific disciplines such as pharmacognosy, botany, chemistry, pharmacology, medicine or clinical pharmacy. The newest findings on Petasites hybridus as a significant plant drug showed very promising aspects of therapeutic utility. Great progress has been made in chemical analytical methods and the determination of pharmacological activities. Substantial advances have also occurred in the production of bioassay procedures and plant materials, particularly utilizing cell- and tissue-culture techniques.

Donaldson K. **Introduction to the healing herbs.** ORL Head Neck Nurs 1998;16(3):9-16.
For centuries, man has used plants for their healing properties. Today we refer to these plants as herbs. These plants play a principal part in all treatment modalities, both ancient and modern. The gentle, nourishing, and synergistic actions of herbal medicine make it an excellent treatment choice for all systems. Properties of ten commonly used herbs will be discussed. The herbs will be reviewed for their history, actions, indications and safety.

Duke CC, Moore DE, Roufogalis BD. **St. John's wort.** N Z Pharm 1998 Jan;18:13-4.
IPA COPYRIGHT: ASHP The characteristics, biological activity, common uses, clinical trials, and adverse effects of Hypericum perforatum (St. John's wort) are discussed.

Duncan MG. **The effects of nutritional supplements on the treatment of depression, diabetes, and hypercholesterolemia in the renal patient.** J Ren Nutr 1999;9(2):58-62.
The independent use of nutritional supplements has increased dramatically over the past several years. St. John's Wort for the treatment of depression, chromium for improvement of abnormal glucose and insulin regulation, and garlic for hypercholesterolemia, are among the more popular nutritional supplements being used by the population at large for their respective conditions. Depression, diabetes, and hypercholesterolemia are common to the renal patient. However, the efficacy of St. John's Wort, chromium, and garlic for these problems in the patient with impaired

renal function is not known. This article reviews the pharmacology, efficacy, safety, and pharmokinetics of these three food supplements in the nonrenal patient. There are encouraging data suggesting successful treatment in the otherwise normal individual. However, clinical studies examining the safety of these three supplements for the treatment of depression, diabetes, and hypercholesterolemia in the patient with renal disease are lacking and preclude recommendation of their use.

Dunford A, Eldin S. **Useful plants [letter; comment].** J R Soc Med 1997;90(3):178-9.

Eliason BC. **Alternative medicine--the case of herbal remedies [letter].** N Engl J Med 1999;340(7):564; Discussion 566.

Eliason BC, Kruger J, Mark D, Rasmann DN. **Dietary supplement users: demographics, product use, and medical system interaction.** J Am Board Fam Pract 1997;10(4):265-71.
BACKGROUND: Dietary supplements-defined as vitamins and minerals, herbal products, tissue extracts, proteins and amino acids, and other products-are purchased to improve health and prevent disease. Little has been published, however, about the characteristics of either the products or the people who use them. METHODS: Consecutive customers visiting two health food stores during a 15-day period were interviewed by telephone. They were asked about their use of dietary supplements, demographics, and their use of the established health care system. RESULTS: Of the 194 customers contacted, 136 (70.1 percent) completed the survey. Respondents took a total of 805 supplements, most often to prevent a health problem (84.3 percent). Herbal products were most commonly used. Garlic, ginseng, and Ginkgo biloba were the herbs most frequently used. Fifty products were found to have previously reported toxicities, including vitamin A, which 9 customers were taking in megadoses. Most customers were white (94.1 percent), female (75.7 percent), had at least 1 year of college education (70.6 percent), had health insurance (95.6 percent), and had a regular physician (85.3 percent). CONCLUSION: Most of the dietary supplements consumed appear to be safe, but 50 of 805 had previously reported toxicities including megadoses of vitamin A. Garlic, ginseng, and Ginkgo biloba were the most commonly ingested herbs, and the medical literature supports their effectiveness for some conditions in humans. Customers of two health food stores had average to above-average education and took dietary supplements to stay healthy. They used the conventional health care system but did not typically consult their physician about dietary supplements. The pattern of use suggests that physicians might not be adequately addressing preventive and wellness issues in discussions with their patients. Furthermore, physicians might need to learn about dietary supplements so they can communicate with patients about them.

Etkin NL. **Indigenous patterns of conserving biodiversity: pharmacologic implications.** J Ethnopharmacol 1998;63(3):233-45.
The accelerating rate at which the world's botanical resources are being depleted today has inspired redoubled efforts on the part of global conservation programs. For the most part, this reflects the actions of outsiders who are culturally and politically detached from the threatened environments, and who identify species for conservation through western economic models. In view of this, ethnopharmacologists--and primarily those representing the social sciences--have drawn attention to the cogency of indigenous knowledge of biotic diversity and its conservation.

This paper reviews how local paradigms of plant management promote conservation, and problematizes the issue specifically to the use of plants by Hausa peoples in northern Nigeria. The pharmacologic implications of indigenous patterns of plant use and conservation derive from the manifold and overlapping contexts in which plants, especially wild species, are used by local communities. These applications identify the importance of particular species and should be employed in assigning priority for the conservation of plants.

Falch B, Reichling J, Saller R. **[Ginger: not only a spice. Investigation of effects and effectivity].** Dtsch Apoth Ztg 1997 Nov 20;137:47-52, 55-60.(Ger)
IPA COPYRIGHT: ASHP The occurrence, morphological, microscopical, and organoleptic characteristics, constituents, traditional and modern uses, pharmacological effects, clinical and toxicological investigations, dosages, and methods of the application of ginger (Zingiber officinale Roscoe) rhizome and its medical preparations are discussed.

Fisher E, Lacy E. **Nutrition: nonvitamin food supplements.** Pharm Times 1997 Nov;63:97-105.
IPA COPYRIGHT: ASHP An overview of nonvitamin food supplements is presented, including bee pollen, bioflavonoids, carnitine, chromium, ubidecarenone (coenzyme Q-10), ginseng, kelp, melatonin, and tryptophan; the problems associated with the studies performed on nonvitamin food supplements, the sources of claims made for them, potential problems with self-administration of nonvitamin food supplements by the patient, the possible adverse effects of such supplements, and the process of counseling patients on the relative merits of supplementing one's diet with these substances are also discussed. This article qualifies for 2 hours U.S. CE credit by the ACPE.

Gaedcke F. **[St. John's Wort and its preparations: evaluation of quality with the aid of a selective reproducible HPLC procedure].** Dtsch Apoth Ztg 1997 Oct 16;137:117-21. (Ger)
IPA COPYRIGHT: ASHP The assessment of the pharmaceutical quality of the active principles of St. John's Wort (Hypericum perforatum), including hypericin and pseudohypericin, using a specially developed method with HPLC is discussed.

Germer S, Franz G. **[Ginger: manifold medicinal crude drug. Uses and thin layer chromatographic (TLC) assay according to the German Pharmacopeia 1997].** Dtsch Apoth Ztg 1997 Nov 20;137:40-6. (Ger)
IPA COPYRIGHT: ASHP A discussion of the crude drug ginger (Zingiber officinale Roscoe) is presented, including historical and botanical aspects, cultivation and harvesting, processing the rhizome, potential adulteration, contents of active substances, and uses. Pharmacopeial methods of TLC analysis of the active ingredients in ginger extracts are included.

Gillespie SG. **Herbal drugs and phytomedicinal agents.** Pharm Times 1997 Dec;63:53-62.
IPA COPYRIGHT: ASHP An overview of herbal drugs and phytomedicinal agents is presented, including a discussion of the history of herbal medicine, an outline of the regulation of herbal drugs in the United States and Europe, the extent and the demographics of use of herbal drugs, the characteristics of herbal drugs regarding composition, standardization, and dosage forms, and

the indications, contraindications, dose, and side effects of selected herbal drugs. This article qualifies for 2 hours U.S. CE credit by the ACPE.

Goldman LS. **Use of herbal medicines among C-L populations [letter].** Psychosomatics 1998;39(5):482.

Goodyear K, Lewith G, Low JL. **Randomized double-blind placebo-controlled trial of homoeopathic 'proving' for Belladonna C30.** J R Soc Med 19998;91(11):579-82.
Homoeopathic drug pictures are developed by recording the symptomatic effects of homoeopathic remedies given to healthy volunteers (a 'proving'). In a double-blind randomized controlled trial we tested the hypothesis that individuals using an infinitesimal dilution of Belladonna (thirtieth potency, C30) would record more true symptoms, on a questionnaire that contained both true and false Belladonna proving symptoms, than those receiving placebo. 60 volunteers entered the study and 47 completed data collection. We were unable to distinguish between Belladonna C30 and placebo using our primary outcome measure. For the secondary outcome measure we analysed the number of individuals who proved to the remedy according to our predefined criteria: 4 out of 19 proved in the Belladonna C30 group and 1 out of 27 in the placebo group (difference not statistically significant). This pilot study does not demonstrate a clear proving reaction for Belladonna C30 versus placebo, but indicates how the question might be further investigated.

Gori M, Campbell RK. **Natural products and diabetes treatment.** Diabetes Educ 1998;24(2):201-2, 205-8.
Many natural products are promoted to improve the health status of patients with diabetes by people making a profit on these products. Few of these claims have any scientific basis. Certain natural products are potentially damaging to patients with chronic diseases, especially if the products are used instead of proven scientific treatment regimens. Many individuals believe that if a product is natural it must be effective and safe. What is ironic is that if the products were safe and effective, and if studies would have been done on humans to prove safety and effectiveness, the sales of the products would greatly increase (as opposed to present limited sales as herbs from health food stores). Some of the products do have a beneficial effect, especially as a placebo if the patient believes that the product is going to work. As can be seen from the summary of products that are listed here that claim to improve the treatment of patients with diabetes, very few are available in a standard form that would produce a known positive effect. The few products that do have a mild impact on lowering blood glucose levels are much less effective than standard treatments. In a recent review of the role of plant-derived drugs and herbal medicines in healthcare, no natural products were listed as having a beneficial effect on diabetes. Diabetes care providers need to confront the issue of the use of natural products with their patients. Patients should be taught the importance of using proven, effective treatment regimens. Any patient who decides to use a natural product should be followed closely to make sure that no toxic effects occur and that treatment objectives are achieved.

Grabarczyk H, Horoszkiewicz M, Bloszyk E. **[Plant extracts in cosmetics].** Farm Pol 1997;53(6):250-7. (Pol)

Grauds C. **At last--standardized botanical products.** Pharm Times 1997 Apr;63:107.
IPA COPYRIGHT: ASHP The development of standardized botanical products is described, including the process of extraction of the plant material, how standards might be defined differently among competitive companies, and establishing therapeutic validity for standardized botanical products.

Grauds C. **Herbal ephedra and the pharmacist.** Pharm Times 1998 Mar;64:60, 62.
IPA COPYRIGHT: ASHP An overview of the popular herb ephedra (Ephedra species; Ma Huang), an herbal equivalent and precursor to the drugs ephedrine and pseudoephedrine, is presented, including the importance of pharmacists providing consultation to patients using this herb, indications for ephedra use, side effects, contraindications, and U.S. Food and Drug Administration (FDA) warnings and restrictions on ephedra-containing products.

Grauds C. **Strong herb sellers: up-and-comers for 1998.** Pharm Times 1998 May;64:48, 50.
IPA COPYRIGHT: ASHP The top 10 selling herbs as a result of a growing herbal market are listed, and research on the efficacy of Hypericum perforatum (St. John's wort) for depression and its potential drug interactions are briefly presented.

Gresser G. **[Broom: medicinal and poisonous plant, plantation net and devil's broom].** Dtsch Apoth Ztg 1998 Mar 5;138:51-2, 55-9. (Ger)
IPA COPYRIGHT: ASHP An overview of the etymology, botanical characteristics, distribution range, active constituents, including biogenic amines, flavonoids and iso-flavonoids, along with the therapeutic uses and toxicity of the plant broom, Cytisus scoparius (L) LINK (Leguminose), is presented.

Grush LR, Nierenberg A, Keefe B, Cohen LS. **St. John's Wort during pregnancy.** JAMA 1998 Nov 11;280:1566.
IPA COPYRIGHT: ASHP The cases of 2 women, ages 38 and 43 yr, who took Hypericum perforatum (St. John's Wort) in preference to standard antidepressant therapy during pregnancy are reported; the first patient experienced a recurrence of major depression during her first trimester of pregnancy and initiated H. perforatum at 900 mg/day, and the second patient discontinued fluoxetine hydrochloride and methylphenidate hydrochloride, which had been prescribed for refractory depression, and substituted 900 mg/day of H. perforatum. In the first patient, pregnancy and labor were uneventful, and the infant had Apgar scores of 9 at 1 and 5 min. The patient discontinued H. perforatum and began breastfeeding. The baby developed jaundice on day 5, which required brief phototherapy. The patient resumed H. perforatum on day 20 at 300 mg/day, but continued breastfeeding. Examination of the baby at 4 and 33 days was within the normal range.

Halberstein RA. **Traditional botanical remedies on a small Caribbean island: Middle (Grand) Caicos, West Indies.** J Altern Complement Med 1997;3(3):227-39.
A descriptive survey of 18 medicinal plants utilized on Middle (Grand) Caicos Island in the West Indies revealed that each species has multiple applications. Phytochemical constituents, ascertained from published sources, suggest pharmacological/physiological efficacy in the ethnomedical treatment of various disorders. Traditional preparation procedures may enhance the

chemotherapeutic value of the plant derivatives, while at the same time reducing their potential toxicity. The majority of species used in Middle Caicos are also exploited in other cultures but often for very different purposes.

Hammond GB, Fernandez ID, Villegas LF, Vaisberg AJ. **A survey of traditional medicinal plants from the Callejon de Huaylas, Department of Ancash, Peru.** J Ethnopharmacol 1998;61(1):17-30.
The medicinal uses of local flora from the Callejon de Huaylas, Department of Ancash, northeastern Peru, are reported. This geographical area has an old tradition of herbal healing. A total of 33 species have been documented through interactions with village elders, traditional doctors and herbalists. Of the 33 medicinal plant species surveyed in the Callejon de Huaylas, six have not been previously reported, seven have received only minor phytochemical coverage in the literature, and the medicinal uses of seven other plants have not been corroborated with traditional medicinal reports from around the world. The traditional medicinal uses of six medicinal plants have been corroborated with previously published reports but their biological activities have yet to be confirmed in the laboratory. The medicinal uses of four other plants have been corroborated with previously published reports and their biological activities have been confirmed in the laboratory. The purported medicinal use of three plant species could not be confirmed in the laboratory.

Harrison P. **Herbal medicine takes root in Germany [see comments].** CMAJ 1998;158(5):637-9.
The sale of Herbal Medicine is a growth industry in Germany, where physicians routinely prescribe these products and annual sales have surpassed $ 2 billion. Pam Harrison says the rising popularity has been driven by German patients, who began demanding herbal alternatives to synthetic drugs. Medical schools responded by reintroducing lessons on a topic that had been phased out of the medical curriculum.

Havlick HD. **From the customer's perspective.** Natural Pharm 1998 Aug;2:1, 10-1.
IPA COPYRIGHT: ASHP The importance of pharmacists in keeping abreast of natural and herbal products in light of the fact that more consumers purchase their natural products from pharmacies rather than health food stores is discussed, including what consumers look for when purchasing an herbal product, and how pharmacists might better serve their customers and increase their customer base.

Heiligenstein E, Guenther G. **Over-the-counter psychotropics: a review of melatonin, St John's wort, valerian, and kava-kava.** J Am Coll Health 1998;46(6):271-6.
Use and availability of alternative healthcare products have revived in the last few years. The prevalence of supplement use in the United States is largely unknown but is thought to be widespread. In this article, four of the common substances used to treat emotional problems are reviewed. The plant or substance description, clinical indications, evidence of therapeutic efficacy, mechanisms of therapeutic actions, dosages and regimens, different commercially available preparations, and adverse effects and toxicities are described for melatonin, St John's wort, valerian, and kava-kava. That a product is "natural" does not mean that it is either safe or

effective. Many supplements are potent drugs that lack sufficient data on safety, dose-response relationships, drug interactions, and purity.

Heinrich M, Ankli A, Frei B, Weimann C, Sticher O. **Medicinal plants in Mexico: healers' consensus and cultural importance.** Soc Sci Med 1998;47(11):1859-71.
Medicinal plants are an important element of indigenous medical systems in Mexico. These resources are usually regarded as part of a culture's traditional knowledge. This study examines the use of medicinal plants in four indigenous groups of Mexican Indians, Maya, Nahua, Zapotec and - for comparative purposes - Mixe. With the first three the methodology was similar, making a direct comparison of the results possible. In these studies, the relative importance of a medicinal plant within a culture is documented using a quantitative method. For the analysis the uses were grouped into 9-10 categories of indigenous uses. This report compares these data and uses the concept of informant consensus originally developed by Trotter and Logan for analysis. This indicates how homogenous the ethnobotanical information is. Generally the factor is high for gastrointestinal illnesses and for culture bound syndromes. While the species used by the 3 indigenous groups vary, the data indicate that there exist well-defined criteria specific for each culture which lead to the selection of a plant as a medicine. A large number of species are used for gastrointestinal illnesses by two or more of the indigenous groups. At least in this case, the multiple transfer of species and their uses within Mexico seems to be an important reason for the widespread use of a species. Medicinal plants in other categories (e.g. skin diseases) are usually known only in one culture and seem to be part of its traditional knowledge.

Heinrich M, Robles M, West JE, Ortiz De Montellano BR, Rodriguez E. **Ethnopharmacology of Mexican asteraceae (Compositae).** Annu Rev Pharmacol Toxicol 1998;38:539-65.
Traditional herbal remedies have increased in popularity in Europe and the United States in recent years but have always been important to people living in rural Mexico and to their Mexican American/Chicano descendants in the United States. Mexican American patients will often be ingesting herbal teas at the same time that they are being treated for their ailments with antibiotics or antiinflammatory agents. The plant family Asteraceae (Compositae) has contributed the largest number of plants to this pharmacopoeia; the reasons for the importance of this family include its large number of species in Mexico and its wide array of natural products that are useful in the treatment of the maladies that have afflicted the inhabitants of rural Mexico. These natural products include sesquiterpene lactones, polyacetylenes, alkaloids, monoterpenes, and various phenolics such as flavonoids. In this review, we emphasize the sesquiterpene lactones, a large group of compounds with antiinflammatory properties and the ability to relax smooth muscles and thereby relieve gastrointestinal distress. These compounds also readily form adducts with glutathione or free thiols and can thereby affect the metabolism, activity, and toxicology of a wide array of pharmacological agents.

Hendriks H. **Pharmaceutical aspects of some Mentha herbs and their essential oils.** Perfum Flavor 1998 Nov-Dec;23:15-23.
IPA COPYRIGHT: ASHP An overview of some herbs and essential oils of the Mentha species that are used in pharmaceuticals, including M. piperita (peppermint), peppermint oil, M. arvensis (cornmint; Japanese mint), cornmint oil, M. pulegium (pennyroyal), pennyroyal oil, M. spicata (spearmint), M. cardiaca (spearmint), and spearmint oil, is presented, including their quality

control, formulations, therapeutic uses, adverse effects, and toxicity; menthol, a constituent of Mentha species essential oils, is mentioned.

Hippius H. **St John's Wort (Hypericum perforatum)--a herbal antidepressant.** Curr Med Res Opin 1998;14(3):171-84.
A number of clinical studies conducted over the past few years have indicated that whole extract of St John's wort (Hypericum perforatum L.) has antidepressant effects. The herbal antidepressant St John's wort offers promising results in the treatment of patients with mild and moderate depression (response rate of 60-70% estimated by analysis of pooled data). St John's wort preparations are well tolerated. Their use rarely leads to adverse drug reactions which, when they do occur, are mainly subjective symptoms (e.g. gastrointestinal, dizziness). The generally good tolerability of St John's wort preparations and the resulting high patient compliance in taking the prescribed medication, in conjunction with their efficacy in mild and moderate depression, make these preparations particularly suitable for use in outpatient practice. Tolerability is also very good in elderly patients. If a sufficiently high-dose course of treatment with St John's wort preparations (900 mg daily) does not lead to a clear improvement in depression after four to six weeks, therapy should be continued with an established ('classical') antidepressant.

Hu SY. **Herbal teas and populace health care in tropical China.** Am J Chin Med 1997;25(1):103-34.
Commercial Chinese herbal tea is the development of the populace in tropical and subtropical China consequential to their fight against infectious diseases and their struggle to explore local plants to relieve fever, to alleviate pain, to restore strength and to modulate immunity against viral epidemics. From these ethnomedical experiences, two types of herbal teas were commercialized, namely, liangcha and medicated teas. Liangcha refers to a ready-made decoction infused from wild plants served in simple stores in cities and towns. Medicated teas are parcelled material prepared from crude drugs with or without tea (Camellia sinensis [L.] O. Ktze,), sold in colorful boxes and bags to people for use at home. Investigations of liangcha were made in Hong Kong and Macao, and studies for medicated teas were done from samples obtained in Chinese stores at Boston. A total of 127 source species of these herbal teas were identified and arranged in two alphabetical lists by the botanical names, each followed by an English common name in parenthesis, part used, frequency in samples, and family. External recognizing characters of medicated teas, discussions of problems encountered in identifying source species, relevant toxicities, and potential new vegetal pharmaceutical resources are given.

Huxtable RJ. **Safety of botanicals: historical perspective [editorial].** Proc West Pharmacol Soc 1998;41:1-10.

Iorio L, Nacca RG, Simonelli R. **Cistercian medicinal herbs for renal therapy in the 15th century.** Am J Nephrol 1997;17(3-4):286-8.
The rule conceived the monastery as a citadel of divine service so that medicine, together with other arts, was the subject of studies and searches which contributed to the foundation of monastic medicine. In the 14th and 15th centuries, Cistercian monks did not limit themselves to the study of the ancient treatises on medicinal herbs, but enlarged their knowledge through

clinical experience to such an extent that they created the principal therapy of diseases for about five centuries.

Jambor J. **[Strategies for the development of herbal drugs market].** Farm Pol 19998;54(5):201-9. (Pol)

Johnson ST, Wordell CJ. **Homeopathic and herbal medicine: considerations for formulary evaluation.** Formulary 1997 Nov;32:1166-8, 1171-3.
IPA COPYRIGHT: ASHP The principles, efficacy, risks, regulation, and examples of homeopathy and herbal medicine therapy, and formulary considerations for these types of alternative medicine are discussed.

Keplinger K, Laus G, Wurm M, Dierich MP, Teppner H. **Uncaria tomentosa (Willd.) DC.--ethnomedicinal use and new pharmacological, toxicological and botanical results.** J Ethnopharmacol 1999;64(1):23-34.
The medicinal system of the Ashaninka Indians in Peru is portrayed. Three categories of medical disorders and healers are recognized. A human is viewed to consist of a physical and a spiritual being who communicate with each other by means of a regulating element. The significance of Uncaria tomentosa (Willd.) DC. (Rubiaceae), locally known as una de gato, in traditional medicine is emphasized by its exclusive use by priests to influence this regulation. Pharmacological and toxicological results obtained with extracts or isolated compounds are summarized. Pentacyclic oxindole alkaloids stimulate endothelial cells in vitro to produce a lymphocyte-proliferation-regulating factor. Tetracyclic oxindole alkaloids act as antagonists. A significant normalization of lymphocyte percentage was observed in vivo although total leucocyte numbers did not change.

Khaliq Y. **Alternative medicine: what pharmacists need to know.** Pharm Pract 1997 Mar;13:44-50, 83-5.
IPA COPYRIGHT: ASHP An overview of alternative medicine with a focus on herbal medicine, homeopathy, and vitamin therapy is presented; the attitudes of patients, physicians, and pharmacists, benefits of alternative medicine, disadvantages of these therapies, such as lack of evidence, toxicity, drug interactions, and lack of regulation and quality control, and the pharmacist's role are discussed.

Klepser TB, Klepser ME. **Unsafe and potentially safe herbal therapies.** Am J Health Syst Pharm 1999;56(2):125-38; Quiz 139-41.
Unsafe and potentially safe herbal therapies are discussed. The use of herbal therapies is on the rise in the United States, but most pharmacists are not adequately prepared educationally to meet patients' requests for information on herbal products. Pharmacists must also cope with an environment in which there is relatively little regulation of herbal therapies by FDA. Many herbs have been identified as unsafe, including borage, calamus, coltsfoot, comfrey, life root, sassafras, chaparral, germander, licorice, and ma huang. Potentially safe herbs include feverfew, garlic, ginkgo, Asian ginseng, saw palmetto, St. John's wort, and valerian. Clinical trials have been used to evaluate feverfew for migraine prevention and rheumatoid arthritis; garlic for hypertension, hyperlipidemia, and infections; ginkgo for circulatory disturbances and dementia; ginseng for

fatigue and cancer prevention; and saw palmetto for benign prostatic hyperplasia. Also studied in formal trials have been St. John's wort for depression and valerian for insomnia. The clinical trial results are suggestive of efficacy of some herbal therapies for some conditions. German Commission E, a regulatory body that evaluates the safety and efficacy of herbs on the basis of clinical trials, cases, and other scientific literature, has established indications and dosage recommendations for many herbal therapies. Pharmacists have a responsibility to educate themselves about herbal therapies in order to help patients discern the facts from the fiction, avoid harm, and gain what benefits may be available.

Kligler B. **Herbal medicines and the family physician [editorial; comment].** Am Fam Physician 1998;58(5):1064-5.

Klink B. **Alternative medicines: is natural really better?** Drug Top 1997 Jun 2;141:99, 103. IPA COPYRIGHT: ASHP The rapid sales growth and risks vs benefits of alternative medicine and herbal products and the role of the pharmacists who sell these products are discussed.

Kosalec I. **[History and future of Echinacea species--natural immunostimulating plants].** Farm Glas 1998 May;54:161-70. (Scr)

Kozyrskyj A. **Herbal products in Canada. How safe are they? [see comments].** Can Fam Physician 1997;43:697-702.
OBJECTIVE: To examine existing evidence and inform family physicians about issues concerning herbal product use in Canada. QUALITY OF EVIDENCE: The Canadian Food and Drug Act and findings of an Expert Advisory Committee on Herbs and Botanical Preparations were consulted to provide an overview of the issues regarding herbal product regulation in Canada. Case reports of herbal toxicity were identified to illustrate some of the hazards of herbal products, and references provided to guide health professional in searching the literature for clinical trials that evaluate these drugs' efficacy. MAIN FINDINGS: Herbal products not registered as drugs in Canada are sold as foods and are exempt from the drug review process that evaluates product efficacy and safety. This places the public at risk of unwanted effects from the use of herbal products that are adulterated with other substances and of forgoing effective conventional therapy. Moreover, consumers are exposed to a plethora of information portraying herbal products as harmless. Some progress has been made to address these concerns by facilitating the registration of herbal products as drugs. CONCLUSIONS: Most herbal products that were evaluated were unsafe or ineffective, or no information was available to evaluate their efficacy. Despite the perception that herbal products are innocuous, family physicians need to be aware that herbal therapy can be harmful in order to help their patients make informed choices.

Krishnaswamy K, Raghuramulu N. **Bioactive phytochemicals with emphasis on dietary practices.** Indian J Med Res 1998;108:167-81.
Diet can modify the pathophysiological processes of various metabolic disorders and can be an effective preventive strategy for various disease processes most of which are known to involve oxidative damage. Both nutrient and non-nutrient components of the diet have been recognized for their anti-oxidant and other potential benefits. Plant foods contain phytochemicals such as flavonoids, phenolic acids, etc., which show biological activity. Some common foods used in

Indian culinary practices were assessed for their anti-oxidant, anti-mutagenic and anti-carcinogenic effects and vitamin D activity and evaluated for their plausible biological effects. Green leafy vegetables had the highest anti-oxidant activity followed by wheat and rice. Cooking decreased this activity. Eugenol, the active principle of clove, was shown to offer protection against CCl4 induced hepatotoxicity in rats. It also showed anti-peroxidative activity in addition to decrease in O2 formation. Studies on the anti-carcinogenic effect of turmeric/curcumin revealed that both are potent anti-mutagens in vivo and reduce the adducted DNA levels in liver of rates challenged with B(a)P. In another study, Syrian hamsters receiving turmeric/curcumin through diet or local paint on cheek pouch had lower tumour burden as well as adducted DNA level against 7-12-DMBA challenge. Turmeric/curcumin were found to be better anti-tumour agents when given in the post initiation phase of carcinogenesis. The beneficial effect of turmeric was found to be due to its anti-oxidant potential. Studies on humans at risk of palatal cancer due to reverse smoking showed that turmeric (1 g/day) for 9 months had a significant impact on the regression of precancerous lesions. Onion and garlic also possess anti-mutagenic principle. Further studies on the bioactive phytochemicals in plants showed that certain plants belonging to Solanaceae (Cestrum diurnum, Lycopersicon esculentum and Solanum melongena) have calcinogenic potential and vitamin D like activity. In view of the vast data on bioactive principles from plants, it is suggested that dietary prevention coupled with other life-style changes in perhaps the right answer for prevention of cancer and other chronic diseases in India.

Kumar M, Berwal JS. **Sensitivity of food pathogens to garlic (Allium sativum).** J Appl Microbiol 1998;84(2):213-5.
The inhibitory activity of garlic (Allium sativum) against Staphylococcus aureus, Salmonella typhi, Escherichia coli and Listeria monocytogenes was measured by the 'turbidity' method. Minimum inhibitory concentration (MIC) of garlic at 80% inhibition level was calculated for these bacteria. All bacterial pathogenic strains tested were inhibited by garlic; E. coli was most sensitive and Listeria monocytogenes was least sensitive. Therefore, garlic has potential for the preservation of processed foods.

La Valle JB. **St. John's Wort: there's no magic bullet.** Drug Store News Chain Pharm 1998 Jan;8:15.
IPA COPYRIGHT: ASHP The problems associated with the consumer rush to take St. John's Wort (Hypericum perforatum) for depression are discussed, including problems with self-diagnosis and treatment of depression, subtherapeutic dosing of the compound, drug interactions with monoamine oxidase (MAO) inhibitors or other antidepressants, side effects, and methods for discontinuation of traditional antidepressants.

Lavalle J. **Ginseng: ancient Chinese cure-all.** Drug Store News For Pharm 1997 Feb;7:42.
IPA COPYRIGHT: ASHP The pharmacology, action, indications, toxicities, contraindications, and dosage of ginseng are presented.

Lazarowych NJ, Pekos P. **Use of fingerprinting and marker compounds for identification and standardization of botanical drugs: strategies for applying pharmaceutical HPLC analysis to herbal products.** Drug Inf J 1998;32(2):497-512.
IPA COPYRIGHT: ASHP The use of HPLC fingerprinting and markers to identify herbal drug

materials, set specifications for raw materials, and standardize botanical preparations during manufacturing is discussed; the method was illustrated using Valeriana officinalis (valerian) and Tanacetum parthenium (feverfew).

Lee OS, Kang HH, Han SH. **Oriental herbs in cosmetics.** Cosmet Toiletries 1997 Jan;112:57-64.
IPA COPYRIGHT: ASHP The use of plant extracts as cosmetic ingredients is presented, including ginseng from Panax ginseng and Swertia for anti-aging preparations, Angelica, Glycyrrhiza (licorice), Lithospermum, and Scutellaria roots as anti-inflammatory agents, Houttuynia, Phellodendron, and Sophora as antimicrobials, Lonicera and Sanguisorba as astringents, Angelica dahurica, Angelica korea, Bupleurum, and Cnidium rhizome as anti-tyrosinase actives, teas as free-radical scavengers, Angelica keiskei, Coptis, and Lonicera as ultraviolet protectants, Morus lhou (mulberry) for skin whitening, and other agents for hair growth and care.

Lepik K. **Safety of herbal medications in pregnancy.** Can Pharm J 1997 Apr;130:29-33.
IPA COPYRIGHT: ASHP A summary of safety information that is relevant to the use of selected herbal medications during pregnancy is presented, including pharmacologic, toxicologic, and reproductive effects of 26 herbal remedies.

Li Y, Wu YL. **How Chinese scientists discovered qinghaosu (artemisinin) and developed its derivatives? What are the future perspectives?** Med Trop (Mars) 1998;58(3 Suppl):9-12.
Since the middle of this century and especially since the 1960s and 1970s. Chinese scientists have put considerable effort and resources into the search for new antimalarial compounds extracted from Chinese traditional herbs. Archaeological findings indicate that qinghao (Artemisia annua L.) has been used as a traditional remedy in China for over two thousand years. Its antimalarial principle was finally isolated in 1971 and named artemisinin or qinghaosu (meaning the principle of qinghao in Chinese). Its rapid action, low toxicity and powerful effect against falciparum malaria made it a favored subject for research. In 1976, the unique structure of the molecule, characterized by an endoperoxide and an alternative O-C-O-C segment, was identified. The specific lactone reduction discovered during the determination of the structure opened the way for the synthesis of qinghaosu derivatives, and thereafter a series of more active and more oil- or water-soluble derivatives was developed. Subsequent studies of the structure/activity relationship led to the discovery of dihydroartemisinin, artemether and artesunate. Now qinghaosu and these three derivatives are being used around the world as effective new antimalarial drugs in the fight against falciparum malaria, including multi-drug-resistant Plasmodium falciparum. At the present time new qinghaosu analogues or derivatives are being developed and studies of their structure/activity relationships, their antimalarial mechanisms, their interaction with ferrous ions and the DNA damage associated with these processes are being actively pursued. In addition, recent studies also indicate that some qinghaosu derivatives have other bioactivities, including antiparasitic (against Schistosoma japonicum, Toxoplasma gondii and so on) and anticancer activities. Research into qinghaosu and its derivatives has already produced and will no doubt continue to produce results of the utmost importance in the fight against malaria and other diseases.

Locock RA. **Herbal medicine: Essiac.** Can Pharm J 1997 Feb;130:18-9, 51.
IPA COPYRIGHT: ASHP The actions and uses of the herbal preparation, Essiac, and its constituents, including Arctium lappa L. (burdock root), Rumex acetosella L. (sheep sorrel herb), Ulmus fulva Michaux (slippery elm bark), Rheum palmatum L. (turkey rhubarb root), Nasturtium officinale (Rorippa nasturtium; watercress), Laminariales species (kelp), Cnicus (blessed thistle), and Trifolium pratense L. (red clover), are presented.

Mamedov NA, Craker LE. **Herbs and plant systematics.** J Herbs Spices Med Plants 1997;5(2):1-2.
IPA COPYRIGHT: ASHP The methodology of plant systematics and the importance of using systematics in the search for new medicinal and aromatic plant materials are discussed.

Manandhar NP. **Native phytotherapy among the Raute tribes of Dadeldhura district, Nepal.** J Ethnopharmacol 1998;60(3):199-206.
The herbal drugs used by the Raute tribe of far-western Nepal are discussed. A total of 47 species of plants including one species of pteridophyte, four monocotyledons and 42 dicotyledons, and 17 types of diseases treated, have been identified from this study. Medicinal uses of 15 species (31%) are unrecorded from other parts of the country.

Masood E. **'Medicinal plants threatened by over-use' [news] [see comments].** Nature 1997;385(6617):570.

McIntyre RV. **Herbal healers [editorial].** J Okla State Med Assoc 1998;91(5):271.

McKinney DE. **Saw palmetto for benign prostatic hyperplasia.** JAMA 1999 May 12;281:1699.
IPA COPYRIGHT: ASHP A physician's viewpoints regarding the quality of medicinal plant products, particularly extracts of saw palmetto (Serenoa repens) for benign prostatic hypertrophy (BPH) are presented, including 4 major points to consider when evaluating a manufacturer's products for patients. Other plant products that may also have value in the treatment of BPH were briefly discussed.

McLaughlin JL, Rogers LL, Anderson JE. **Use of biological assays to evaluate botanicals.** Drug Inf J 1998;32(2):513-24.
IPA COPYRIGHT: ASHP The materials and procedures for 4 bioassays used to screen and direct the fractionation of botanical extracts in drug discovery are described, and the application of the methods in the discovery of Annonaceous acetogenins is discussed.

Menke J. **Herbal remedies.** S D J Med 1997;50(6):207-8.

Milliken W. **Malaria and antimalarial plants in Roraima, Brazil.** Trop Doct 1997;27(Suppl 1):20-5.
One of the numerous problems created by the gold rush which took place in northern Brazil (Roraima State) at the end of the 1980s was a severe epidemic of malaria amongst the indigenous peoples of the region. Worst hit were the Yanomami Indians, who had lived in almost total

isolation prior to this event. The problem has been exacerbated by the development of chloroquine-resistant strains of Plasmodium falciparum. In an effort to identify viable alternatives to dependence on western medicine for malaria treatment, a survey was carried out on the local plant species (wild and cultivated) used for this purpose in Roraima. Fieldwork was carried out amongst seven indigenous peoples, as well as with the non-indigenous settlers. Over 90 species were collected, many of which have been cited as used for treatment of malaria and fevers elsewhere. Knowledge of antimalarial plants was found to vary greatly between the communities, and in some cases there was evidence of recent experimentation. Initial screening of plant extracts has shown a high incidence of significant antimalarial activity amongst the species collected.

Montbriand MJ. **Past and present herbs used to treat cancer: medicine, magic, or poison?** Oncol Nurs Forum 1999;26(1):49-60.
PURPOSE/OBJECTIVES: To provide an overview of the past and present use of herbs, thereby dispelling the belief that herbs are secret cancer remedies unknown to or ignored by the biomedical community. DATA SOURCES: Historical and current pharmacy, medical, and nursing literature. DATA SYNTHESIS: More than 3,000 species of herbs used in treating cancer since 2838 BC are known to biomedicine, yet popular lay literature persists in perpetrating the myth that medicine has ignored the potential uses of herbs. Secrecy about herbs has been fashionable since the Middle Ages. Magical and virtuous herbs, named in a book of secrets from that age, are examined for their historical and current use in cancer treatment. Popular unproven herbs, as well as proven herbs used in chemotherapy, also are discussed. CONCLUSIONS: Greater accessibility to information about the use of herbs historically, popularly, and currently would help dispel the secrecy, giving healthcare professionals and patients and opportunity to make informed choices. IMPLICATIONS FOR NURSING PRACTICE: Nurses with knowledge of herbs can be valuable resources to patients and professional colleagues. Members of the professional community (nurses, doctors, pharmacists, and social workers) need to take collegial responsibility in informing each other and their patients about herbs, including their potential risks, possible benefits, and antidotes for overdose.

Muller JL, Clauson KA. **Top herbal products encountered in drug information requests. Part 2.** Drug Ben Trends 1998 Jun;10:21-3.
IPA COPYRIGHT: ASHP An overview of the indications, dosage, side effects, possible drug interactions, and clinical studies of 2 top selling herbal products, Hypericum perforatum (St. John's Wort) and Serenoa repens (saw palmetto), is presented.

Myerscough M. **Herbal remedies. How much do you know?** Aust Fam Physician 1998;27(11):1037-40.
In this article the importance of knowledge about herbal remedies in general practice is discussed using guarana (Paullinia cupana), St John's wort (Hypericum perforatum), and gingko (Ginkgo biloba) as examples. Obtaining information about herbal remedies can be difficult. Lack of clinical data about the use, safety, efficacy and general practitioner attitudes to herbal remedies creates research opportunities in this area of general practice.

Nemecz G. **Chamomile.** US Pharm 1998 Mar;23:104, 110, 112, 115-6.
IPA COPYRIGHT: ASHP The therapeutic uses of chamomile, including antiphlogistic, spasmolytic, sedative, hypnotic, analgesic, and antimicrobial effects as well as its chemical composition, pharmacological action, toxicity, and dosage, are presented.

Nemecz G. **Saw palmetto.** US Pharm 1998 Jan;23:97-8, 100, 102.
IPA COPYRIGHT: ASHP The history, chemical composition, medicinal uses, and adverse effects of Serenoa repens (saw palmetto) are discussed.

Nemecz G, Combest WL. **Feverfew.** US Pharm 1997 Nov;22:122, 124, 126, 128.
IPA COPYRIGHT: ASHP An overview of the chemical composition and pharmacological effects of feverfew (Tanacetum parthenium), a perennial herb that has shown efficacy in the treatment of migraine headaches, is presented, including a summary of clinical studies of feverfew in the treatment of migraine headaches and arthritis, its anti-inflammatory effects, its effects on platelet aggregation and vascular smooth muscle contraction, its toxicity and adverse effects, and dosage forms and recommended use.

Neuwinger HD, Mebs D. **[Boophone disticha: hallucinogenic African plant].** Dtsch Apoth Ztg 1997 Apr 3;137:51-6. (Ger)
IPA COPYRIGHT: ASHP An overview of the botanical characteristics, uses in African folk medicine, chemistry, toxicology, and pharmacology of the hallucinogenic contents of the plant Boophone disticha (L) Herbert (Amaryllidaceae) is presented.

Norton SA. **Herbal medicines in Hawaii from tradition to convention.** Hawaii Med J 1998;57(1):382-6.
The stories of kava and chaulmoogra demonstrate the importance of herbal products in ancient and recent Hawaiian medicine. Kava is a psychoactive beverage that has been used ceremonially for millennia throughout the Pacific. It is a nonfermented depressant that causes tranquil intoxication in which thoughts and memory remain clear. Its broad pharmacologic activity led to use in Hawaii to treat skin disorders and later in Germany to treat gonorrhea. Kava is now available outside the Pacific basin as a relaxant, emerging as a popular, albeit deritualized, natural product. In the late 19th century, the main treatment for leprosy was chaulmoogra, extracted from Hydnocarpus seeds. Chaulmoogra had been a traditional treatment for skin diseases in Ayurvedic and Chinese medicine. Chaulmoogra from Asian markets was expensive and usually adulterated so the USDA decided to plant Hydnocarpus in Hawaii. Joseph Rock, a botanist at University of Hawaii, trekked through southeast Asia collecting fresh seeds to plant on Oahu. Rock's trees provided chaulmoogra for leprosy patients on Molokai and elsewhere until it was replaced by dapsone. Chaulmoogra, once the treatment for leprosy worldwide, is now nearly forgotten; kava, once poorly known outside the Pacific, is now a widely-used alternative medicine. Hawaii will probably continue its role in the transition of plants from traditional use to conventional use.

Nwosu MO. **Aspects of ethnobotanical medicine in southeast Nigeria.** J Altern Complement Med 1998;4(3):305-10.
OBJECTIVE: To document the diversity and traditional use of tropical plants as medicine by the

indigenous people of southeast Nigeria. DESIGN: Information was obtained by interviews conducted with the aid of questionnaires and facilitators during field surveys carried out from January 1993 to June 1994. Voucher herbarium specimens were identified at the University of Nigeria, Nsukka Herbarium, in collaboration with Bernhard Zepernick (former Curator), Botanisches Museum, Berlin. Specimens were photographed. RESULTS: Data are summarized in the form of a table, summarizing the plants commonly used by the traditional doctors or medicine men. Herbal preparations are arranged alphabetically under family and species. The data are presented in the order: botanical name, collection number, vernacular name, locality, plant habit/status, and reported medicinal applications.

O'Hara M, Kiefer D, Farrell K, Kemper K. **A review of 12 commonly used medicinal herbs.** Arch Fam Med 1998;7(6):523-36.
A large and increasing number of patients use medicinal herbs or seek the advice of their physician regarding their use. More than one third of Americans use herbs for health purposes, yet patients (and physicians) often lack accurate information about the safety and efficacy of herbal remedies. Burgeoning interest in medicinal herbs has increased scientific scrutiny of their therapeutic potential and safety, thereby providing physicians with data to help patients make wise decisions about their use. This article provides a review of the data on 12 of the most commonly used herbs in the United States. In addition, we provide practical information and guidelines for the judicious use of medicinal herbs.

Palsson K, Jaenson TG. **Plant products used as mosquito repellents in Guinea Bissau, West Africa.** Acta Trop 1999;72(1):39-52.
By standardized interviews of people in 23 rural villages, in the Oio region of Guinea Bissau, we collected data on which plant species and plant derived products or methods people use to reduce mosquito biting activity.The following plants were used to reduce numbers of mosquitoes indoors at night: fresh or smouldering Hyptis suaveolens Poit. (Lamiaceae), smoke of the bark of Daniellia oliveri Rolfe (Caesalpiniaceae), smoke of the infructescence of Elaeis guineensis Jacq. (Arecaceae), smoke of the seed capsules of Parkia biglobosa (Jacq.) Benth. (Mimosaceae), smoke of the leaves of Azadirachta indica A.Juss. (Meliaceae) and Eucalyptus sp. (Myrtaceae), fresh Ocimum canum Sims (Lamiaceae), and fresh Senna occidentalis (L.) Link (Caesalpiniaceae). In two field experiments we estimated the 'repellent activity' of certain of these plants and compared their efficacies with those of two commercially available mosquito repellents, i.e. 'positive' controls. In the first experiment we tested: smouldering H. suaveolens (85.4% repellency); fresh H. suaveolens (73.2%); burning of the bark of D. oliveri (74.7%); and smoke of the leaves of Eucalyptus (72.2%). In the second experiment we tested: smouldering H. suaveolens (83.6% repellency); fresh H. suaveolens (66.5%); burning of the bark of D. oliveri (77.9%); smoke of the leaves of A. indica (76.0%); smoke of the infructescence of E. guineensis (69.0%); fresh O. canum (63.6%); and fresh S. occidentalis; (29.4%). All the products tested, except S. occidentalis were significantly more effective than the negative control.

Paulsen SM. **Use of herbal products and dietary supplements by oncology patients--informed decisions?** Highlights Oncol Pract 1998;15(4):94-9, 103-6.
IPA COPYRIGHT: ASHP An overview of various herbal products and dietary supplements used in cancer prevention and treatment is presented, including prasterone (dehydroepiandrosterone),

green teas, adaptogens such as Echinacea and cat's claw (Uncaria species), bovine cartilage, Larrea tridentata (chaparral), linseed oil (flaxseed oil), Viscum album (mistletoe), pau d'arco (a tea derived from the bark of trees of the Tecoma genus), and shark cartilage as well information on clinical studies and toxicity of these products.

Pepping J. **Kava: Piper methysticum.** Am J Health Syst Pharm 1999 May 15;56:957-58, 960.
IPA COPYRIGHT: ASHP A brief overview of the pharmacology, pharmacokinetics, dosage, adverse effects, drug interactions, contraindications, and results of clinical studies of kava, an herb used for its anxiolytic and sedative properties, is presented. Kava is derived from the pulverized roots and rhizomes of several subspecies of a pepper plant Piper methysticum.

Pepping J. **St. John's Wort: Hypericum perforatum.** Am J Health Syst Pharm 1999 Feb 15;56:329-30.
IPA COPYRIGHT: ASHP A brief overview of the pharmacology, dosage, adverse effects, drug interactions, contraindications, and results of clinical studies of Hypericum perforatum (St. John's Wort), an herb used to treat depression, anxiety, and sleep disorders, is presented.

Phillipson D. **Pharmacognostical peregrinations.** Pharm J 1997 Feb 1;258:176-7.
IPA COPYRIGHT: ASHP An account of one London University pharmacognosy professor's experiences with pharmacists in Australia and Malaysia, where he visited in the autumn of 1996, is presented with a focus on their interest in herbal medicine.

Pittenger J. **Herbal treatments find their way into mainstream America.** Wis Med J 1997;96(3):30-1.

Posner H. **Alternative medicine--the case of herbal remedies [letter].** N Engl J Med 1999;340(7):565; Discussion 566.

Prince CE. **Goldenrod (Solidago gigantea, Solidago virgaurea).** Nebr Mortar Pestle 1997 Sep;60:8-9.
IPA COPYRIGHT: ASHP The anti-inflammatory properties, toxicity, and results of animal studies of Solidago gigantea and Solidago virgaurea (goldenrod) are discussed.

Qin GW, Xu RS. **Recent advances on bioactive natural products from Chinese medicinal plants.** Med Res Rev 1998;18(6):375-82.
China has accumulated a rich body of empirical knowledge of the use of medicinal plants for the treatment of various diseases throughout its long history. Chemical studies on Chinese medicinal plants provide a valuable material base for the discovery and development of new drugs of natural origin. In this article recent chemical work on various Chinese medicinal plants is reviewed, including Mussaenda pubescens (Rubiaceae), Isatis indigotica (Cruciferae), Euphorbia fischeriana, and E. ebracteolata (Euphorbiaceae), and Stemona species (Stemonaceae). The structural diversity of the medicinal chemical constituents of the above plants is discussed.

Raja D, Blanche C, Valles Xirau J. **Contribution to the knowledge of the pharmaceutical ethnobotany of La Segarra region (Catalonia, Iberian Peninsula).** J Ethnopharmacol

1997;57(3):149-60.
An ethnobotanical survey was carried out in the region known as La Segarra, situated at the north east of the Iberian Peninsula, in the inner plains of Catalonia, with an area of 720 km2 and a population of 17000. Working with 29 people, data on uses of 142 species belonging to 54 botanical families were obtained and presented, of which 13 uses corresponding to nine plant species were previously unreported.

Rogers MV, Cheek B. **Echinacea (purple coneflower).** Carol J Pharm 1997 Jan-Feb;77:16.
IPA COPYRIGHT: ASHP The pharmacology, dosage forms, dosage, and toxicity of Echinacea (purple coneflower) for immunostimulation are discussed.

Rogers PL, Shin HS, Wang B. **Biotransformation for L-ephedrine production.** Adv Biochem Eng Biotechnol 1997;56:33-59.
L-ephedrine is widely used in pharmaceutical preparations as a decongestant and anti-asthmatic compound. One of the key intermediates in its production is L-phenylacetylcarbinol (L-PAC) which can be obtained either from plants (Ephedra sp.), chemical synthesis involving resolution of a racemic mixture, or by biotransformation of benzaldehyde using various yeasts. In the present review, recent significant improvements in the microbial biotransformation are assessed for both fed-batch and continuous processes using free and immobilised yeasts. From previous fed-batch culture data, maximal levels of L-PAC of 10-12 gl-1 were reported with yields of 55-60% theoretical based on benzaldehyde. However, recently concentrations of more than 22 gl-1 have been obtained using a wild-type strain of Candida utilis. This has been achieved through optimal control of yeast metabolism (via microprocessor control of the respiratory quotient, RQ) in order to enhance substrate pyruvate production and induce pyruvate decarboxylase (PDC) activity. Processes involving purified PDC have also been evaluated and it has been demonstrated that L-PAC levels up to 28 gl-1 can be obtained with yields of 90-95% theoretical based on the benzaldehyde added. In the review the advantages and disadvantages of the various strategies for the microbial and enzymatic production of L-PAC are compared. In view of the increasing interest in microbial biotransformations, L-PAC production provides an interesting example of enhancement through on-line control of a process involving both toxic substrate (benzaldehyde) and end-product (L-PAC, benzyl alcohol) inhibition.

Romano I, Tsourounis C. **Saw palmetto (Serenoa repens) for the treatment of benign prostatic hyperplasia.** Calif J Health Syst Pharm 1998 May-Jun;10:16-7, 33.
IPA COPYRIGHT: ASHP An overview of the pharmacology, pharmacokinetics, clinical studies, and adverse effects of Serenoa repens (Saw palmetto) for the treatment of benign prostatic hyperplasia is presented.

Saller R, Reichling J, Kristof O. **[Phytotherapy--treatment without side effects?].** Dtsch Med Wochenschr 1998;123(3):58-62. (Ger)

Schneck C. **St. John's wort and hypomania [letter].** J Clin Psychiatry 1998;59(12):689.

Seifert P. **Herbal extracts in cosmetics--opportunities and limitations.**Seifen Oele Fette Wachse 1997 Jan;123:28, 30-1.

IPA COPYRIGHT: ASHP Various limitations associated with the opportunities for the fashionable use of herbal extracts in cosmetics are briefly discussed, including differences in the criteria for herbal extracts used in cosmetic and medicinal applications, the criteria for natural cosmetics, utility of the drug extract ratio as a measure of the quality or activity of plant extracts, and standardization of plant extracts.

Shaw D. **Risks or remedies? Safety aspects of herbal remedies in the UK.** J R Soc Med 1998;91(6):294-6.

Shaw D, Leon C, Murray V, Volans G. **Patients' use of complementary medicine [letter].** Lancet 1998;352(9125):408.

Shepard GH Jr. **Psychoactive plants and ethnopsychiatric medicines of the Matsigenka.** J Psychoactive Drugs 1998;30(4):321-32.
For the Matsigenka of the Peruvian Amazon, health and well-being in daily life depend upon harmonious relationships within the social group and with the spirit world. Psychoactive plants play a crucial role in curing disrupted social relationships while giving humans access to the otherwise remote, parallel world of spirits. Different species and cultivars of psychoactive plants, as well as varying admixtures and doses, are used to obtain different intensities and qualities of psychoactive experience, depending upon the individual's goals. Strongly psychoactive plants are used by shamans to travel to the realm of spirits. A number of mild to strongly psychoactive plants are used by male hunters to purify their souls and improve their aim. Mildly psychoactive plants are used to improve women's concentration for spinning and weaving cotton, to control negative emotions such as grief and anger, to manipulate the content of dreams, and to pacify sick or frightened children. A majority of such remedies come from the botanical families of Rubiaceae, Solanaceae and Cyperaceae, known sources of psychoactive compounds. Interdisciplinary research into the culture, botany and pharmacology of psychoactive plants in indigenous medical systems contributes to a better understanding of the role of psychological states in human health and well-being.

Shinchi K, Ishii H, Imanishi K, Kono S. **Relationship of cigarette smoking, alcohol use, and dietary habits with Helicobacter pylori infection in Japanese men.** Scand J Gastroenterol 1997;32(7):651-5.
BIOSIS COPYRIGHT: BIOL ABS. Background: Little is known of factors determining infection with Helicobacter pylori. Methods: In a cross-sectional study of 566 men aged 50-55 years, who received a preretirement health examination at the Self Defense Forces Fukuoka Hospital between January 1993 and December 1994, we examined the association of smoking, alcohol use, and dietary habits with H. pylori infection. Results: The overall seropositivity as determined with IgG antibody was 79.3% (449 of 566). The rank was inversely associated with the infection (trend, P = 0.048). Neither smoking nor alcohol drinking was related to the infection. The prevalence adjusted for rank tended to be lower in men consuming raw vegetables (trend, P = 0.12) daily than those with less consumption. Unexpectedly, the consumption of tofu (soybean curd) was significantly, negatively related to the infection (trend, P = 0.013). The seropositivity was unrelated to the consumption of pickled vegetables, soy paste soup, green tea, or garlic. Conclusion: The findings suggest that fresh vegetables may be protective against H.

pylori infection. The study does not support either an increased risk of the infection associated with salty foods or a protective effect of green tea or garlic.

Square D. **Sage advice from my garden.** CMAJ 1998;159(12):1495-7.

Stueland DT, Ault BJ, Gunderson PD. **Change in cholinesterase levels and self-reported symptoms over two years.** J Agromed 1997; 4(1/2):151-6.
The application and reliability of self reported symptoms and serum cholinesterase (ACH) levels as measures of effects of farm chemical exposures over time were analyzed. Twenty two ginseng producers in central Wisconsin participated in 2 years of on site testing. Each year they reported on farming practices and health seeking behavior and completed a 20 item questionnaire related to possible farm chemical exposure symptoms. Plasma and red cell ACH were also measured. No seizure symptoms were reported. The mean age of participants was 41.5 years. Thirteen of the participants were men and 21 were owner operators. The mean initial plasma ACH levels changed from 16.15 units/milliliter (U/ml) in 1994 to 16.25U/ml in 1995. Red blood cell ACH levels were 37.95U/ml in 1994 and 42.32U/ml in 1995 at the start of the season. In 1994 the follow up study showed an increase to 39.55U/ml, but a decrease in 1995 to 38.80U/ml. Changes in symptoms from 1994 to 1995 correlated with the change in initial plasma ACH levels over the same year. Each year the participants experienced a drop in ACH activity. Self reported symptoms remained highly correlated and showed, overall, only minor changes, suggesting that symptoms and ACH testing may be reliable for on site field testing.

Sukumaran M, Chung H, Gollapudi DP. **Cultural factors in the treatment of a catatonic Chinese patient [letter].** Gen Hosp Psychiatry 1997;19(5):378-80.

Tello CG, Ford P, Iacopino AM. **In vitro evaluation of complex carbohydrate denture adhesive formulations.** Quintessence Int 1998;29(9):585-93.
OBJECTIVE: Acemannan, a complex mannose carbohydrate derived from the aloe vera plant, has an inherent stickiness/viscosity. Prototype Acemannan denture adhesive formulations were evaluated for pH changes, cytotoxicity to human gingival fibroblasts and adhesive strength in both dry and wet conditions. METHOD AND MATERIALS: The denture adhesive formulations consisted of five combinations of Acemannan with varying concentrations of preservatives and two other formulations without preservatives. The pH of each formulation was measured over 24 hours. Assessment of cytotoxicity was accomplished using the in vitro, tetrazolium-based colorimetric assay on cultures of human gingival fibroblasts after exposure to the adhesive formulations for up to 24 hours. The adhesive strength was evaluated with a universal testing machine under initial dry conditions and after immersion in a constant-temperature water bath for up to 20 minutes. RESULTS: Formulations 1 and 2 achieved and maintained pH values above 6.0 (the critical pH for hydroxyapatite dissolution) approximately 6 hours into the study. None of the prototypes demonstrated an initial pH above the critical pH. Formulations 1, 2, 3, and 5 exhibited significant cytotoxicity to human gingival fibroblasts over 24 hours. Formulations 4, 20:1, and 150:1 demonstrated minimal cytotoxicity. Formulation 1 exhibited the poorest adhesive strength, while the most viscous formulation (prototype 150:1) was by far the best performer. Generally, adhesive bond strengths for all prototypes were quite high and relatively stable over time in a wet environment. CONCLUSION: To achieve the ideal adhesive

in terms of strength, pH, and cytotoxicity, Acemannan formulation 150:1 should be adjusted to contain the preservative concentration of formulation 4 and have an initial pH value of 6.0 or higher.

Thompson CA. **As patients embrace herbal remedies, dearth of scientific evidence frustrates clinicians.** Am J Health Syst Pharm 1997 Dec 1;54:2656, 2658, 2664.
IPA COPYRIGHT: ASHP Sources of information regarding the efficacy and side effects of herbal remedies for physicians and pharmacists are described, clinical studies evaluating the efficacy of some herbal products are summarized, and differences between formulations of herbal products that may affect the efficacy of the product are discussed.

Thompson CA. **USP moves forward in providing information on botanical products [news].** Am J Health Syst Pharm 1998;55(6):527, 530.

Thornton Z. **Health care the herbal way.** East Pharm 1997 Aug;40:71-2.
IPA COPYRIGHT: ASHP A brief overview of the therapeutic use of herbal medicines is presented, and adverse reactions, self-medication, and the quality control of herbal products are considered.

Turow V. **Herbal therapy for children [letter].** Pediatrics 1998;102(6):1492-3.

Van Rensen I, Blume H, Ihrig M, Morck H, Dingermann T, Veit M. **[Evaluation of phytopharmaceuticals in pharmacy practice].** Pharm Ztg 1998 Feb 19;143:11-8, 21. (Ger)
IPA COPYRIGHT: ASHP An overview of phytopharmaceuticals, including nomination and standardization of pharmaceutical quality, efficacy, clinical research, therapy study types and designs, safety critiques, terms of registration, and advertisements, is presented; it was noted that patients need the expertise of the counseling pharmacist in regard to herbal medication.

Vann A. **The herbal medicine boom: understanding what patients are taking [see comments].** Cleve Clin J Med 1998;65(3):129-34.

Varga CA, Veale DJ. **Isihlambezo: utilization patterns and potential health effects of pregnancy-related traditional herbal medicine.** Soc Sci Med 1997;44(7):911-24.
Isihlambezo is a herbal decoction used by many Zulu women in South Africa as a preventative health tonic during pregnancy. Though the practice is cited by ethnographers and medical practitioners, few studies have focused on specific elements of isihlambezo use and preparation. Moreover, though some evidence exists suggesting negative effects of its ingestion, the maternal-fetal health impact and toxicity of isihlambezo have not been adequately studied. We examined two aspects of this traditional antenatal health practice: (1) the potential impact of urbanization and access to Western clinic-based care on popularity and utilization patterns of isihlambezo, and (2) the potential maternal-fetal health effects of its use. Interviews were conducted among rural and urban women in clinic and non-clinic settings regarding socio-behavioral aspects of isihlambezo use. The pharmacology of certain plant ingredients of isihlambezo was investigated through laboratory assays, literature review, and interviews with traditional healers. There were significant differences by area of interview in nearly all aspects of isihlambezo use examined.

Though isihlambezo was most popular among urbanites and clinic non-attenders, it was considered an important antenatal health care alternative by the majority of women surveyed. Mixing traditional and clinic-based antenatal care was also strongly advocated. Pharmacological analysis suggested the possibility of both therapeutic and harmful consequences of isihlambezo. It was suggested that the following factors might contribute the popularity of isihlambezo among urban women: high cost and inferior quality of clinic care, use of isihlambezo as a means of adapting to urbanization-related stress, and socio-cultural transition.

Vazquez FM, Suarez MA, Perez A. **Medicinal plants used in the Barros Area, Badajoz Province, Spain.** J Ethnopharmacol 1997;55(2):81-5.
A study of the wild and cultivated medicinal plants used in the Barros Area (southern Spain) is reported, 48 plants distributed among 20 different families are used in the treatment of various human diseases. The use of Bellis annua L. Centaurea ornata Wild., Leuzea conifera (L.) DC., Pulicaria paludosa Link and Asparagus aphyllus L. is reported.

Williamson JS, Wyandt CM. **Herbal therapies: facts and the fiction.** Drug Top 1997 Aug 4;141:78-87.
IPA COPYRIGHT: ASHP An overview of herbal therapies is presented, including the history of disease treatment with herbal remedies, counseling patients about the appropriate use of herbal products, and the risks and benefits of common herbal remedies such as Medicago sativa (alfalfa), Aloe vera (aloe vera), Arnica montana (arnica), Vaccinium myrtillus (bilberry), Uncaria tomentosa (cat's claw), Angelica sinensis (dong quai), Echinacea purpurea (echinacea), Ephedra sinica (ephedra), Chrysanthemum parthenium (feverfew), Allium sativum (garlic), Ginkgo biloba (ginko biloba), Panax ginseng (ginseng), hypericum perforatum (St. John's wort), and Serenoa repens (saw palmetto). A table of the purported properties and uses of 153 herbs is provided. This article qualifies for 2 hours U.S. CE credit by the ACPE.

Williamson JS, Wyandt CM. **Herbal update.** Drug Top 1998 Jun 1;142:66-75.
IPA COPYRIGHT: ASHP The rational use and contraindications of herbal therapy, patient information, drug interactions, and the legal status of herbal preparations are presented including popular American and European herbs such as Aloe vera, Arnica montana, Vaccinium myrtillus (bilberry), Uncaria tomentosa (cat's claw), Angelica sinensis (Dong quai), Echinacea purpurea, evening primrose oil, Tanacetum parthenium (feverfew), Allium sativum, Zingiber officinale (ginger), Ginkgo biloba, Panax ginseng, Crataegus species (hawthorn), Aesculus hippocastanum, Piper methysticum (kava-kava), Silybum marianum, Hypericum perforatum (St. John's wort), Serenoa species (Saw palmetto), and Valeriana officinalis (Valerian). This article qualifies for 2 hours U.S. CE credit by the ACPE.

Williamson JS, Wyandt CM. **What the pharmacist should know about food and drug interactions.** Hosp Pharm Rep 1998 Apr;12:43-52.
IPA COPYRIGHT: ASHP An overview of the effects of food, tobacco, ethyl alcohol, and herbal products on drug action is presented, including a discussion of the mechanisms of drug-food interactions, counseling patients about when it is appropriate to take a drug with food and when it is contraindicated, counseling patients about the effects of alcohol and tobacco use on drug action, and potentially significant food-drug interactions involving nutritional agents, hormonal

agents, respiratory agents, diuretics/cardiovascular agents, anti-infective agents, GI agents, CNS agents, antineoplastic agents, immunosuppressive agents, and dietary supplements. This article qualifies for 2 hours U.S. CE credit by the ACPE.

Winkelaar PG. Medicolegal file. **Tacit approval of alternative therapy.** Can Fam Physician 1999;45:905.

Winston D, Dattner AM. **The American system of medicine.** Clin Dermatol 1999;17(1):53-6.

Wong HC. **Is feverfew a pharmacologic agent? [letter].** CMAJ 1999;160(1):21-2.

Wright R, Vanvuren B. **Ginkgo biloba.** Nebr Mortar Pestle 1997 Jun;60:10-1.
IPA COPYRIGHT: ASHP An overview of Ginkgo biloba, from a tree native to China and an herbal remedy used for 5000 yr, is presented, including its mechanism of action, therapeutic use in conditions associated with decreased peripheral and cerebral vascularity such as cerebral ischemia, its pharmacodynamics, dosage, adverse effects, and potential drug interactions. It is noted that in Germany and France, Ginkgo biloba is among the most commonly prescribed drugs, while in the United States it is available as an OTC natural product.

Wynn RL, Meiller TF. **A brief survey of herbal medicines and other remedies.** Gen Dent 1997;45(2):112-5.

Xue T, Zhang L. **Avenues of discovery in bioprospecting [letter; comment].** Nature 1998;393(6686):617.

Zhang YY, Don HY, Guo YZ, Ageta H, Harigaya Y, Onda M, Hashimoto K, Ikeya Y, Okada M, Maruno M. **Comparative study of Scutellaria planipes and Scutellaria baicalensis.** Biomed Chromatogr 1998;12(1):31-3.
Scutellaria planipes, a species of Scutellaria, was explored by comparing to Scutellaria baicalensis, a pharmacopoeia species. Four principle flavonoids in both the plant roots were analyzed by using a reversed-phase chromatographic system with a chemically bonded ODS silica gel column and phosphate buffer:methanol (68:32 and 1:1) as mobile phase. Their contents were similar in both plant roots. Antiallergic and antibacterial activities in vitro and acute toxicity were compared. The results provided valuable data for S. planipes as a potential medicinal resource.

Zink T, Chaffin J. **Herbal 'health' products: what family physicians need to know [see comments].** Am Fam Physician 1998;58(5):1133-40.
Patients who self-medicate with herbs for preventive and therapeutic purposes may assume that these products are safe because they are "natural," but some products cause adverse effects or have the potential to interact with prescription medications. The United States lacks a regulatory system for herbal products. Although only limited research on herbs has been published, St John's wort shows promise as a treatment for depression. Ginkgo biloba extract is possibly effective for cerebrovascular insufficiency and dementia. Feverfew is used extensively in Canada for migraine prophylaxis but needs more rigorous study. Ephedrine has been regulated by many

states because its misuse has been associated with several deaths. Echinacea is being tried as an agent for immune stimulation, and garlic is under study for cholesterol-lowering properties, but both require more study. Physicians should educate themselves and their patients about the efficacy and adverse interactions of herbal agents and the limitations of our present knowledge of them.

Adverse Effects

Phytotherapy: how to minimize risks. Presc Intl 1997;6(27):25-6.
IPA COPYRIGHT: ASHP Various ways to minimize risks associated with herbal remedy therapies are described, including an overview of adverse effects associated with various herbal remedies, the need for health professionals to be aware of unreliable labels on plant based products as well as contamination potential, and the levels of regulatory control that exist on herbal remedies in France.

Pulmonary embolism with a plant based product. Presc Intl 1997;6(31):144.
IPA COPYRIGHT: ASHP The removal of a plant based formulation from the market in France following its implication in a case of deep vein thrombosis and pulmonary embolism in an infant, and the importance of removing herbal products with no guarantees of efficacy and safety from pharmacy shelves are briefly discussed.

Abdel-Hafez AA, Meselhy MR, Nakamura N, Hattori M, Watanabe H, Murakami Y, El-Gendy MA, Mahfouz NM, Mohamed TA. **Effects of paeoniflorin derivatives on scopolamine-induced amnesia using a passive avoidance task in mice; structure-activity relationship.** Biol Pharm Bull 1998;21(11):1174-9.
Paeoniflorin (1) and its derivatives having in common a cage-like pinane skeleton with hemiketal-acetal system, were evaluated for their effects on memory impairment induced by scopolamine in mice using a step-down type passive avoidance task. In the test session, 1 and its derivatives were intraperitoneally (i.p.) administered at doses of 0.002, 0.01, 0.02 and 0.2 mmol/kg, and 30 min later (15 min before the experiment), scopolamine (1 mg/kg, i.p.) was given. These compounds showed dose-dependent attenuation in a dose range of 0.002-0.02 mmol/kg and also enhancement of scopolamine-induced decrease in step-down latency. The effects of these compounds, except that of 2',3',4',5'-O-tetraacetyl-3-O-methylpaeoniflorin (8), followed a bell-shaped dose response profile. 8-Debenzoyl-6-deglucosyl-3-O-methylpaeoniflorin (6) showed no significant increase in the step-down latency at all tested doses. Maximum step-down latency was obtained by 3-O-methylpaeoniflorin (3) and 2',3,3',4',5'-penta-O-methylpaeoniflorin (7) (the minimal effective dose was 0.002 mmol/kg). Relative to 3, debenzoylation, as in 8-debenzoyl-3-O-methylpaeoniflorin (4), slightly increased the latency, while deglucosylation, as in 6-deglucosyl-3-O-methylpaeoniflorin (5), significantly reduced the prolongation of latency. Removal of both glucose and benzoyl moieties resulted in the loss of activity as seen in 6. These results revealed that, in addition to the cage-like pinane skeleton, the benzoyl and the glucosyl moieties are important structural elements of the paeoniflorin skeleton as its effects on scopolamine-induced amnesia.

Al-Fakhri SA. **Herbal medicine: possible cause of aspiration pneumonia: case report.** Saudi Pharm J 1998;6(1):88-91.
IPA COPYRIGHT: ASHP The case report of a 3-wk-old girl who developed aspiration pneumonia possibly due to aspiration of an herbal medicine in powder form consisting of Commiphora molmol (myrrh), Ferula foetida L. (apiacea), Astragalus sarcocolla, and Saccharum officinarum Linne. is presented. The child was successfully treated with nebulized albuterol (salbutamol) and budesonide and oral prednisolone.

Al-Suwaidan SN, Gad El Rab MO, Al-Fakhiry S, Al Hoqail IA, Al-Maziad A, Sherif AB. **Allergic contact dermatitis from myrrh, a topical herbal medicine used to promote healing.** Contact Dermatitis 1998;39(3):137.

Aldana L, Gonzalez De Mejia E, Craigmill A, Tsutsumi V, Armendariz-Borunda J, Panduro A, Rincon AR. **Cypermethrin increases apo A-1 and apo B mRNA but not hyperlipidemia in rats.** Toxicol Lett 1998;95(1):31-9.
The hepatotoxic effect of cypermethrin and the expression of hepatic genes at the mRNA level, as molecular markers of liver damage, were evaluated in rats following exposure to cypermethrin. The expression of hepatic genes was compared with conventional liver functional tests, and correlations were made by studying the liver at the ultrastructural level. Cypermethrin treated rats presented a significant decrease, of 79% and 22%, on the expression of albumin and apo E genes at 5 days, respectively. The levels of apo A-1 and apo B mRNA were increased up to four- and fivefold, respectively. This increase did not correlate with the serum values of HDL and VLDL lipoprotein particles. Intracytoplasmic lipid droplets were observed after the first 2 days following cypermethrin administration, suggesting that apo A-1 and B mRNA were translated but not secreted. There were significant correlations between the low values of the albumin gene expression, the decrease in the HDL concentrations, and the ultrastructural alterations, respectively. These alterations were mainly a large amount and increased size of mitochondria in the animals exposed to cypermethrin. It is concluded that under the experimental conditions used, cypermethrin may alter the metabolism of lipids and proteins in rat liver.

Alexander RG, Wilson DA, Davidson AG. **Medicines Control Agency investigation of the microbial quality of herbal products.** Pharm J 1997 Aug 16;259:259-61.
IPA COPYRIGHT: ASHP To assess the microbiological quality of licensed herbal products by determining the nature and quantity of microorganisms present, 425 herbal products were examined by pharmacopeial and validated inhouse methods; total aerobic bacterial counts and total fungal counts were measured. Most licensed herbal products were found to comply with European Pharmacopeial limits. However, some solid oral dosage forms were found to contain undesirable organisms. It was suggested that additional quantitative tests for specific microorganisms in future editions of the European Pharmacopeia may be justified.

Alpertunga B, Omurtag GZ, Ozmentese N. **Investigation about the genotoxic activities of some herbal teas used as folk medicine.** Acta Pharm Turc 1997;39(3):105-10.

Ameri A. **The effects of Aconitum alkaloids on the central nervous system.** Prog Neurobiol 1998;56(2):211-35.

Preparations of Aconitum roots are employed in Chinese and Japanese medicine for analgesic, antirheumatic and neurological indications. The recent surge in use of phytomedicine derived from traditional Chinese medicine as well as increasing concerns about possible toxic effects of these compounds have inspired a great deal of research into the mechanisms by which certain Aconitum alkaloids may act on the central nervous system. The pharmacological effects of preparations of Aconitum roots are attributed to several diterpenoid alkaloids. The main alkaloid of these plants is aconitine, a highly toxic diterpenoid alkaloid which is known to suppress the inactivation of voltage-dependent Na+ channels by binding to neurotoxin binding site 2 of the alpha-subunit of the channel protein. In this article the pharmacology of several structurally related Aconitum alkaloids is highlighted and their therapeutic vs toxic potential is discussed. Neurochemical and neurophysiological studies will be reviewed with emphasis on the effects of the alkaloids in regions of the brain that have been implicated in pain transmission and generation of epileptic activity. Considering the chemical structure of the Aconitum alkaloids as well as their mechanism of action, a subdivision in three groups becomes obvious: the first group comprises such alkaloids which possess high toxicity due to two ester boundings at the diterpene skeleton. The members of this group activate voltage-dependent sodium channels already at resting potential and inhibit noradrenaline reuptake. Activation of sodium channels and in consequence excessive depolarization with final inexcitability and suppression of pain transmission account for their antinociceptive properties. The second group comprises less toxic monoesters which have been shown to possess strong antinociceptive, antiarrhythmic and antiepileptiform properties due to a blockade of the voltage-dependent sodium channel. Electrophysiological studies have revealed a use-dependent inhibition of neuronal activity by these alkaloids. They seem to be competitive antagonists of the group I-alkaloids. The third group of Aconitum alkaloids are lacking an ester side chain in the molecule. Toxicity is markedly reduced when compared with the two other groups. They fail to affect neuronal activity, but are reported to have antiarrhythmic actions suggesting that they may have different affinities to various subtypes of the alpha-subunit of the Na+ channel in brain and heart.

Angell M, Kassirer JP. **Alternative medicine--risks of untested and unregulated remedies.** N Engl J Med 1998 Sep 17;339:839-41.
IPA COPYRIGHT: ASHP The risks of untested and unregulated herbal medicine, the most common of all forms of alternative medicine, are discussed.

Anibarro B, Fontela JL, De La Hoz F. **Occupational asthma induced by garlic dust.** J Allergy Clin Immunol 1997;100(6 Pt 1):734-8.
BACKGROUND: Garlic dust has not been a frequently encountered cause of IgE-mediated disease. OBJECTIVE: We report on 12 patients (all of them garlic workers) with the clinical criteria for occupational asthma. METHODS: Skin prick tests and serum-specific IgE determinations were performed with common inhalants, garlic, and other members of the Liliaceae family (onion, leek, and asparagus). Bronchial challenge test with garlic powder was performed in all patients. Garlic and onion extract proteins were separated by sodium dodecylsulfate-polyacrylamide gel electrophoresis. Immunoblot and IgE immunoblot inhibition analyses were performed with patients' sera on extracts of garlic, onion, and pollens of Phleum pratense and Chenopodium album. RESULTS: Garlic sensitization was demonstrated by bronchial challenge test in seven patients (group 1) and ruled out in the remaining five (group 2).

Clinical data were similar in both groups. The patients with garlic allergy had a mean age of 27 years, and all of them had pollen allergy; sensitization to other members of the Liliaceae family was also common. Electrophoresis of garlic extract revealed two major protein bands at approximately 12 and 54 kd. During IgE immunoblotting, the pool of sera reacted with garlic proteins mainly at 54 kd. Preincubation with onion, Phleum, and Chenopodium partially abolished the IgE binding to several allergens of garlic. CONCLUSION: We report on seven patients in whom an occupational garlic allergy was demonstrated. Garlic allergy is relatively rare but seems to affect young subjects with pollen allergy, and sensitization to other members of the Liliaceae family is common. The results of this study confirm the presence of some structurally similar allergens in garlic, onion, and certain pollens.

Aphale AA, Chhibba AD, Kumbhakarna NR, Mateenuddin M, Dahat SH. **Subacute toxicity study of the combination of ginseng (Panax ginseng) and ashwagandha (Withania somnifera) in rats: a safety assessment.** Indian J Physiol Pharmacol 1998;42(2):299-302.
Ginseng (Panax ginseng) and Ashwagandha (Withania somnifera) are widely used as geriatric tonics. Both individually have not shown any toxicity on long term administration. Study was planned to assess the safety of the combination by doing subacute toxicity study in rats with 90 days oral administration using three doses. Food consumption, body weight, haematological, biochemical and histopathological parameters were studied. There was significant increase in body weight, food consumption and liver weight, and improved hematopoiesis was observed. Brain, heart, lung, liver, spleen, kidneys, stomach, testis and ovaries were normal on gross examination and histopathologically. Subacute toxicity studies in rats did not reveal any toxicity.

Apted J. **Primin sensitivity in a patient sensitive to Streptocarpus [letter].** Australas J Dermatol 1998;39(3):199-200.

Asero R. **Relevance of pollen-specific IgE levels to the development of Apiaceae hypersensitivity in patients with birch pollen allergy.** Allergy 1997;52(5):560-4.
A large clinical/serologic study was carried out to determine the prevalence of Apiaceae (carrot, celery, and fennel) hypersensitivity in patients with birch pollen allergy, and to investigate its relationship with apple and hazelnut allergy and with birch pollen-specific IgE levels. A total of 196 birch pollen-hypersensitive patients with oral allergy syndrome (OAS) caused by different vegetable foods were examined in the cross-sectional part of the study. Of this total, 195 patients had apple and/or hazelnut allergy, and 103 had Apiaceae sensitivity; only one patient had Apiaceae allergy alone. Apiaceae-positive patients showed significantly higher birch pollen-specific IgE levels than negative ones (median 13 vs 7 AU/ml; $P < 0.0001$). The prospective part of the study was performed on 103 birch pollen-hypersensitive patients who were OAS-free at the time of the first visit and were periodically followed-up for OAS. Patients who developed Apiaceae sensitivity showed much higher birch-specific IgE levels than patients who developed apple/hazelnut allergy only (median 15.5 vs 8.5 AU/ml; $P < 0.05$), whereas those who remained OAS-free showed the lowest specific IgE levels (median 5 AU/ml). This study suggests that most Apiaceae determinants cross-react with apple or hazelnut determinants, whereas only some apple or hazelnut determinants cross-react with Apiaceae-allergenic determinants; moreover, it shows that birch-specific IgE levels heavily influence the onset of OAS as a whole, and probably play a critical role in the development of allergies to distinct vegetable foods as well.

Asero R, Mistrello G, Roncarolo D, Antoniotti PL, Falagiani P. **A case of garlic allergy.** J Allergol Clin Immunol 1998;101(3):427-28.
BIOSIS COPYRIGHT: BIOL ABS. RRM CASE STUDY ALLIUM-SATIVUM HUMAN ADULT FEMALE GARLIC ALLERGY ALLERGY URTICARIA DERMATOLOGY IMMUNE SYSTEM DISEASE INTEGUMENTARY SYSTEM DISEASE.

Avila H, Rivero J, Herrera F, Fraile G. **Cytotoxicity of a low molecular weight fraction from Aloe vera (Aloe barbadensis Miller) gel.** Toxicon 1997;35(9):1423-30.
The cytotoxicity of a low mol. wt fraction (LMWF) obtained from Aloe vera gel was determined by two different assays. Firstly, exposure of monolayers of chicken fibroblasts to LMWF induced disruption of intercellular junctions and detachment of individual cells from the bottom of the flask, with formation of cell-free gaps in the monolayer. Secondly, LMWF inhibited the production of reactive oxygen species by human polymorphonuclear leukocytes stimulated by zymosan, as followed by luminol-dependent chemiluminescence. The toxic activity of LMWF was compared to that of sodium dodecyl sulfate (a well-known toxic substance), aloe-emodin and aloin (an anthraquinone and its precursor present in Aloe vera cortex) using the chemilumescence assay, and was found to be of similar potency to these toxic substances on a weight-to-weight basis. These results confirm that Aloe vera gel contains toxic low mol. wt compounds, and every effort must be made to limit the amount of these toxins in the commercially prepared Aloe vera gel products.

Bagheri H, Broue P, Lacroix I, Larrey D, Olives JP, Vaysse P, Ghisolfi J, Montastruc JL. **Fulminant hepatic failure after herbal medicine ingestion in children [letter].** Therapie 1998;53(1):82-3.

Barnes J, Mills SY, Abbot NC, Willoughby M, Ernst E. **Different standards for reporting ADRs to herbal remedies and conventional OTC medicines: face-to-face interviews with 515 users of herbal remedies.** Br J Clin Pharmacol 1998;45(5):496-500.
AIMS: To determine whether adverse drug reactions (ADRs) to herbal remedies would be reported differently from similar ADRs to conventional over-the-counter (OTC) medicines by herbal-remedy users. METHODS: Face-to-face interviews (using a structured questionnaire) with 515 users of herbal remedies were conducted in six pharmacy stores and six healthfood stores in the UK. The questionnaire focused on the likely course of action taken by herbal-remedy users after experiencing an ADR associated with a conventional OTC medicine and a herbal remedy. RESULTS: Following a 'serious' suspected ADR, 156 respondents (30.3%) would consult their GP irrespective of whether the ADR was associated with the use of a herbal remedy or a conventional OTC medicine, whereas 221 respondents (42.9%) would not consult their GP for a serious ADR associated with either type of preparation. One hundred and thirty-four respondents (26.0%) would consult their GP for a serious ADR to a conventional OTC medicine, but not for a similar ADR to a herbal remedy, whereas four respondents (0.8%) would consult their GP for a serious ADR to a herbal remedy, but not for a similar ADR to a conventional OTC medicine. Similar differences were found in attitudes towards reporting 'minor' suspected ADRs. CONCLUSIONS: Consumers of herbal remedies would act differently with regard to reporting an ADR (serious or minor) to their GP depending on whether it was associated with a herbal remedy or a conventional OTC medicine. This has implications for

herbal pharmacovigilance, particularly given the increasing use of OTC herbal remedies. The finding that a high proportion of respondents would not consult their GP or pharmacist following ADRs to conventional OTC medicines is also of concern.

Bateman J, Chapman RD, Simpson D. **Possible toxicity of herbal remedies.** Scott Med J 1998;43(1):7-15.
Herbal remedies are rapidly gaining popularity throughout the world as a result of dissatisfaction with conventional medicines. It is a widely held belief that herbal preparations are "natural" and are therefore intrinsically harmless. However, their effects can be very powerful and potentially lethal if used incorrectly and their use as a substitute for conventional medicines may be ineffective. Toxic effects have been attributed to several factors including hepatotoxicity of main constituents, contamination of preparations by heavy metals or microorganisms, and adverse reactions due to age, and genetic and concomitant disease characteristics of the user.

Bernd A, Simon S, Ramirez Bosca A, Kippenberger S, Diaz Alperi J, Miquel J, Villalba Garcia JF, Pamies Mira D, Kaufmann R. **Phototoxic effects of Hypericum extract in cultures of human keratinocytes compared with those of psoralen.** Photochem Photobiol 1999;69(2):218-21.
Extracts of Hypericum perforatum (St. John's wort) are used in the treatment of depression. They contain the plant pigment hypericin and hypericin derivates. These compounds have light-dependent activities. In order to estimate the potential risk of phototoxic skin damage during antidepressive therapy, we investigated the phototoxic activity of hypericin extract using cultures of human keratinocytes and compared it with the effect of the well-known phototoxic agent psoralen. The absorbance spectrum of our Hypericum extract revealed maxima in the whole UV range and in parts of the visible range. We cultivated human keratinocytes in the presence of different Hypericum concentrations and irradiated the cells with 150 mJ/cm2 UVB, 1 J/cm2 UVA or 3 h with a white light of photon flux density 2.6 mumol m-2 s-1. The determination of the bromodeoxyuridine incorporation rate showed a concentration- and light-dependent decrease in DNA synthesis with high hypericin concentrations (> or = 50 micrograms/mL) combined with UVA or visible light radiation. In the case of UVB irradiation a clear phototoxic cell reaction was not detected. We found phototoxic effects even with 10 ng/mL psoralen using UVA with the same study design as in the case of the Hypericum extract. These results confirm the phototoxic activity of Hypericum extract on human keratinocytes. However, the blood levels that are to be expected during antidepressive therapy are presumably too low to induce phototoxic skin reactions.

Betz JM, Andrzejewski D, Troy A, Casey RE, Obermeyer WR, Page SW, Woldemariam TZ. **Gas chromatographic determination of toxic quinolizidine alkaloids in blue cohosh Caulophyllum thalictroides (L.) Michx.** Phytochemical Analysis 1998;9(5):232-6.
BIOSIS COPYRIGHT: BIOL ABS. Blue cohosh (Caulophyllum thalictroides (L.) Michx., Berberidaceae) is a North American perennial herb which is found as an ingredient in dietary supplement products in the United States. The plant contains the alkaloids N-methylcytisine, baptifoline, anagyrine and magnoflorine. Some of the alkaloids, including the quinolizidine alkaloid anagyrine, are toxic to range animals and have been implicated as teratogens in higher animals. Since the traditional use of the herb involves administration to women of reproductive

age to treat menstrual cramps, and to pregnant women la the last 3-4 weeks of pregnancy to ease parturition, therefore the safety of these products to the fetus is of concern. Three of these alkaloids have been determined in authentic blue cohosh and several dietary supplements. Levels found were: 5-850 ppm for N-methylcytisine, 2-390 ppm for anagyrine, and 9-900 ppm for baptifoline. The lower alkaloid concentrations were found in products containing liquid extracts. Alkaloid identities were confirmed by mass spectrometry.

Bieler CA, Stiborova M, Wiessler M, Cosyns JP, Van Ypersele De Strihou C, Schmeiser HH. **32P-post-labelling analysis of DNA adducts formed by aristolochic acid in tissues from patients with Chinese herbs nephropathy.** Carcinogenesis 1997;18(5):1063-7.
Recently, we reported that aristolochic acid (AA) a naturally occurring nephrotoxin and carcinogen is implicated in a unique type of renal fibrosis, designated Chinese herbs nephropathy (CHN). Indeed, we identified the principal aristolochic acid-DNA adduct in the kidney of five such patients. We now extend these observations and demonstrate the presence of additional AA-DNA adducts by the 32P-post-labelling method not only in the kidneys, but also in a ureter obtained after renal transplantation. Using the nuclease P1 version of the assay not only the major DNA adduct of aristolochic acid, 7-(deoxyadenosin-N6-yl)-aristolactam I (dA-AAI), but also the minor adducts, 7-(deoxyguanosin-N2-yl)-aristolactam I (dG-AAI) and 7-(deoxyadenosin-N6-yl)-aristolactam II (dA-AAII) were detected, and identified by cochromatographic analyses with TLC and HPLC. Quantitative analyses of six kidneys revealed relative adduct levels from 0.7 to 5.3/10(7) for dA-AAI, from 0.02 to 0.12/10(7) for dG-AAI and 0.06 to 0.24/ 10(7) nucleotides for dA-AAII. The detection of the dA-AAII adduct is consistent with the occurrence of aristolochic acid II (AAII) in the herb powder imported under the name of Stephania tetrandra and confirms that the patients had indeed ingested the natural mixture of AAI and AAII. 32P-post-labelling analyses of further biopsy samples of one patient showed the known adduct pattern of AA exposure not only in the kidney, but also in the ureter, whereas in skin and muscle tissue no adduct spots were detectable. In an attempt to explain the higher level of the dA-AAI adduct compared to the dG-AAI adduct level in renal tissue even 44 months after the end of regimen, the persistence of these two purine adducts was investigated in the kidney of rats given a single oral dose of pure AAI. In contrast to the dG-AAI adduct, the dA-AAI adduct exhibited a lifelong persistence in the kidney of rats. Our data demonstrate that AA forms DNA adducts in human tissue by the same activation mechanism(s) reported from animal studies. Thus, the carcinogenic/mutagenic activity of AA observed in animals could also be responsible for the urothelial cancers observed in two of the CHN patients.

Blanc PD, Kuschner WG, Katz PP, Smith S, Yelin EH. **Use of herbal products, coffee or black tea, and over-the-counter medications as self-treatments among adults with asthma.** J Allergy Clin Immunol 1997;100(6 Pt 1):789-91.
BACKGROUND: There are few data on the use of alternative therapies in adult asthma and their impact on health outcomes. OBJECTIVE: The objective of this study was to study the prevalence and morbidity of asthma self-treatment with herbs, coffee or black tea, and over-the-counter (OTC) medications containing ephedrine or epinephrine. METHODS: We carried out a cross-sectional analysis of interview data for 601 adults with asthma recruited from a random sample of pulmonary and allergy specialists. We estimated the 12-month prevalence of reported use of herbal products, coffee or black tea, or OTC products to self-treat asthma and their

association with emergency department visits and hospitalization. RESULTS: Herbal asthma self-treatment was reported by 46 (8%; 95% confidence interval [CI] 6% to 10%); coffee or black tea self-treatment by 36 (6%; 95% CI 4% to 8%), epinephrine or ephedrine OTC use by 36 (6%; 95% CI 4% to 8%), and any of the three practices by 98 subjects (16%; 95% CI 13% to 19%). Adjusting for demographic and illness covariates, herbal use (odds ratio [OR] 2.5; 95% CI 1.1 to 5.6) and coffee or black tea use (OR 3.1; 95% CI 1.2 to 7.8) were associated with asthma hospitalization; OTC use was not (OR 0.8; 95% CI 0.3 to 2.5). CONCLUSIONS: Even among adults with access to specialty care for asthma, self-treatment with nonprescription products was common and was associated with increased risk of reported hospitalization. This association does not appear to be accounted for by illness severity or other disease covariates. It may reflect delay in utilization of more efficacious treatments.

Borins M. **The dangers of using herbs. What your patients need to know.** Postgrad Med 1998;104(1):91-5, 99-100.
Herbal remedies are becoming increasingly popular among patients as treatment for such varied medical problems as arthritis, depression, diabetes, menstrual irregularity, and pulmonary conditions. However, there are many negative effects of herbal preparations. Dr Borins discusses the potential side effects of various herbs and the lack of standardization and control that can contribute to contamination and toxicity of herbal products.

Bove GM. **Acute neuropathy after exposure to sun in a patient treated with St. John's Wort.** Lancet 1998 Oct 3;352:1121-2.
IPA COPYRIGHT: ASHP The case of a 35-yr-old woman who took 500 mg of Hypericum perforatum as a ground preparation daily for mild depression, based on information in a magazine article, and developed subacute polyneuropathy after exposure to the sun is presented. After 4 wk of taking H. perforatum, the patient developed stinging pain on her face and the dorsum of each hand, which were areas that had received sun exposure. She sought help when the same symptoms developed on the exposed areas of her arms and legs a few h after sunbathing. The patient was diagnosed with subacute toxic neuropathy. H. perforatum was stopped. The symptoms began to improve after 3 wk and disappeared gradually over the next 2 months.

Boyle FM. **Adverse interaction of herbal medicine with breast cancer treatment [letter; comment].** Med J Aust 1997;167(5):286.

Brockmoller J, Reum T, Bauer S, Kerb R, Hubner WD, Roots I. **Hypericin and pseudohypericin: pharmacokinetics and effects on photosensitivity in humans.** Pharmacopsychiatry 1997;30(Suppl 2):94-101.
Extracts of St. John's wort (Hypericum perforatum) are used in treatment of depression. They contain various substances with the naphthodianthrones hypericin and pseudohypericin as characteristic ingredients. These compounds were shown to cause phototoxicity in cell culture and in animals. A placebo-controlled randomized clinical trial with monitoring of hypericin and pseudohypericin plasma concentration was performed to evaluate the increase in dermal photosensitivity in humans after application of high dose hypericum extracts. The study was divided into a single dose and a multiple dose part. In the single dose period, each of 13

volunteers received in a double blind fourfold complete crossover design, either placebo, or 900, 1800 or 3600 mg of a standardized hypericum extract (LI 160) containing zero, 2.81, 5.62 and 11.25 mg of total hypericin (total hypericin is the sum of hypericin and pseudohypericin). Maximum total hypericin plasma concentrations were observed about 4 h after dosage and were 0, 0.028, 0.061 and 0.159 mg/L, respectively. Before and 4 h after drug intake, the subjects were exposed at small areas of their back to increasing doses of solar simulated irradiation (SSI, with combined ultraviolet A, UV-A, and UV-B light) and another part was exposed to selective UV-A light irradiation. Minimal erythema dose was determined 5, 20 and 68 h after irradiation. Comparison of SSI sensitivity without and with hypericum extract did not show and difference and there was no dose-related trend in light sensitivity. Sensitivity to selective UV-A light was increased only after the highest dose from a minimal tanning dose of 10.8 J/ cm2 (mean) after placebo to 8.7 J/cm2 after 3600 mg extract with marginal statistical significance ($p = 0.03$ by one sided paired t-test). There was no correlation between total hypericin plasma concentrations and photosensitivity. In the multiple dose part, 50 volunteers received 600 mg hypericum extract t.i.d. with a daily dose of 5.6 mg of total hypericin. Comparison of UV light sensitivity before dosing with day 15 of treatment showed a slightly increased SSI sensitivity expressed by decrease of the MED from 0.17 to 0.16 J/cm2 ($p = 0.005$ by Wilcoxon test), and similarly, sensitivity to UV-A light increased (the mean tanning dose decreased from 9.9 to 7.8 J/cm2, $p < 0.0001$). This increase in cutaneous light sensitivity could be compensated by reducing irradiation time by 21%. Doses used in this study were higher than typical doses in current commercial preparations. In spite of these high doses in the double blind single dose part, frequency of side effects was equal to placebo medication and UV light sensitivity was not or only marginally increased. The study does not, however, exclude phototoxic reactions with doses above 11.25 mg of total hypericin and plasma levels above 100 micrograms/L. Furthermore, phototoxicity may be different after application of pure hypericin, since some constituents in the plant extract may exhibit protective effects.

Brusick D, Mengs U. **Assessment of the genotoxic risk from laxative senna products.** Environ Mol Mutagen 1997;29(1):1-9.
Laxative senna products and several of their specific components have been submitted to a large number of genetic tests. While most studies gave negative responses, results from some of the studies suggest that components of senna products, particularly emodin and aloe-emodin, have genotoxic activity. Assessment of the genotoxicity profile of these substances, in light of other data from animal and human metabolism or kinetic studies, human clinical trials and rodent carcinogenicity studies do not support concerns that senna laxatives pose a genotoxic risk to humans when consumed under prescribed use conditions.

Brustbauer R, Wenisch C. **[Bradycardic atrial fibrillation after drinking herbal tea].** DMW 1997;122(30):930-2. (Ger)
BIOSIS COPYRIGHT: BIOL ABS. History and clinical findings: One day after drinking what she thought to be a tea made from borage leaves a 72-year-old woman developed nausea, vomiting and diarrhoea, later also flickering in her eyes and palpitations. She was in a good general state with a blood pressure of 120/75 mm Hg and an irregular heart rate of 52/min. Physical examination was otherwise unremarkable. She had not been on any medication. Investigations: The usual laboratory tests were normal. The electrocardiogram showed atrial

fibrillation with a slow ventricular rate with pauses of up to 1.5 s, intermittently type I and II 2~ AV block, and depressed concave ST segments. The level of digoxin was 3.93 ng/ml, that of digitoxin 133.5 ng/ml. Treatment and course: The patient's symptoms quickly improved under symptomatic treatment. Further questioning suggested that she had probably mistaken foxglove leaves for those of borage when picking them to make a brew. Conclusion: If cardiac arrhythmias have occurred after intake of self-picked herbal leaves one should consider digitalis intoxication resulting from misidentification.

Bruynzeel DP. **Bulb dermatitis. Dermatological problems in the flower bulb industries.** Contact Dermatitis 1997;37(2):70-7.
The irritant and allergenic properties of the most important flower bulbs are described, as well as the clinical symptoms they cause. The tulip contains the allergen tulipalin A; sensitization and irritation are responsible for the development of tulip fingers. The same clinical picture can be caused by Alliums like the onion and garlic. The narcissus causes lily rash, a dermatitis rarely caused by sensitization. The hyacinth evokes itching in practically everyone: an irritant reaction caused by calcium oxalate crystals. Patch testing is complicated as the allergens are not all identified.

Burnakis TG. **It's only natural.** Hosp Pharm 1998 Aug;33:1006-7.
IPA COPYRIGHT: ASHP Some adverse effects and drug interactions of alternative medicines are reported, including the development of severe chronic interstitial nephritis in a patient with previously normal renal function after self-medication with chromium picolinate, the occurrence of drug interactions between ginseng and both warfarin and digoxin, and the development of spontaneous bleeding in 2 subjects who had taken Ginkgo biloba.

Caballero T, Martin-Esteban M. **Association between pollen hypersensitivity and edible vegetable allergy: A review.** J Invest Allergol Clin Immunol 1998;8(1):6-16.
BIOSIS COPYRIGHT: BIOL ABS. Over the last three decades several authors have described the existence of an association between sensitivity to different pollens and sensitivity to diverse edible vegetables. An association between ragweed pollinosis and hypersensitivity to Cucurbitaceae vegetables (e.g., watermelon, melon, cucumber) and banana has been reported. Other authors have found a relationship between birch pollinosis and sensitization to hazelnut, apple, carrot, potato, kiwi and other vegetables. Additionally, several papers have shown the association between mugwort pollinosis and sensitization to celery, carrot, spices, nuts, mustard and Leguminoseae vegetables. Later some studies showed association between grass pollinosis and sensitization to tomato, potato, green-pea, peanut, watermelon, melon, apple, orange and kiwi. Finally, an association between sensitization to plantain pollen and melon hypersensitivity was also described. The association between pollinosis and edible vegetable sensitization has been explained by the combination of different hypotheses, such as the following. 1) presence of lectins in edible vegetables; 2) existence of IgE to carbohydrates of the glycoproteins (crossreactive carbohydrate determinants); and, 3) existence of common allergens between pollens and edible vegetables. Up to now three allergens have been identified as responsible for cross-reactivity in these associations: profilin, a 14 kd protein that regulates actin; Bet v 1, the 18 kd birch pollen allergen; and a 60-69 kd allergen. It is important to study in depth these

associated sensitizations and the common allergens responsible for them in order to improve diagnostic methods and treatment of these syndromes.

Calore EE, Cavaliere MJ, Haraguchi M, Gorniak SL, Dagli ML, Raspantini PC, Calore NM, Weg R. **Toxic peripheral neuropathy of chicks fed Senna occidentalis seeds.** Ecotoxicol Environ Saf 1998;39(1):27-30.
Plants of the genus Senna (formerly Cassia) are poisonous to livestock and other laboratory animals, leading to a syndrome of a widespread muscle degeneration, incoordination, recumbence, and death. The main histologic lesion is necrosis of skeletal muscle fibers. Recently, a mitochondrial myopathy with ragged-red and cytochrome oxidase (COX)-negative muscle fibers was recognized in hens chronically intoxicated with parts of seeds of S. occidentalis. The purpose of the present work was to investigate if there was peripheral nerve involvement in the acute intoxication of chicks with S. occidentalis seeds. Teasing of individual fibers revealed signs of extensive axonal damage with myelin ovoids. Ultrathin sections confirmed the axonal damage. Axons were filled with membranes, some residual disorganized filaments, and enlarged mitochondria. In some instances the axon disappeared and there was secondary degeneration of the myelin sheath. The present work is the first description of the neurotoxic effect of S. occidentalis intoxication. Future work should attempt to determine the mechanisms involved in this neuropathy.

Calore EE, Cavaliere MJ, Haraguchi M, Gorniak SL, Dagli ML, Raspantini PC, Perez Calore NM. **Experimental mitochondrial myopathy induced by chronic intoxication by Senna occidentalis seeds.** J Neurol Sci 1997;146(1):1-6.
Histochemical and electron microscopic studies of biceps femoris, pectoralis major and rectus femoris of chronically treated birds with seeds of the poisonous plant Senna occidentalis (0.2% external/internal tegment), were performed. The muscles had similar features of human mitochondrial myopathy as ragged-red fibers, cytochrome-oxidase negative fibers, and weak activity of the oxidative enzymes. Fibers with lipid storage were also present. Acid phosphatase activity in rare muscle fibers was also detected, and represents probably a secondary degenerative process. By electron microscopy, enlarged mitochondria with disrupted or excessively branched cristae were seen. The present study presents a new experimental model of mitochondrial myopathy that may be useful for the best knowledge of this group of diseases and for experimental trials of drugs that could reverse the mitochondrial impairment in the mitochondrial myopathies.

Campana MA, Panzeri AM, Moreno VJ, Dulout FN. **Genotoxic evaluation of the pyrethroid lambda-cyhalothrin using the micronucleus test in erythrocytes of the fish Cheirodon interruptus interruptus.** Mutat Res 1999;438(2):155-61.
In order to develop experimental models able to detect genotoxic effects of pollutants in aquatic organisms, the genotoxicity of the pyrethroid lambda-cyhalothrin was studied using the micronucleus test in erythrocytes of Cheirodon interruptus interruptus. The frequency of micronuclei was examined in blood smears obtained from fishes exposed in vivo to three different concentrations (0.05; 0. 01; 0.001 ug/l) of the compound and sacrificed at nine sampling times (24, 48, 72, 96 h and 8, 12, 15, 19 and 23 days). As a positive control fishes were exposed to 5 mg/l of cyclophosphamide. Results obtained demonstrated the genotoxic effects of

the pyrethroid in the experimental model employed. The variation in the micronuclei frequencies in the different sampling times could be related to the blood cell kinetics and the erythrocyte replacement. The results could be considered as a validation of the MN test in fishes for the assessment of genotoxic pollutants. Copyright 1999 Published by Elsevier Science B.V.

Cantor C. **Kava and alcohol [letter; comment].** Med J Aust 1997;167(10):560.

Catania PN. **Problems with herbal remedies in anticoagulated home care patients.** Home Care Provid 1998;3(5):253-5.
The increasing popularity of alternative therapies, including herbal remedies, poses new challenges for home health care providers. The cost of herbal remedy use now exceeds $1 billion annually in the United States and is expected to increase. The use of traditional medicine in combination with alternative therapy may lead to complications for patients and their caregivers as evidenced by the adverse effects of certain herbal products in patients who receive traditional anticoagulant or antiplatelet medication.

Cavaliere MJ, Calore EE, Haraguchi M, Gorniak SL, Dagli ML, Raspantini PC, Calore NM, Weg R. **Mitochondrial myopathy in Senna occidentalis-seed-fed chicken.** Ecotoxicol Environ Saf 1997;37(2):181-5.
Plants of the genus Senna (formerly Cassia) have been recognized as the cause of a natural and experimental syndrome of muscle degeneration frequently leading to death in animals. Histologically, it demonstrated skeletal and cardiac muscle necrosis, with floccular degeneration and proliferation of sarcolemmal nuclei. Recently, it was described as an experimental model of mitochondrial myopathy in hens chronically treated with Senna occidentalis. Currently, skeletal muscles of chicks intoxicated with seeds of the poisonous plant S. occidentalis were studied by histochemistry and electron microscopy. Since birth, the birds were fed ground dried seeds of this plant with a regular chicken ration at a dose of 4% for 11 days. Microscopic examination revealed, besides muscle-fiber atrophy, lipid storage in most fibers and a moderate amount of cytochrome oxidase-negative fibers. By electron microscopy, enlarged mitochondria with disrupted or excessively branched cristae were seen. This picture was characteristic of mitochondrial myopathy. These findings have hitherto remained unnoticed in skeletal muscle of young birds treated with S. occidentalis.

Ceha LJ, Presperin C, Young E, Allswede M, Erickson T. **Anticholinergic toxicity from nightshade berry poisoning responsive to physostigmine.** J Emerg Med 1997;15(1):65-9.
The woody nightshade, Solanum dulcamara, belongs to the genus Solanum and its primary toxin is solanine. We report a large nightshade ingestion in a 4-yr-old girl who presented to the emergency department in acute anticholinergic crisis. The child was given 0.2 mg of intravenous physostigmine (0.02 mg/kg). Within 50 min, the patient received two additional equal doses with complete resolution of symptoms. After 36 h of observation, the child was discharged. Our patient presented with symptoms more suggestive of the deadly nightshade species, Atropa belladonna, which is native to Europe; however, a detailed laboratory analysis of the suspect berries revealed no atropine or hyoscyamine. Analysis did reveal sterols consistent with solanine. This is a unique case presentation of woody nightshade, S. dulcamara, poisoning presenting with anticholinergic crisis and responding to physostigmine.

Cerrato PL. **Natural tranquilizers?** RN Mag 1998 Dec;61:61-2, 68-9.
IPA COPYRIGHT: ASHP A brief overview of the anxiolytic effects of extracts of kava and valerian and the dosage, adverse effects, contraindications, and drug interactions of these preparations is presented.

Chang HL, Kuo ML, Lin JM. **Mutagenic activity of incense smoke in comparison to formaldehyde and acetaldehyde in Salmonella typhimurium TA102.** Bull Environ Contam Toxicol 1997;58(3):394-401.

Chang IM. **Liver-protective activities of aucubin derived from traditional oriental medicine.** Res Commun Mol Pathol Pharmacol 1998;102(2):189-204.
The iridoid glycosides including aucubin (AU), catalpol (CA), swertimarin (SW), and gardenoside (GA) are frequently found as natural constituents of many traditional oriental medicinal plants including Chinese herbs. Among these iridoid glycosides, AU was systematically studied for its potent liver-protective activities using experimental systems of hepatic damage. AU showed high liver-protective activity against carbon tetrachloride-induced hepatic damage in mice. Also AU showed significant protective activity against alpha-amanitin-induced hepatic damage in mice, and it prevented a depression of liver RNA biosynthesis caused by alpha-amanitin administration. Potent antidotal effects on mushroom poisoning in beagle dogs ingested with aqueous extract of Amanita virosa was observed; beagle dogs completely survived, even when AU administration was withheld for half an hour after mushroom poisoning. In addition, AU was found to suppress hepatitis B viral DNA replication in vitro. Conversion of AU to its aglycone form appeared to be a prerequisite step for an exhibition of such antiviral activity.

Chang MW, Song GY, Cha HS. **[Effect of ginseng extracts on production of vacuolating toxin by Helicobacter pylori].** J Korean Soc Microbiol 1997;32(5):539-51. (Kor)
BIOSIS COPYRIGHT: BIOL ABS. This study was carried out to survey the prevalence of Helicobacter pylori infection and the incidence of vacuolating toxin producing H. pylori from the gastric biopsy specimens of patients with 178 gastritis, 57 gastric ulcer, 455 gastric cancer and 44 healthy person in Pusan, Korea. Further aim of this study was to evaluate the effect of ginseng extract, sofalcone, ginsenosides (F1, Rb3, Re, Rg1), sangwha, green, arrowroot, ginger, and jujube tea on the activity and production of vacuolating toxin by H. pylori in vitro. The isolation rates of H. pylori by culture method from gastric biopsy specimens were 34.1% in healthy person, 42.1% in gastritis, 36.8% in gastric ulcer, and 39.3% in gastric cancer. The isolation rates of vacuolating toxin producing H. pylori from gastric biopsy specimens were 80% in healthy person, 82.7% in gastritis, 81% in gastric ulcer, and 83.8% in gastric cancer. The growth of H. pylori was not influenced by the addition of 10 mug/ml or 100 mug/ml of Ginseng extract and 10 mug/ml of sofalcone in the medium, but the production of vacillating toxin of H. pylori was significantly inhibited by the addition of 100 mug/ml of Ginseng extract and sofalcone. The activity of vacuolating toxin in the culture supernatant of H. pylori was significantly diminished (1/2-1/16 compared to control) by the addition of 10 mg/ml of sangwha, green, arrowroot, and ginger tea, and 1 mug/ml of ginsenosides F1, Rb3, Re, and Rg1. These results suggest that the isolation rates of vacuolating toxin producing H. pylori were significantly higher than that of the foreign reports. Ginseng extract and sofalcone have direct inhibitory effect on the activity of vacuolating toxin production by H. pylori without considerable growth inhibition and sangwha,

green, arrowroot, and ginger tea have direct inhibitory effect on the activity of vacuolating toxin of H. pylori.

Chang NY. **[Experimental study on the antistimulative and antineoplastic effects of Radix ginseng used in combination with Fafces trogopterus].** J Chin Mater Med 1997;22(11):694-6. (Chi)
IPA COPYRIGHT: ASHP To investigate the effects of Radix ginseng used in combination with Fafces trogopterus, neoplastic mice received R. ginseng either alone or with F. trogopterus. The mice that received the combination demonstrated better antistimulative effects and extended life span than those who received R. ginseng alone.

Chen F, Sun S, Kuhn DC, Lu Y, Gaydos LJ, Shi X, Demers LM. **Tetrandrine inhibits signal-induced NF-kappa B activation in rat alveolar macrophages.** Biochem Biophys Res Commun 1997;231(1):99-102.
Tetrandrine is a bisbenzylisoquinoline alkaloid isolated from a natural Chinese herbal medicine. While this alkaloid has been shown to exhibit antifibrotic and anti-inflammatory activities, its mechanism of action is unknown. The present study was designed to investigate the inhibitory effect of tetrandrine on NF-kappa B activation in the alveolar macrophage. Three different provocative stimuli were used to activate NF-kappa B in these cells. The results indicate that tetrandrine can inhibit the activation of NF-kappa B and NF-kappa B-dependent reporter gene expression by LPS, PMA, and silica in a dose-dependent manner. In contrast, at the doses used, tetrandrine did not interfere with Sp-1 DNA binding activity or Sp-1-dependent reporter gene expression in these cells. Western blot analysis suggests that the inhibitory effect of tetrandrine on NF-kappa B activation can be attributed to its ability to suppress signal-induced degradation of I kappa B alpha, a cytoplasmic inhibitor of the NF-kappa B transcription factor.

Chen T, Li J, Cao J, Xu Q, Komatsu K, Namba T. **A new flavanone isolated from rhizoma smilacis glabrae and the structural requirements of its derivatives for preventing immunological hepatocyte damage.** Planta Med 1999;65(1):56-9.
From the rhizome of Smilax glabra Roxb., a new flavanone was isolated and named as smitilbin (1), together with 6 known compounds, engeletin (2), astilbin (3), dihydroquercetin (4), eurryphin (5), resveratrol (6), and 5-O-caffeoylshikimic acid (7). These compounds were applied to the assay of liver nonparenchymal cells (NPC) against hepatocytes (HC) isolated from mice with an immunological liver injury. Against the NPC-caused elevation of ALT (alanine transminase) in culture supernatant from HC, the pretreatment of NPC with flavanoids (1-3) dose-dependently blocked the ALT release while 4, the aglycone of 3, did not. The chromone 5 showed a much stronger inhibition. Compound 6 also showed the activity. However, 1-7 did not show any suppression of NPC or CCl4-induced ALT release when they were used to pretreat HC. These results suggest that compounds 1-3, 5, and 6 could protect the hepatocyte damage from NPC through selectively producing the dysfunction of NPC with an essential requirement of rhamnose, and the chromone part in their structures may be critical for exhibiting the activity rather than through protecting the hepatocyte membranes.

Chen Xiaoliang, Gui Xiaoming, Xie Zhenjia. **[Influence of processing methods on alkaloid, toxicity and effect of Strychnos nux-vomica L].** Zhongguo Zhongyao Zazhi 1998;23(3):151-3,

191. (Chi)
BIOSIS COPYRIGHT: BIOL ABS. Determination has been made on the contents of strychnine, brucine and ephedrin in different processed products of Strychnos nux-vomica. The acute toxicity, analgesic and antiphlogistic actions of these products have also been detected. The result shows that the product processed with Ephedra sinica can reduce toxicity and promote 'curative effect. Among the different processing methods the preparation with Ephedra and Liqorice root and the preparation with Ephedra and alcohol appear better and thus useful in practical application.

Cheng KT, Tsay HS, Chen CF, Chou TW. **Determination of the components in a Chinese prescription, yu-ping-feng san, by RAPD analysis.** Planta Med 1998;64(6):563-5.
In this study, the RAPD (random amplified polymorphic DNA) technique was employed for the first time to determine the components in a Chinese herbal prescription. Forty decamer oligonucleotide primers were screened in the RAPD analysis to identify three Chinese medicines, the dried root of Astragalus membranaceus (Fisch.) Bge., the dried root of Ledebouriella seseloides Wolff, and the dried rhizome of Atractylodes macrocephala Koidz, in a Chinese prescription. Only primer OPP-10 simultaneously generated three distinct markers were each specific to one component. The marker with 200 bp is specific to Astragalus membranaceus; the 440 bp marker is specific to Atractylodes macrocephala; and the remaining marker with 500 bp was present in Ledebouriella seseloides. The presence of the three herbal medicines in the mixed sample, the Chinese prescription, was determined when the primer OPP-10 RAPD reaction was performed. The technique was proved to contribute to the identification of components in the Chinese medicinal preparations.

Cheng TJ, Wong RH, Lin YP, Hwang YH, Horng JJ, Wang JD. **Chinese herbal medicine, sibship, and blood lead in children.** Occup Environ Med 1998;55(8):573-6.
OBJECTIVES: Risk factors for increased blood lead concentration (BPb) has been investigated. However, the effect of sibship and Chinese herbal medicine on BPb has not been systematically studied. In this study BPb data from voluntary testing was used to determine if Chinese herbal medicine and sibship were associated with BPb. METHODS: 319 children aged 1-7 were tested for BPb. Meanwhile, parents were interviewed to obtain information including consumption of Chinese herbal medicine, living environment, lifestyle, and sibship of the children tested. RESULTS: The mean (SD) BPb of 319 preschool children was 4.4 (2.4) micrograms/dl. The consumption of Ba-baw-san (a Chinese herbal medicine) was significantly associated with increased BPb in children ($p = 0.038$). Further multivariate regression analysis of BPb in 50 pairs of siblings showed the factors of being brothers explained 75% of variation for BPb, and being sisters and brother-sister explained 51% and 41% of variation respectively. CONCLUSION: Chinese herbal medicine and children's play patterns within the family expressed in different types of sibship are the main determinants of low concentrations of BPb in preschool children of Taiwan.

Cheng TO. **Warfarin danshen interaction [letter].** Ann Thorac Surg 1999;67(3):894.

Chou CT, Chang SC. **The inhibitory effect of common traditional anti-rheumatic herb formulas on prostaglandin E and interleukin 2 in vitro: a comparative study with**

Tripterygium wilfordii. J Ethnopharmacol 1998;62(2):167-71.
To understand the clinical efficacy of traditional anti-rheumatic herbal medicines on acute and severe arthritis or immune diseases, four herbal formulas and one herb were tested in vitro to determine their effects on prostaglandin E2 (PGE2) and interleukin 2 (IL2). Peripheral blood mononuclear cells from healthy subjects were incubated with different concentrations of four herbal formulas including Shaur Yau Gan Tsao Tang (SYGTT), Shang Jong Shiah Tong Yong Tong Feng Wan (SJSTY), Shu Jin Lih An Saan (SJLAS), Ma Shing Yih Gan Tang (MSYGT) and one herb, Tripterygium wilfordii (T2) with and without mitogen stimulation. PGE2 and IL2 from culture supernatant were measured by enzyme immunoassay. The results showed that SYGTT, SJSTY, SJLAS at concentration of 100 microg and MSYGT at 500 microg/ml can significantly inhibit PGE2 release ($P < 0.05$) from mononuclear cells. However, T2 at 2 microg/ml expressed the same response. For the inhibition of IL2, the concentration of SYGTT, SJSTY and SJLAS must exceed 100 symbol microg/ml. MSYGT failed to inhibit IL2 at even concentrations of 500 microg/ml but T2 at a very low concentration (0.6 microg/ml) could strongly inhibit it. The findings suggest that the majority of traditional anti-rheumatic herbal formulas or herbs, except for T2, should not be used to treat acute and critical arthritis or immune diseases.

Chughtai SR, Ahmad MA, Naseem K, Mohmand AS. **Genotoxicity testing of some spices in diploid yeast.** Pakistan J Botany 1998;30(1):33-8.
BIOSIS COPYRIGHT: BIOL ABS. A study was conducted to assess the mutagenic and recombinogenic potential of 10 commonly consumed spices and condiments viz., bay leaves, black pepper, cardamom small, caraway, red chilies, cinnamon, coriander, fennel, garlic and curry powder in the diploid yeast Saccharomyces cerevisiae. Aqueous extracts of these spices were tested for the induction of mitotic gene conversion and reverse mutation in the diploid strain D7 of the yeast. All except cinnamon failed to induce detectable recombination and mutations in the growing cells of the yeast without exogenous metabolic activation. Treatments with an aqueous extracts of cinnamon significantly increased the rate of gene conversion and reverse mutation. Cinnamon caused cells death and inhibition of cell division. Ethyl methane sulphonate (EMS) used as a positive control exhibited recombinogenic and mutagenic effects.

Church D. **Alternative remedies [letter; comment].** N Z Med J 1998;111(1060):59.

Ciordia R. **Beware "St. John's Wort," potential herbal danger [letter].** J Clin Monit Comput 1998;14(3):215.

Clark SM, Wilkinson SM. **Phototoxic contact dermatitis from 5-methoxypsoralen in aromatherapy oil.** Contact Dermatitis 1998;38(5):289-90.
BIOSIS COPYRIGHT: BIOL ABS. RRM CASE STUDY HUMAN PATIENT ADULT FEMALE HUMAN PHOTOTOXIC CONTACT DERMATITIS TOXICITY 5-METHOXYPSORALEN AROMATHERAPY OIL HERBAL REMEDIES PRODUCT INFORMATION TOXICOLOGY DERMATOLOGY ALLERGY INTEGUMENTARY SYSTEM DISEASE.

Cockayne SE, Gawkrodger DJ. **Occupational contact dermatitis in an aromatherapist.** Contact Dermatitis 1997,37(6):306-7.
A case study of a 32 year old woman who worked as a holistic beauty therapist for 12 years was presented. At presentation she had a 9 month history of patchy eczema on her hands and body. Her condition improved when she was off work. Treatment had included topical corticosteroids and emollients. At work she performed aromatherapy massages and facials with essential oils. Her hobby was gardening and she always wore gloves during this activity. Positive patch test results were noted to nickel-sulfate (12503536), paratertiary-butylphenol-formaldehyde-resin, fragrance mix, lemon-grass-oil (8007021), lavender-absolute (8000280), cananga-oil (83863303), Bulgarian rose-oil (8007010), ylang-ylang (8006813), patchouli (8014093), clary-sage (8016635), her own pedicure foot lotion, and her own facial lotion. Her facial lotion contained hazel-nut-oil, beeswax, avocado-oil, carnuba, basil-oil, tonka-bean absolute, bitter-orange-oil, and chamomile oil. The pedicure foot lotion contained the essential oils of peppermint, black pepper, juniper, eucalyptus and rosemary. No common allergen was found in all of the compounds that gave a positive result. The authors note that patch testing with a perfume series and with the patient's own products was absolutely essential, where aromatherapy is suspected as a source of allergic contact dermatitis.

Combest WL, Nemecz G. **Herbal remedies in the pharmacy.** US Pharm 1997 Jul;22:50, 52, 55-6, 59.
IPA COPYRIGHT: ASHP An update on herbal remedies used as over-the-counter products in pharmacies is presented, including a discussion of the increase in the use of herbal remedies in the United States, Food and Drug Administration regulations regarding herbal remedies and phytomedicinals, a list of herbs considered unsafe and their potential side effects, quality control and standardization issues regarding herbal remedies, potential dangers of self-treatment with herbal remedies, and information for the pharmacist to prepare them to give advice on herbal remedies to patients.

Cosyns JP, Goebbels RM, Liberton V, Schmeiser HH, Bieler CA, Bernard AM. **Chinese herbs nephropathy-associated slimming regimen induces tumours in the forestomach but no interstitial nephropathy in rats.** Arch Toxicol 1998;72(11):738-43.
Chinese herbs nephropathy (CHN), a rapidly progressive interstitial fibrosis of the kidney, has been described in approximately 100 young Belgian women who had followed a slimming regimen containing some Chinese herbs. In 4 patients multifocal transitional cell carcinomas (TCC) were observed. Aristolochic acid (AA), suspected as the causal factor of CHN, is a well known carcinogen but its ability to induce fibrosis has never been demonstrated. The objective of this study was to evaluate the latter using doses of AA, durations of intoxication and delays of sacrifice known to yield tumours in rats. We also tested the hypothesis that a possible fibrogenic role of AA was enhanced by the other components of the slimming regimen. Male and female rats were treated orally with 10 mg isolated AA/kg per day for 5 days/week, or with approximately 0.15 mg AA/ kg per day 5 days/week contained in the herbal powder together with the other components prescribed in the slimming pills for 3 months. The animals were killed respectively 3 and 11 months later. At sacrifice, animals in both groups had developed the expected tumours but not fibrosis of the renal interstitium. Whether the fibrotic response observed in man is due to species and/or strain related differences in the response to AA or to

other factors, remains to be determined. Interestingly, despite the addition of fenfluramine and diethylpropion, two drugs incriminated in the development of valvular heart disease, no cardiac abnormalities were observed.

Cosyns JP, Jadoul M, Squifflet JP, Wese FX, Van Ypersele De Strihou C. **Urothelial lesions in Chinese-herb nephropathy [see comments].** Am J Kidney Dis 1999;33(6):1011-7.
Rapidly progressive renal fibrosis after a slimming regimen including Chinese herbs containing aristolochic acid (AA) has been identified as Chinese-herb nephropathy (CHN). We reported urothelial atypia in three patients with CHN, with the subsequent development in one patient of overt transitional cell carcinoma (TCC). Therefore, it was decided to remove the native kidneys, as well as the ureters, in all patients with CHN. Nineteen kidneys and ureters removed during and/or after renal transplantation from 10 patients were studied to assess critically urothelial lesions and to characterize the cellular expression of p53, a tumor-suppressor gene overexpressed in several types of malignancies. Multifocal high-grade flat TCC in situ (carcinoma in situ; CiS) was observed, mainly in the upper urinary tract, in four patients, a prevalence of 40%. In one of those patients, a superficially invasive flat TCC of the right upper ureter, as well as two additional foci of noninvasive papillary TCC, were found in the right pelvis and left lower ureter, respectively. This patient also presented recurrent noninvasive papillary TCC of the bladder. Furthermore, in all cases, multifocal, overall moderate atypia was found in the medullary collecting ducts, pelvis, and ureter. All CiS and papillary TCC, as well as urothelial atypia, overexpressed p53. These results show that the intake of Chinese herbs containing AA has a dramatic carcinogenic effect. Carcinogenesis is associated with the overexpression of p53, which suggests a role for a p53 gene mutation. The relationship of this mutation with the reported presence of AA DNA adducts in the kidney remains to be explored.

Crone CC, Wise TN. **Survey of alternative medicine use among organ transplant patients.** J Transpl Coord 1997;7(3):123-30.
Herbal medicine and health food supplements have become increasingly popular. However, many of these pharmacologically active compounds remain poorly understood. Patients with chronic and life-threatening conditions often use alternative therapies while receiving conventional medical care, and his population is at increased risk for complications and adverse drug interactions due to poor health and complex drug regimens. Patients awaiting or who had received solid organ transplants were surveyed about their use of herbal medicines and health food supplements. Twenty percent of respondents acknowledged experience with these products, which they used to prolong the function of a failing organ or to obtain relief from fatigue and insomnia. Transplant staff often were unaware of their patients' use of these treatments, despite patients' claims to the contrary. The potential for unexpected drug interactions, toxicity, and other adverse reactions resulting from the use of herbal medicines or supplements must be recognized and identified by transplant teams.

Cutler SJ, Cutler HG. **Natural central nervous system agents.** US Pharm 1997 Nov;22:87-8, 90, 93-4.

De Boer D, Egberts T, Maes RA. **Para-methylthioamphetamine, a new amphetamine designer drug of abuse.** Pharm World Sci 1999;21(1):47-8.

A case study is described of a patient who was intoxicated after the intake of so-called herbal stimulants. A visit to a physician after the intoxication prompted to this investigation and the case was examined for its direct cause. An interview with the patient revealed that the source of the herbal stimulants was a so-called 'S-5 tablet'. Information provided on the packings of the tablet only indicated the presence of natural alkaloids and vitamins. Toxicological analysis however proved that the 'S-5 tablet' contained para-methylthioamphetamine (MTA), mainly. MTA is a relative unknown amphetamine designer drug, which has only been studied as a model compound in some structure-activity relationship studies. The fact that MTA appeared in tablets was therefore completely unexpected. Not only the potential abuse of this new amphetamine designer drug is a serious matter of concern, but also the misleading information provided with the tablet.

De Broe ME. **On a nephrotoxic and carcinogenic slimming regimen [editorial; comment].** Am J Kidney Dis 1999;33(6):1171-3.

De Broe ME, et al . **Clinical nephrotoxins: renal injury from drugs and chemicals.** Dordrecht(Netherlands), Norwell(MA): Kluwer Academic Publishers; 1998. 481 P.
BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK ANIMAL HUMAN ANIMAL MODEL NEPHROTOXICITY ENVIRONMENTAL TOXINS TOXIN PHARMACEUTICAL AGENTS XENOBIOTICS RENAL DYSFUNCTION RENAL INJURY KIDNEY ANTI-INFECTIOUS AGENTS ANALGESICS IMMUNOSUPPRESSIVE DRUGS HERBAL REMEDIES ADVERSE RENAL EFFECTS URINARY SYSTEM CELL CULTURE MODEL TOXICOLOGY UROLOGIC DISEASE EXCRETORY SYSTEM.

De Soriano G, Chase D. **Safety of herbal remedies [letter].** J R Soc Med 1998;91(10):561.

Deng JF, Lin TJ, Kao WF, Chen SS. **The difficulty in handling poisonings associated with Chinese traditional medicine: a poison control center experience for 1991-1993.** Vet Hum Toxicol 1997;39(2):106-14.
The purpose of this prospective case series was to outline the characteristics of Chinese traditional medicine poisonings and develop essential information for poison prevention and management. All phone inquiries made to the Poison Center related to Chinese traditional medicines from January 1, 1991 to December 31, 1993 were included. Standardized questionnaires were used to capture relevant information. Among the 318 phone inquiries about Chinese traditional medicines, 273 cases were classified as poisonings; and 22 mortalities occurred (6.9%). All of the poisonings occurred because of suicide attempts, accidents, or erroneous or improper use or processing. In our study, 47% of the potential toxic effects of Chinese traditional medicines were either unknown or could not be found in the literature. There existed undefinable uncertainty in attributing the clinical effects to the exposures to Chinese traditional medicines. We recommend that the strategy in handling Chinese traditional medicine poisonings to decrease mortality should be comprised of confirmation of the generic name of the substances and the specific part of the plant used, awareness of improper processing methods, maintenance of records on a broad review of systems and laboratory data, identification of active principles and potential interactions among the individual active agents; verification of histopathologic effects of the toxins; development of information on toxicodynamics and

toxicokinetics; intensive supportive care for poisoned patients, and investigation of potential antidotes. There are several regulatory options available to health authorities to control the unrestricted use of these potentially toxic medicines and to help safeguard the public.

Dewitt MS, Swain R, Gibson LB Jr. **The dangers of jimson weed and its abuse by teenagers in the Kanawha Valley of West Virginia.** W V Med J 1997;93(4):182-5.
Jimson weed (Datura stramonium, a member of the Belladonna alkyloid family) is a plant growing naturally in West Virginia and has been used as a home remedy since colonial times. Due to its easy availability and strong anticholinergic properties, teens are using Jimson weed as a drug. Plant parts can be brewed as a tea or chewed, and seed pods, commonly known as "pods" or "thorn apples," can be eaten. Side effects from ingesting jimson weed include tachycardia, dry mouth, dilated pupils, blurred vision, ballucinations, confusion, combative behavior, and difficulty urinating. Severe toxicity has been associated with coma and seizures, although death is rare. Treatment consists of activated charcoal and gastric lavage. Esmolol or other beta-blocker may be indicated to reduce severe sinus tachycardia. Seizures, severe hypertension, severe hallucinations, and life-threatening arrhythmias are indicators for the use of the anticholinesterase inhibitor, Physostigmine. This article reviews the cases of nine teenagers who were treated in hospitals in the Kanawha Valley after ingesting jimson weed. We hope this article will help alert primary care physicians about the abuse of jimson weed and inform health officials about the need to educate teens about the dangers of this plant.

Dipaola RS, Zhang H, Lambert GH, Meeker R, Licitra E, Rafi MM, Zhu BT, Spaulding H, Goodin S, Toledano MB, et al. **Clinical and biologic activity of an estrogenic herbal combination (PC-SPES) in prostate cancer [see comments].** N Engl J Med 1998;339(12):785-91.
BACKGROUND: Herbal mixtures are popular alternatives to demonstrated therapies. PC-SPES, a commercially available combination of eight herbs, is used as a nonestrogenic treatment for cancer of the prostate. Since other herbal medicines have estrogenic effects in vitro, we tested the estrogenic activity of PC-SPES in yeast and mice and in men with prostate cancer. METHODS: We measured the estrogenic activity of PC-SPES with transcriptional-activation assays in yeast and a biologic assay in mice. We assessed the clinical activity of PC-SPES in eight patients with hormone-sensitive prostate cancer by measuring serum prostate-specific antigen and testosterone concentrations during and after treatment. RESULTS: In complementary yeast assays, a 1:200 dilution of an ethanol extract of PC-SPES had estrogenic activity similar to that of 1 nM estradiol, and in ovariectomized CD-1 mice, the herbal mixture increased uterine weights substantially. In six of six men with prostate cancer, PC-SPES decreased serum testosterone concentrations (P

Drew AK, Myers SP. **Safety issues in herbal medicine: implications for the health professions [see comments].** Med J Aust 1997;166(10):538-41.
The use of herbal medicines in Australia is widespread. A number of factors make assessment of adverse effects associated with these products more complex than for pharmaceuticals. Problems have resulted from contamination with heavy metals and adulteration with prescription drugs in overseas herbal products. A classification is proposed for adverse effects associated with herbal medicines, and medical practitioners are encouraged to include use of these preparations in a

patient's drug history and in reports of suspected adverse drug reactions. It may be necessary to develop a separate database to promote adverse drug reaction reporting for herbal medicine and the wider field of complementary and alternative medicine.

Emmanuel NP, Jones C, Lydiard RB. **Use of herbal products and symptoms of bipolar disorder [letter].** Am J Psychiatry 1998;155(11):1627.

Ernst E. **Harmless herbs? A review of the recent literature.** Am J Med 1998;104(2):170-8. Herbal medicines have become a popular form of therapy. They are often perceived as being natural and therefore harmless. This article reviews the recent literature on the adverse effects of herbal remedies. Examples of allergic reactions, toxic reactions, adverse effects related to an herb's desired pharmacological actions, possible mutagenic effects, drug interactions, drug contamination, and mistaken plant identities are provided. Because of underreporting, our present knowledge may well be just the "tip of the iceberg." Little is known about the relative safety of herbal remedies compared to synthetic drug treatments, although for some herbal remedies, the risks may be less than for conventional drugs.

Ernst E, Rand JI, Barnes J, Stevinson C. **Adverse effects profile of the herbal antidepressant St. John's wort (Hypericum perforatum L.).** Eur J Clin Pharmacol 1998;54(8):589-94. This paper provides a systematic review of adverse drug reactions (ADRs) associated with the use of extracts of the herb St. John's wort (Hypericum perfbratum L.) for the treatment of mild to moderate depression. METHODS: Searches of four computerized literature databases were performed for records of (ADRs). Manufacturers of hypericum products, the international drug monitoring centre of the World Health Organization (WHO) and the national drug safety monitoring bodies of Germany and the United Kingdom were also contacted for information. RESULTS: Information on (ADRs) originates from case reports, clinical trials, post-marketing surveillance and drug monitoring studies. Collectively, the data suggest that hypericum is well tolerated, with an incidence of adverse reactions similar to that of placebo. The most common adverse effects are gastrointestinal symptoms, dizziness/confusion and tiredness/sedation. A potential serious adverse effect is photosensitivity, but this appears to occur extremely rarely. CONCLUSIONS: Hypericum has an encouraging safety profile. However, as most of the current data originate from short-term investigations, more long-term studies are desirable.

Farrell GC. **Drug-induced hepatic injury.** J Gastroenterol Hepatol 1997;12(9-10):242-50. Drugs and other chemical toxins account for less than 5% of cases of jaundice or acute hepatitis and fewer cases of chronic liver disease, but they are an important cause of more severe types of hepatic injury. Drug reactions produce an array of hepatic lesions that mimic all known hepatobiliary diseases; this poses a diagnostic challenge for physicians and pathologists. Diagnosis of drug-induced hepatic injury is circumstantial, with positive rechallenge being the only factor that unequivocally implicates a particular agent. Nonetheless, other aspects of the temporal relationship between drug ingestion and adverse reaction, exclusion of other diseases, the presence of extrahepatic features of drug hypersensitivity and some findings on liver biopsy can lend support to the diagnosis. Some of these issues will be explored in this review by considering contemporary paradigms of drug-induced hepatic injury. Factors that predispose to dose-dependent hepatic injury will be considered in relation to acetaminophen, an example of

acute hepatotoxicity, and methotrexate, an agent that can produce hepatic fibrosis. Flucloxacillin will be discussed as an example of drug-induced cholestatic hepatitis often associated with prolonged cholestasis and the vanishing bile duct syndrome. Minocycline and diclofenac will be mentioned as two drugs for which drug hepatitis is an exceedingly rare complication. Finally, the evidence that Chinese herbal medicines can be hepatotoxic will be reviewed.

Fau D, Lekehal M, Farrell G, Moreau A, Moulis C, Feldmann G, Haouzi D, Pessayre D. **Diterpenoids from germander, an herbal medicine, induce apoptosis in isolated rat hepatocytes [see comments].** Gastroenterology 1997;113(4):1334-46.
BACKGROUND & AIMS: Germander was withdrawn from the market after its use for weight control caused an epidemic of hepatitis. Its toxicity was shown to be caused by diterpenoids and their cytochrome P4503A-mediated metabolic activation into electrophilic metabolites that deplete cellular thiols. The aim of the present study was to determine the mechanisms of cell death. METHODS: Isolated rat hepatocytes were incubated for 2 hours with germander diterpenoids (100 micrograms/mL). RESULTS: Diterpenoids decreased cell glutathione, increased cytosolic [Ca2+], activated Ca(2+)-dependent tissue transglutaminase forming a cross-linked protein scaffold, and caused internucleosomal DNA fragmentation and the ultrastructural features of apoptosis. Cell death was prevented by decreasing metabolic activation (with troleandomycin), preventing depletion of glutathione (with cystine), blocking activation of Ca(2+)-modulated enzymes (with calmidazolium), or inhibiting internucleosomal DNA fragmentation (with aurintricarboxylic acid). Apoptosis was increased and diterpenoids caused overexpression of p53 and interleukin 1 beta-converting enzyme in rats treated with dexamethasone (cytochrome P4503A inducer). Apoptosis was also increased by a diet deficient in sulfur amino acids. CONCLUSIONS: The germander furano diterpenoids cause apoptosis within 2 hours in isolated rat hepatocytes. Electrophilic metabolites may stimulate apoptosis by decreasing thiols, increasing [Ca2+], and activating Ca(2+)-dependent transglutaminase and endonucleases.

Ferguson JE, Chalmers RJ, Rowlands DJ. **Reversible dilated cardiomyopathy following treatment of atopic eczema with Chinese herbal medicine.** Br J Dermatol 1997;136(4):592-3.
Chinese herbal medicines are increasingly being used as an alternative treatment for chronic skin disease. Most patients and many doctors remain insufficiently aware of their potential toxicity. We report a patient with eczema who developed a severe cardiomyopathy following a 2-week course of Chinese herbal medicine. The connection between the two conditions was not made until 2 weeks after presentation when the patient was specifically asked if she had ingested any unusual substances. The belief that herbs, as natural products available without prescription, are harmless, is commonplace and patients may not consider them worthy of mention during a standard medical history.

Fernandez L, Duque S, Sanchez I, Quinones D, Rodriguez F, Garcia-Abujeta JL. **Allergic contact dermatitis from rosemary (Rosmarinus officinalis L.).** Contact Dermatitis 1997;37(5):248-9.
BIOSIS COPYRIGHT: BIOL ABS. RRM CASE STUDY NOTE ROSMARINUS-OFFICINALIS HUMAN PLANT MALE HUMAN MIDDLE AGE DERMATOLOGY HEALTH PHARMACOGNOSY ROSEMARY LEAF PLASTER ANTIINFLAMMATORY

HERBAL REMEDY ALLERGIC CONTACT DERMATITIS ALLERGY INTEGUMENTARY SYSTEM DISEASE IMMUNE SYSTEM DISEASE.

Figueiredo MR, Kaplan MA. **Pyrrolizidine alkaloids: a word of caution.** Cienc Cultur 1997;49(5-6):331-8.
BIOSIS COPYRIGHT: BIOL ABS. Most plants bearing pyrrolizidine alkaloids (PAs) are toxic to men and animals. These natural products are recognized to be hepatotoxic, pneumotoxic, carcinogenic and mutagenic. Thus, the presence of toxic pyrrolizidine alkaloids in certain medicinal plants entails a serious health risk. Moreover, people are exposed to undetermined toxicity hazards of pyrrolizidine alkaloid-containing plants due to the consumption of milk and meat from chronically PA-poisoned animals and honey from wild bees. Symphytum officinale (comfrey) has been used freely as tea, topical cream, salad and beverage. This is a clear and actual example of how lack of knowledge about chemistry and toxicology of a plant made easy its spreading in the consumer society as beneficial and safe.

Fox C. **Technically speaking.** Cosmet Toiletries 1998 Sep;113:29-32.
IPA COPYRIGHT: ASHP An overview of current discoveries related to cosmetic products is presented, including a discussion of the role of essential fatty acids in maintaining skin function, herbal irritations related to creams prescribed by Chinese herbalists, the incidence of lanolin allergies among high-risk populations, moisturizers, silicone elastomers, and conditioners for hair care, and new emulsions and antiperspirant products.

Frasca T, Brett AS, Yoo SD. **Mandrake toxicity. A case of mistaken identity.** Arch Intern Med 1997;157(17):2007-9.
A 31-year-old man ingested an unknown amount of mandrake plant purchased at a local health food store and came to the emergency department with severe nausea and vomiting. He was hospitalized overnight but recovered uneventfully without obvious adverse systemic effects. This plant was almost certainly Podophyllum peltatum based on chromatographic identification of podophyllotoxin in a sample. However, the patient had mistakenly believed he was taking the anticholinergic and hallucinatory plant Mandragora officinarum, which is also known as mandrake. Other users of herbal substances and authors of the medical literature have also confused these 2 versions of mandrake. Given the growing popularity of alternative therapies, physicians should understand the distinction between these substances and should be aware of the medical effects of other commonly used herbal remedies.

Friede M, Hasenfuss I, Wustenberg P. **[Traffic- and work-safety under the effect of St. Johns Wort].** Fortschr Med 1998;116(34):44-5. (Ger)

Friese J, Gleitz J, Gutser UT, Heubach JF, Matthiesen T, Wilffert B, Selve N. **Aconitum sp. alkaloids: the modulation of voltage-dependent Na+ channels, toxicity and antinociceptive properties.** Eur J Pharmacol 1997;337(2-3):165-74.
Alkaloids from Aconitum sp., used as analgesics in traditional Chinese medicine, were investigated to elucidate their antinociceptive and toxic properties considering: (1) binding to Na+ channel epitope site 2, (2) alterations in synaptosomal Na+ and Ca2+ concentration ([Na+]i, [Ca2+]i), (3) arrhythmogenic action of isolated atria, (4) antinociceptive and (5) acute toxic

action in mice. The study revealed a high affinity group (Ki 1 microM) and a low affinity group (Ki 10 microM) of alkaloids binding to site 2. The compounds of the high affinity group induce an increase in synaptosomal [Na+]i and [Ca2+]i (EC50 3 microM), are antinociceptive (ED50, 25 microg/kg), provoke tachyarrhythmia and are highly toxic (LD50 70 microg/kg), whereas low affinity alkaloids reduce [Ca2+]i, induce bradycardia and are less antinociceptive (ED50 20 mg/kg) and less toxic (LD50 30 mg/kg). These results suggest that the alkaloids can be grouped in Na+ channel activating and blocking compounds, but none of the alkaloids seem to be suitable as analgesics because of the low LD50/ED50 values.

Garcia-Bravo B, Bernal AP, Garcia-Hernandez MJ, Camacho F. **Occupational contact dermatitis from anethole in food handlers.**Contact Dermatitis 1997;37(1):38.
Two case reports of food handlers developing occupational contact dermatitis from anethole (104461) were presented. In the first case, a 39 year old woman who cooked Seville cakes had exhibited a hand dermatitis that was resistant to treatment for 20 years. Upon entering the workplace, the lesions spread up the forearms and rhinitis and blepharitis developed. Standard series patch tests were conducted. The patient reacted positively to anise-oil (8007703) and anethole, the main ingredient in anise-oil, at 2 and 4 days. In the second case, a 38 year old woman who worked in the same cake factory had severe dermatitis on her hands, forearms, scalp, and face. Upon entering the workplace, rhinitis and blepharitis developed. Standard series patch tests were performed. The patient exhibited positive reactions to Kathon-CG (55965849), anise-oil, anethole, and Roman-chamomile at 2 and 4 days. The authors conclude that these cases may be the first reports of occupational contact dermatitis from anethole in food handlers.

Garges HP, Varia I, Doraiswamy PM. **Cardiac complications and delirium associated with valerian root withdrawal [letter].** JAMA 1998;280(18):1566-7.

Gianni L, Dreitlein WB. **Some popular OTC herbals can interact with anticoagulant therapy.** US Pharm 1998 May 23;23:80, 83-4, 86.
IPA COPYRIGHT: ASHP The interaction of Ginkgo biloba, Tanacetum parthenium (feverfew), Allium sativum (garlic), Zingiber officinale (ginger), and vitamin E with anticoagulant therapy and a resulting increase in the risk of bleeding in some patients are discussed.

Giavina-Bianchi PF Jr, Castro FF, Machado ML, Duarte AJ. **Occupational respiratory allergic disease induced by Passiflora alata and Rhamnus purshiana.** Ann Allergy Asthma Immunol 1997;79(5):449-54.
BACKGROUND: There has been an increase in the incidence of occupational asthma along with better understanding of its pathophysiologic mechanisms and etiologic factors. There are no reports of patients with asthma and rhinitis to Passiflora alata (passion flower) and Rhamnus purshiana (cascara sagrada). METHODS: We describe two substances of plant origin as causal agents of occupational allergic respiratory diseases in a patient who worked in a pharmacy devoted to the manual preparation of products. RESULTS: Skin testing and Western blot confirmed the sensitization of the patient to these plant extracts in vivo and in vitro, respectively. Bronchial challenge confirmed the cause-effect relationship between the allergen exposure and the diseases. CONCLUSIONS: We conclude that Passiflora and cascara sagrada are two new etiologic agents of IgE-mediated occupational asthma and rhinitis. The present study also serves

to alert physicians to the risks associated with work in pharmacies devoted to manual preparation of plant extracts, emphasizing the importance of the use of protective measures in these environments.

Goday Bujan JJ, Oleaga Morante JM, Yanguas Bayona I, Gonzalez Guemes M, Soloeta Arechavala R. **Allergic contact dermatitis from krameria triandra extract.** Contact Dermatitis 1998;38(2):120-1.

Goh CL. **The need for epidemiological studies [editorial; comment].** Am J Contact Dermat 1997;8(3):135-6.

Gordon JB. **SSRIs and St.John's Wort: possible toxicity? [letter].** Am Fam Physician 1998;57(5):950,953.

Greenberger P. **News from the Society for the Advancement of Women's Health Research. Herbal medicines: are supplements safe? [news].** J Womens Health 1998;7(9):1077-9.

Gulick RM, Mcauliffe V, Holden-Wiltse J, Crumpacker C, Liebes L, Stein DS, Meehan P, Hussey S, Forcht J, Valentine FT. **Phase I studies of hypericin, the active compound in St. John's Wort, as an antiretroviral agent in HIV-infected adults. AIDS Clinical Trials Group Protocols 150 and 258.** Ann Intern Med 1999;130(6):510-4.
BACKGROUND: Hypericin, the active compound in St. John's Wort, has antiretroviral activity in vitro. Many HIV-infected persons use St. John's wort. OBJECTIVE: To evaluate the safety and antiretroviral activity of hypericin in HIV-infected patients. DESIGN: Phase I study. SETTING: Four clinical research units. PATIENTS: 30 HIV-infected patients with CD4 counts less than 350 cells/mm3. INTERVENTION: Intravenous hypericin, 0.25 or 0.5 mg/kg of body weight twice weekly or 0.25 mg/kg three times weekly, or oral hypericin, 0.5 mg/kg daily. MEASUREMENTS: Safety was assessed at weekly visits. Antiretroviral activity was assessed by changes in HIV p24 antigen level, HIV titer, HIV RNA copies, and CD4 cell counts. RESULTS: Of the 30 patients who were enrolled, 16 discontinued treatment early because of toxic effects. Severe cutaneous phototoxicity was observed in 11 of 23 (48% [95% CI, 27% to 69%]) evaluable patients, and dose escalation could not be completed. Virologic markers and CD4 cell count did not significantly change. CONCLUSIONS: Hypericin caused significant phototoxicity and had no antiretroviral activity in the limited number of patients studied.

Gurley BJ, Gardner SF, White LM, Wang PL. **Ephedrine pharmacokinetics after the ingestion of nutritional supplements containing Ephedra sinica (ma huang).** Ther Drug Monit 1998;20(4):439-45.
Nutritional supplements containing Ephedra sinica (ma huang), a botanical source of ephedrine alkaloids, have been linked to several episodes of ephedrine toxicity and at least 17 deaths, yet these products remain unregulated. Ten subjects were enrolled in a randomized, crossover study aimed at characterizing the pharmacokinetics of ephedrine after the ingestion of three commercially available ma huang products compared with a 25-mg ephedrine capsule. Pharmacokinetic parameters for botanical ephedrine were similar to those for synthetic ephedrine hydrochloride. Gender-based comparisons of Vss/F and CL/F revealed higher values for women

than for men (Vss/F, 3.49 +/- 1.04 vs 2.98 +/- 0.73 l/kg; CL/F, 0.48 +/- 0.11 vs 0.37 +/- 0.11 l/hour x kg). The current study suggests that the increased incidence of ma huang toxicity does not stem from differences in the absorption of botanical ephedrine compared with synthetic ephedrine; rather, it results from accidental overdose often prompted by exaggerated off-label claims and a belief that "natural" medicinal agents are inherently safe.

Hagemann TM. **Gastrointestinal medications and breastfeeding.** J Hum Lact 1998;14(3):259-62.
Medications used to treat gastrointestinal symptoms are increasingly being used as more have been gained nonprescription status. Most of the gastrointestinal medications, such as laxatives, antacids, and antidiarrheal agents, are used short term. Women who breastfeed should be aware of the risks of taking any medications, whether prescription or nonprescription. There is little information describing transfer into breast milk for many of these products. Cimetidine, atropine, cascara, cisapride, loperamide, magnesium sulfate, and senna are the only products identified by the AAP as compatible with breast feeding. Metoclopramide is listed by the AAP as a drug whose effect on nursing infants is unknown but may be of potential concern, although studies published to date have not reported any adverse effects. The safest laxatives and antidiarrheals are those that are not absorbed and should be considered first-line therapy for conditions of constipation or loose stools. Famotidine and nizatidine are excreted into breast milk to a lesser extent than cimetidine or ranitidine and may be the preferred histamine antagonists. Despite the limited data on the use of cisapride in nursing women, it is considered safe by the AAP and may be preferred over metoclopramide for first-line prescription treatment of heartburn. Although most of these agents appear safe in the nursing infant, caretakers should be aware of the potential adverse reactions that may occur in infants whose mothers require these products.

Hamid S, Rojter S, Vierling J. **Protracted cholestatic hepatitis after the use of prostata [letter].** Ann Intern Med 1997;127(2):169-70.

Haraguchi M, Calore EE, Dagli ML, Cavaliere MJ, Calore NM, Weg R, Raspantini PC, Gorniak SL. **Muscle atrophy induced in broiler chicks by parts of Senna occidentalis seeds.** Vet Res Commun 1998;22(4):265-71.
Senna occidentalis (formerly Cassia occidentalis) is a common contaminant of agricultural commodities. It is toxic to cattle and poultry, reportedly being responsible for skeletal myodegeneration in these animals. All parts of the plant present toxicity, but the seeds are the most toxic. The toxin(s) responsible for the myodegeneration have not been definitively identified, nor is it known which part of the seeds is most toxic. Intoxication by this plant leads to weight loss with considerable economic repercussions. The effects of the whole seed and of parts of S. occidentalis seeds (1% in commercial feed) were compared on the pectoralis major muscle of broiler chicks intoxicated from birth until 22 days of life. There were severe clinical signals and reduced body weight in birds that received the external tegment of the seed, whereas no adverse effects were observed in birds that received the whole seed or other parts of the seed. Histological and morphometric studies showed an intense muscle fibre atrophy (both type 1 and type 2 fibres were affected) in the group that received 1% external tegment. This study may be the first step to identifying the substance(s) involved in this pathological process.

Haraguchi M, Gorniak SL, Calore EE, Cavaliere MJ, Raspantini PC, Calore NM, Dagli ML. **Muscle degeneration in chicks caused by Senna occidentalis seeds.** Avian Pathol 1998;27(4):346-51.
BIOSIS COPYRIGHT: BIOL ABS. Acute intoxication with Senna occidentalis seeds was studied in chicks. Seven-day-old chicks were fed ground dried seeds of this plant mixed with regular chicken ration at a concentration of 4% by weight for 15 days. Feed intake and body weight were markedly affected and a high level of lethality was observed. Necropsy examination of chicks from the experimental group revealed paleness and atrophy of thoracic muscles. Degenerative and necrotic fibres were observed in skeletal muscle by histological examination. Muscle histochemistry showed accumulation of lipids and numerous acid phosphatase-positive muscle fibres. Electron microscopy revealed atrophic muscle fibres, lipid storage, dilatation of the sarcoplasmic reticulum and abnormal mitochondria.

Hasegawa S, Nakayama K, Iwakiri K, An E, Gomi S, Dan K, Katsumata M, Minami M, Wakabayashi I. **Herbal medicine-associated lead intoxication.** Intern Med 1997;36(1):56-8.
A female patient visited our hospital with abdominal pain and anemia. Examination for a gastrointestinal disease gave no diagnostic information. Laboratory studies of the parameters of heme biosynthesis revealed an enzymatic inhibition by lead. The diagnosis of lead poisoning was confirmed by detection of an elevated blood lead level. Excessive lead ingestion was thought to be caused by herbal medicines and/or by an earthen teapot.

Hata M, Sasaki E, Ota M, Fujimoto K, Yajima J, Shichida T, Honda M. **Allergic contact dermatitis from curcumin (turmeric).** Contact Dermatitis 1997;36(2):107-8.

Heki U, Fujimura M, Ogawa H, Matsuda T, Kitagawa M. **Pneumonitis caused by saikokeisikankyou-tou, an herbal drug.** Intern Med 1997;36(3):214-7.
A 57-year-old man was admitted to our hospital because of dyspnea and abnormal shadow on chest roentgenogram. He had received two herbal drugs: Saikokeisikankyou-tou (SKT) for one month and Licium Halimifolium Mil (LHM) for two weeks. After admission, all medication was stopped and his symptoms were gradually diminished. Transbronchial lung biopsy specimens showed interstitial pneumonia. Lymphocyte stimulation test, skin test and challenge test were positive to these herbal drugs. We diagnosed him as drug-induced pneumonitis. This is the first report on pneumonitis caused by Saikokeisikankyou-tou diagnosed by lymphocyte stimulation test, skin test and challenge test.

Higenbottam TW. **Bronchiolitis obliterans following the ingestion of an Asian shrub leaf.** Thorax 1997;52(Suppl 3):68-72.

Hilepo JN, Bellucci AG, Mossey RT. **Acute renal failure caused by 'cat's claw' herbal remedy in a patient with systemic lupus erythematosus [letter].** Nephron 1997;77(3):361.

Hofman M, Diaz JE, Martella C. **Oil of wintergreen overdose [letter].** Ann Emerg Med 1998;31(6):793-4.

Holland EG, Degruy FV. **Drug-induced disorders [see comments].** Am Fam Physician 1997;56(7):1781-8, 1791-2.
Recent estimates suggest that each year more than 1 million patients are injured while in the hospital and approximately 180,000 die because of these injuries. Furthermore, drug-related morbidity and mortality are common and are estimated to cost more than $136 billion a year. The most common type of drug-induced disorder is dose-dependent and predictable. Many adverse drug events occur as a result of drug-drug, drug-disease or drug-food interactions and, therefore, are preventable. Clinicians' awareness of the agents that commonly cause drug-induced disorders and recognition of compromised organ function can significantly decrease the likelihood that an adverse event will occur. Patient assessment should include a thorough medication history, including an analysis of all prescribed and over-the-counter medications, vitamins, herbs and "health-food" products to identify drug-induced problems and potentially reversible conditions. An increased awareness among clinicians of drug-induced disorders should maximize their recognition and minimize their incidence.

Hsu HY, Lin CC, Chen JY, Yang JJ, Zhang R. **Toxic effects of Erycibe obtusifolia, a Chinese medicinal herb, in mice.** J Ethnopharmacol 1998;62(2):101-5.
Extract of stem of Erycibe obtusifolia (EO) at doses of 10, 20 and 30 mg/kg was experimentally tested through oral and intraperitoneal administration. Toxic effects of EO were assessed through functional changes of the liver and kidneys. Mice died immediately following the i.p. injection at the dose of 10 mg/kg. However, no death occurred after the oral administration at the dose of 10, 20 or 30 mg/kg under close observations for at least 2 weeks. Changes of several functional parameters in both the liver and kidney appeared simultaneously after the oral administration. Although the higher dose increased the levels of serum glutamate-oxalate-transaminase (sGOT), serum glutamate-pyruvate-transaminase (sGPT), and blood urea nitrogen (BUN), and decreased the levels of hematocrit at 6 h after the treatment, no distinct dose-dependent relationship existed between the administered doses and the changes in functional parameters observed.

Hullar TE, Sapers BL, Ridker PM, Jenkins RL, Huth TS, Farraye FA. **Herbal toxicity and fatal hepatic failure [letter].** Am J Med 1999;106(2):267-8.

Hung OL, Shih RD, Chiang WK, Nelson LS, Hoffman RS, Goldfrank LR. **Herbal preparation use among urban emergency department patients.** Acad Emerg Med 1997;4(3):209-13.
OBJECTIVE: To determine the prevalence of herbal preparation use among patients presenting to an urban teaching hospital ED. METHODS: A prospective anonymous survey on herbal preparation use was performed. Consecutive, acutely ill or injured adult (> or = 18 years old) ED patients were offered the survey over a 1-month period. The survey also asked for information related to patient age, ethnicity, gender, employment, education, cigarette smoking history, ethanol consumption, use of illicit drugs, chief complaint, and HIV status. RESULTS: Of 2,473 eligible subjects, 623 (25%) participated. The overall reported prevalence of herbal preparation use among the participants was 21.7%. Women were more likely to use herbal preparations than men (28.5% vs 17.2%, p = 0.013). Prevalence rates in different ethnic populations were: whites, 18.2%; Hispanics, 13.9%; blacks, 26.4%; and Asians, 36.8%. Asians had a significantly higher use rate than the other ethnic groups (p = 0.039). Neither HIV positivity, educational level, employment status, nor age was significantly associated with herbal preparation use. The most

commonly reported herbal preparations were goldenseal tea, garlic, and ginger. Several of the herbal preparations reported as used by patients in this study have been associated with severe systemic toxicity in the medical literature. CONCLUSION: Although the survey response rate was low, the prevalence of herbal preparation use among acutely ill or injured patients presenting to this urban ED remains significant. A directed history toward specific herbal preparation use may provide relevant pharmacologic information and uncover cases of herbal-preparation-induced toxicity.

Izzat MB, Yim AP, El-Zufari MH. **A taste of Chinese medicine!** Ann Thorac Surg 1998;66(3):941-2.
We report a case of profound anticoagulation caused by interaction between warfarin and danshen, a widely used Chinese herbal medicine, in a patient who had undergone mitral valve replacement. Patients taking warfarin should be warned not to take this herb. In addition, physicians should be alert to the possibility of an interaction with herbal medicine when anticoagulation control becomes difficult and no other causes are apparent.

Jappe U, Bonnekoh B, Hausen BM, Gollnick H. **Garlic-related dermatoses: case report and review of the literature.** Am J Contact Dermat 1999;10(1):37-9.
BACKGROUND: Garlic is widely appreciated as a spice and as a vegetable as well as an over-the-counter phytotherapeutic. From a dermato-allergological standpoint, several garlic-related adverse reactions have to be distinguished. OBJECTIVE: The corresponding literature is reviewed briefly, with regard to our present observation of a cook, who contracted garlic-induced contact dermatitis being analyzed for its complex pathomechanism. METHODS: The patient showed a positive type-IV patch test reaction for diallyl disulfide, a low molecular weight garlic ingredient; and strong, non-irritant reactions after 20 min and 24 hrs in the scratch chamber test with fresh total garlic. RESULTS: Thus, in this case of an occupational dermatosis, protein contact dermatitis had to be considered, as well as allergic type-IV contact dermatitis as a co-existing pathomechanism. CONCLUSIONS: The spectrum of garlic-related adverse reactions comprises irritant contact dermatitis, with the rare variant of zosteriform dermatitis; induction of pemphigus, allergic asthma and rhinitis; contact urticaria; protein contact dermatitis; allergic contact dermatitis, including the hematogenic variant; as well as combinations thereof, as evidenced by our present case observation.

Jappe U, Franke I, Reinhold D, Gollnick HP. **Sebotropic drug reaction resulting from kava-kava extract therapy: a new entity?** J Am Acad Dermatol 1998;38(1):104-6.

Jensen-Jarolim E, Leitner A, Hirschwehr R, Kraft D, Wuthrich B, Scheiner O, Graf J, Ebner C. **Characterization of allergens in Apiaceae spices: anise, fennel, coriander and cumin.** Clin Exp Allergy 1997;27(11):1299-306.
BACKGROUND: Symptoms elicited by IgE-mediated food allergy range from mild local to severe systemic reactions. Allergens in spices are particularly dangerous due to their hidden presence in many dishes. OBJECTIVES AND METHODS: According to clinical observations, mugwort and birch pollen allergy, and hypersensitivity to spices are frequently associated, but the crossreacting compounds were not defined so far. We tested sera of 15 patients who experienced adverse reactions to spiced food and characterized their IgE-binding patterns on

anise, fennel, coriander and cumin extracts through immunoblot and inhibition experiments. RESULTS: The use of anti-Bet v 1 (MoAb) and anti-profilin (rabbit) antibodies revealed the presence of crossreacting allergens in the tested spice extracts. Inhibition experiments showed that IgE-binding to allergens in Apiaceae spices could be blocked by preincubation of sera with rBet v 1 or rBet v 2 (birch profilin). Moreover, we detected crossreacting allergenic molecules in the molecular weight range of 60 kDa. IgE-binding to spice allergens occurred only with sera of 10/15 (66%) patients with allergy to pollen (birch, mugwort) and/or celeriac. In five out of 15 (33%) patients with a history of adverse reaction to spices, but without pollen and celeriac allergy, no IgE-binding to any spice protein could be demonstrated. It is possible that these clinical reactions could be elicited by other types of hypersensitivity (Type II, III, IV), however, as spices contain highly reactive substances, the symptoms may most likely be classified as food-intolerant. CONCLUSIONS: Bet v 1- and profilin-related allergens may, besides higher molecular weight allergenic molecules, be responsible for Type I allergy to anise, fennel, coriander or cumin, members of the Apiaceae.

Jensen-Jarolim E, Reider N, Fritsch R, Breiteneder H. **Fatal outcome of anaphylaxis to camomile-containing enema during labor: a case study.** J Allergy Clin Immunol 1998;102(6 Pt 1):1041-2.

Jones TK, Lawson BM. **Profound neonatal congestive heart failure caused by maternal consumption of blue cohosh herbal medication.** J Pediatr 1998;132(3 Pt 1):550-2.
A newborn infant whose mother ingested an herbal medication, blue cohosh, to promote uterine contractions presented with acute myocardial infarction associated with profound congestive heart failure and shock. The infant remained critically ill for several weeks, although he eventually recovered. Other causes of myocardial infarction were carefully excluded. Blue cohosh, Caulophyllum thalictroides, contains vasoactive glycosides and an alkaloid known to produce toxic effects on the myocardium of laboratory animals. We believe this represents the first described case of deleterious human fetal effects from maternal consumption of blue cohosh.

Joo JS, Ehrenpreis ED, Gonzalez L, Kaye M, Breno S, Wexner SD, Zaitman D, Secrest K. **Alterations in colonic anatomy induced by chronic stimulant laxatives: the cathartic colon revisited.** J Clin Gastroenterol 1998;26(4):283-6.
Cathartic colon is a historic term for the anatomic alteration of the colon secondary to chronic stimulant laxative use. Because some have questioned whether this is a real entity, we investigated changes occurring on barium enema in patients ingesting stimulant laxatives. Our study consisted of two parts. In part 1, a retrospective review of consecutive barium enemas performed on two groups of patients with chronic constipation (group 1, stimulant laxative use [n=29]; group 2, no stimulant laxative use [n=26]) was presented to a radiologist who was blinded to the patient group. A data sheet containing classic descriptions of cathartic colon was completed for each study. Chronic stimulant laxative use was defined as stimulant laxative ingestion more than three times per week for 1 year or longer. To confirm the findings of the retrospective study, 18 consecutive patients who were chronic stimulant laxative users underwent barium enema examination, and data sheets for cathartic colon were completed by another radiologist (part 2). Colonic redundancy (group 1, 34.5%; group 2, 19.2%) and dilatation (group

1, 44.8%; group 2, 23.1%) were frequent radiographic findings in both patient groups and were not significantly different in the two groups. Loss of haustral folds, however, was a common finding in group 1 (27.6%) but was not seen in group 2 ($p < 0.005$). Loss of haustral markings occurred in 15 (40.5%) of the total stimulant laxative users in the two parts of the study and was seen in the left colon of 6 (40%) patients, in the right colon of 2 (13.3%) patients, in the transverse colon of 5 (33.3%) patients, and in the entire colon of 2 (13.3%) patients. Loss of haustra was seen in patients chronically ingesting bisacodyl, phenolpthalein, senna, and casanthranol. We conclude that long-term stimulant laxative use results in anatomic changes in the colon characterized by loss of haustral folds, a finding that suggests neuronal injury or damage to colonic longitudinal musculature caused by these agents.

Joselice e Silva M, Alves AJ, Do Nascimento SC. **Synthesis and cytotoxic activity of N-substituted thiosemicarbazones of 3-(3,4-methylenedioxy)phenylpropanal.** Farmaco 1998;53(3):241-3.
Five new N-substituted thiosemicarbazones of 3-(3,4-methylenedioxy)phenylpropanal were synthesized. Safrole, a natural product obtained from sassafras oil (Ocotea pretiosa), was oxidized to alcohol using BH3-THF and H2O2, followed by oxidation to aldehyde using pyridinium dichromate (PDC) and condensation with five N-substituted derivatives of thiosemicarbazide. Tests were performed to evaluate the cytotoxic activity with continuous chain KB cells (epidermoide carcinoma of the floor of the mouth). Compounds 5 and 6 showed IC50 values of 1.5 and 4.6 micrograms/ml, respectively.

Kamiyama T, Nouchi T, Kojima S, Murata N, Ikeda T, Sato C. **Autoimmune hepatitis triggered by administration of an herbal medicine.** Am J Gastroenterol 1997;92(4):703-4.
Although herbal medicines are believed to be safe with few side effects, there are several reports on drug-induced liver injury caused by them. However, there are no reports of autoimmune hepatitis triggered by herbal medicines. We report here the case of a patient with autoimmune hepatitis that became clinically apparent after administration of Dai-saiko-to (Da-Chai-Hu-Tang), an herbal medicine that is used as a standard medicine in Japan.

Kaplowitz N. **Hepatotoxicity of herbal remedies: insights into the intricacies of plant-animal warfare and cell death [editorial; comment].** Gastroenterology 1997;113(4):1408-12.

Kobayashi F, Nakamura H, Numata M, Wasada M, Shiraishi K, Itakura M, Matsuzaki S. **[A case of drug-induced liver injury caused by Saiko-Keishi-Kankyoto with thrombocytopenia].** Nippon Shokakibyo Gakkai Zasshi 1997;94(10):681-6. (Jpn)

Koh D, Lee BL, Ong HY, Ong CN. **Colophony in topical traditional Chinese medicaments.** Contact Dermatitis 1997;37(5):243.

Larrey D. **Hepatotoxicity of herbal remedies.** J Hepatol 1997;26(Suppl 1):47-51.

Lee CT, Wu MS, Lu K, Hsu KT. **Renal tubular acidosis, hypokalemic paralysis, rhabdomyolysis, and acute renal failure--a rare presentation of Chinese herbal nephropathy.** Ren Fail 1999;21(2):227-30.

We encountered a 66-year-old Chinese man presented with hypokalemic paralysis, rhabdomyolysis and acute renal failure after administration of mixed Chinese herbs. Proximal renal tubular acidosis and selective glucosuria were the main tubular dysfunctions. The renal failure recovered smoothly and rapidly after resuscitation and the tubular function abnormalities regained spontaneously after medicine withdrawal. It should be recognized that renal tubular acidosis with hypokalemic paralysis, rhabdomyolysis and subsequent acute renal failure may develop after taking Chinese mixed herbal medicine.

Leow YH. **Contact dermatitis due to topical traditional Chinese medication.** Clin Dermatol 1997;15(4):601-5.

Lerner JH. **Herbal therapy: there are risks.** RN 1997;60(8):53-4.

Levi M, Guchelaar HJ, Woerdenbag HJ, Zhu YP. **Acute hepatitis in a patient using a Chinese herbal tea--a case report.** Pharm World Sci 1998;20(1):43-4.
A case is presented of reversible acute hepatitis in a patient using a Chinese herbal tea. Upon identification of the tea mixture Aristolochia species, including A. debilis, which contains the highly toxic aristolochic acid, could be identified. We conclude that the acute hepatitis as described in this patient is most likely to be caused by (one of) the active ingredients of the Chinese herbal tea. Furthermore, this case illustrates that so-called natural products can cause unexpected severe adverse reactions.

Liao YL, Chiang YC, Tsai TF, Lee RF, Chan YC, Hsiao CH. **Contact leukomelanosis induced by the leaves of Piper betle L. (Piperaceae): a clinical and histopathologic survey.** J Am Acad Dermatol 1999;40(4):583-9.
BACKGROUND: In April 1997, an unusual pigmentary disorder was noticed by dermatologists in Taiwan. All patients had a history of using facial dressings with steamed leaves of Piper betle L. (Piperaceae). OBJECTIVE: Our purpose was to clarify the evolution and the origin of this unique leukomelanosis. METHODS: Fifteen patients with an unusual pigmentary disorder, who visited our clinic in September and October 1997, were asked to complete a questionnaire designed to elicit the history related to the disorder. Eight of these 15 patients underwent skin biopsies: 6 on the mottled hyperpigmented area (group A) and 2 on the hypopigmented area (group B). All 8 specimens were prepared with hematoxylin-eosin, Masson-Fontana, and S-100 stains. RESULTS: The results of the questionnaire revealed that these patients had all experienced a temporary erythematous reaction in the first few days of the use of the facial dressing, and 9 of them also complained of an accompanying stinging sensation. A bleaching effect became noticeable approximately 1 week to 1 month later. Eight patients reported that the hyperpigmentation and confetti-like hypopigmentation occurred after overexposure to the sun. In both groups, histopathologic examination revealed some melanophages in the dermis. Masson-Fontana staining of specimens from group A showed local interspersed depigmentation and hyperpigmentation in the basal epidermis and pigmentary incontinence in the dermis. This picture was different from the homogeneous depigmentation within basal epidermis in specimens from group B. In both groups, S-100 staining was negative for melanocytes in the depigmented area. CONCLUSION: The clinical course and histopathologic findings suggest that the evolution of this pigmentary disorder can be divided into 3 stages. The first stage is the immediate

bleaching stage, when an irritant reaction is usually conspicuous. The second stage consists of prominent hyperpigmentation visible both grossly and microscopically. The final stage is characterized by confetti-like depigmentation. It may be induced by chemicals in the betel leaves such as phenol, catechol, and benzene derivatives, perhaps through inhibition of melanin synthesis or melanocytotoxicity.

Liaudet L, Buclin T, Jaccard C, Eckert P. **Severe ergotism associated with interaction between ritonavir and ergotamine.** Br Med J 1999 Mar 20;318:771.
IPA COPYRIGHT: ASHP Severe ergotism attributed to an interaction of 600 mg of ritonavir every 12 h for human immunodeficiency virus (HIV) infection and 0.3 mg ergotamine tartrate twice daily, taken as a combination product with 0.2 mg of belladonna extract and 20 mg of phenobarbital for gastric discomfort, is reported in a 28-yr-old female patient; the patient was also receiving 20 mg/day of fluoxetine for depression. On admission, treatment with intravenous sodium nitroprusside, heparin, and morphine was started. Peridural anesthesia was needed for intractable pain. After 3 days she developed cyanosis and edema in both legs. Intravenous nifedipine, iloprost, and nitrates were also given, but she developed bilateral gangrene of the toes, necessitating transmetatarsal amputation 5 wk later. A proposed mechanism for this interaction, and the possible role of fluoxetine in this severe reaction, are also discussed.

Lichtensteiger CA, Johnston NA, Beasley VR. **Rhamnus cathartica (buckthorn) hepatocellular toxicity in mice.** Toxicol Pathol 1997;25(5):449-52.
The toxicity of the plant Rhamnus cathartica was assessed in mice after the plant was identified as a potential cause of an idiopathic neurologic disease in horses. Another member of the Rhamnaceae family, Karwinskia humboldtiana, is neurotoxic to mammals and birds and can induce hepatic degeneration and necrosis. To investigate the toxicity of R. cathartica, a 34-day feeding trial in mice was conducted using a complete rodent diet with 0, 5, or 25% added R. cathartica. No clinical signs or gross lesions were seen, and all major tissues were histologically normal except the liver. The livers of mice fed R. cathartica had marked hepatocellular swelling. Results from periodic acid-Schiff reaction staining and from electron microscopy confirmed that the swelling was due to deposits of monoparticulate glycogen (beta particles) in the cytoplasm. Glycogen deposition is an uncommon toxic change in cells. Apparently, compound(s) in R. cathartica directly or indirectly interfered with glycogen metabolism (either glycogenesis or glycogenolysis). Mechanistic and chronicity studies with R. cathartica are needed to investigate the pathophysiology of the glycogen disturbance and to determine if hepatic injury progresses and if other organs will be injured.

Lopez-Rubio A, Rodriguez J, Crespo JF, Vives R, Daroca P, Reano M. **Occupational asthma caused by exposure to asparagus: detection of allergens by immunoblotting.** Allergy 1998;53(12):1216-20.
BACKGROUND: Vegetables of the Liliaceae family, such as garlic or onion, have been reported to cause occupational asthma. However, there are few data on adverse reactions to asparagus. We evaluated the role of asparagus as a cause of asthma in a patient with respiratory symptoms occurring at work (horticulture) and studied relevant allergens. METHODS: A 28-year-old man complained of rhinoconjunctivitis and asthma when harvesting asparagus at work. Eating cooked asparagus did not provoke symptoms. A positive skin test reaction was observed

with raw asparagus, Alternaria alternata, and grass-pollen extracts. The methacholine test demonstrated mild bronchial hyperresponsiveness. The patient had an immediate asthmatic response after challenge with raw asparagus extract. Bronchial provocation tests with boiled asparagus, A. alternata, and control extracts were negative. Two unexposed subjects with seasonal allergic asthma did not react to the raw asparagus extract. RESULTS: The double-blind, placebo-controlled food challenge with raw asparagus was negative. Serum asparagus-specific IgE was 13.9 kU(A)/l. By SDS-PAGE immunoblot, at least six IgE-binding components, ranging from 22 to 73 kDa, were detected only in raw asparagus. CONCLUSIONS: We report a case of occupational asthma caused by asparagus inhalation, confirmed by specific bronchoprovocation. Immunoblot analysis showed that asparagus allergens are very labile and quite sensitive to heat denaturation.

Luty S, Latuszynska J, Halliop J, Tochman A, Obuchowska D, Przylepa E, Korczak E. **Toxicity of dermally applied alpha-cypermethrin in rats.** Ann Agric Environ Med 1998;5(2):109-16.
The aim of the study was to assess the immunotoxic effect of dermally applied alpha-cypermethrin in rats based on phagocytic and bactericidal activity of neutrophils of peripheral blood, and the general toxic effect based on histological and ultrastructural examination of internal organs. The preparation was dermally applied in doses of 50 mg/kg and 250 mg/kg. It was administered to the tail skin of female Wistar rats, 4 hours daily for 28 days. After the experiment, the animals were anaesthetized and heart blood was taken in order to evaluate the activity of granulocyte system. The following organs were taken for histological examinations: brain, lung, heart, liver, spleen, kidneys, thymus and lymphatic nodes. Lung, liver, kidney and heart were used for ultrastructural studies. The results of the study showed that bactericidal and phagocytic activity of neutrophils was stimulated after administration of 50 mg/kg alpha-cypermethrin. Dermal application of the preparation resulted in slight histological changes in liver, kidney, lung and brain. Pathological changes in heart were observed only on the level of ultrastructure.

Mack RB. **"Boldly they rode ... into the mouth of hell". Pennyroyal oil toxicity.** N C Med J 1997;58(6):456-7.

Malak J. **Chinese herb nephropathy is not a (dex)fenfluramine nephropathy but a serotonin nephropathy [letter; comment].** J Altern Complement Med 1998;4(2):131-2.

Manteiga R, Park DL, Ali SS. **Risks associated with consumption of herbal teas.** Rev Environ Contam Toxicol 1997;150:1-30.
Plants have been used for medicinal purposes for centuries. Health-oriented individuals are turning to herbal teas as alternatives to caffeinated beverages such as coffee, tea, and cocoa and for low-caloric supplements. The popularity of herbal tea consumption has increased significantly during the past two decades in the U.S. Hundreds of different teas made up of varied mixtures of roots, leaves, seeds, barks, or other parts of shrubs, vines, or trees are sold in health food stores. Although chemists have been characterizing toxic plant constituents for over 100 years, toxicological studies of herbal teas have been limited and, therefore, the safety of many of these products is unknown. Plants synthesize secondary metabolites that are not essential in the production of energy and whose role may be in the defense mechanisms as plant

toxins to their interactions with other plants, herbivores, and parasites. Pyrrolizidine alkaloids (PAs) were among the first naturally occurring carcinogens identified in plant products, and their presence in herbal teas is a matter of public health significance. Some herbal tea mixtures and single-ingredient herbal teas have been analyzed for toxic/mutagenic potential by bioassay and chromatographic techniques. Numerous human and animal intoxications have been associated with naturally occurring components, including pyrrolizidine alkaloids, tannins, and safrole. Thus, the prevention of human exposure to carcinogens or mutagens present in herbal tea mixture extracts is crucial. Preparation of infusion drinks prepared from plants appears to concentrate biologically active compounds and is a major source of PA poisoning. The quantity and consumption over a long period of time is of major concern. It is recommended that widespread consumption of herbal infusions should be minimized until data on the levels and varieties of carcinogens, mutagens, and toxicants are made available.

Martin CM. **It's only natural: herbal remedies claim their niche.** Consult Pharm 1997 Jun;12:631-6.
IPA COPYRIGHT: ASHP An overview of herbal medicines is presented, including research, regulatory issues, and possible benefits and adverse events associated with the use of these popular remedies. Lists of herbs to avoid and resources for natural medicines are presented. Many of the popular herbs on the market that are considered common home remedies are discussed. Herbal dangers with Ginkgo biloba and ginseng are specifically addressed.

Matsuda R, Takahashi D, Chiba E, Kawana I, Tomiyama M, Ebira H, Ikegami T, Kitamura H, Ishii M. **[A case of drug induced hepatitis and interstitial pneumonia caused by a herbal drug, Dai-saiko-to].** Nippon Shokakibyo Gakkai Zasshi 1997;94(11):787-91. (Jpn)

Matsushima T. **[Drug-induced pneumonitis and related diseases].** Nippon Naika Gakkai Zasshi 1997;86(3):457-62. (Jpn)

Mccain WC, Lee R, Johnson MS, Whaley JE, Ferguson JW, Beall P, Leach G. **Acute oral toxicity study of pyridostigmine bromide, permethrin, and DEET in the laboratory rat.** J Toxicol Environ Health 1997;50(2):113-24.
This study investigated the lethal interaction of pyridostigmine bromide (PB), permethrin, and DEET when given to adult male rats by gavage and was separated into two phases. Phase I determined the acute oral lethal dose-response relationship of each compound with the vehicle, propylene glycol. Phase II was divided into two portions: a dose-response study using probit units obtained from phase I [lethal dose (LD) 16, 30, 50, 70, and 84], and an interaction study that contained low levels (calculated LD16, additive LD32) of the two compounds while the concentration of the third compound was varied. Rats were fasted overnight, dosed, and observed for 14 d. A significant increase in lethality occurred when PB, permethrin, and DEET were given concurrently when compared to expected additive values. Furthermore, solutions containing PB and permethrin or PB and DEET also caused a significant increase in lethality when compared to expected additive values. This information suggests that lethality in this study was more than an additive effect.

McGovern TW, Barkley TM. **Botanical briefs: leafy spurge--Euphorbia esula l.** Cutis 1998;62(5):221-2.

McGovern TW, Barkley TM. **Botanical briefs: Peruvian lily--Alstroemeria (L.) spp.** Cutis 1999;63(3):137-8.

McGovern TW, Barkley TM. **Botanical briefs: stinging nettle-Urtical dioica L.** Cutis 1998;62(2):63-4.

McGovern TW, Barkley TM. **Botanical dermatology.** Int J Dermatol 1998;37(5):321-34. BIOSIS COPYRIGHT: BIOL ABS. RRM LITERATURE REVIEW HUMAN BOTANICAL DERMATOLOGY DERMATOLOGY CONTACT URTICARIA DERMATITIS PHYTOPHOTODERMATITIS ALLERGIC CONTACT DERMATITIS OCCUPATIONAL PLANT DERMATOSIS INTEGUMENTARY SYSTEM DISEASE IMMUNE SYSTEM DISEASE.

McIntyre M. **Chinese herbs: risk, side effects, and poisoning: the case for objective reporting and analysis reveals serious misrepresentation [comment] [see comments].** J Altern Complement Med 1998;4(1):15-6.

Mennecier D, Saloum T, Dourthe PM, Bronstein JA, Thiolet C, Farret O. **[Acute hepatitis after phytotherapy (letter)].** Presse Med 1999;28(18):966. (Fre)

Miller CA. **How safe are herbs?** Geriatr Nurs 1998;19(3):163-4.

Miller LG. **Herbal medicinals: selected clinical considerations focusing on known or potential drug-herb interactions.** Arch Intern Med 1998;158(20):2200-11.
Herbal medicinals are being used by an increasing number of patients who typically do not advise their clinicians of concomitant use. Known or potential drug-herb interactions exist and should be screened for. If used beyond 8 weeks, Echinacea could cause hepatotoxicity and therefore should not be used with other known hepatoxic drugs, such as anabolic steroids, amiodarone, methotrexate, and ketoconazole. However, Echinacea lacks the 1,2 saturated necrine ring associated with hepatoxicity of pyrrolizidine alkaloids. Nonsteroidal anti-inflammatory drugs may negate the usefulness of feverfew in the treatment of migraine headaches. Feverfew, garlic, Ginkgo, ginger, and ginseng may alter bleeding time and should not be used concomitantly with warfarin sodium. Additionally, ginseng may cause headache, tremulousness, and manic episodes in patients treated with phenelzine sulfate. Ginseng should also not be used with estrogens or corticosteroids because of possible additive effects. Since the mechanism of action of St John wort is uncertain, concomitant use with monoamine oxidase inhibitors and selective serotonin reuptake inhibitors is ill advised. Valerian should not be used concomitantly with barbiturates because excessive sedation may occur. Kyushin, licorice, plantain, uzara root, hawthorn, and ginseng may interfere with either digoxin pharmacodynamically or with digoxin monitoring. Evening primrose oil and borage should not be used with anticonvulsants because they may lower the seizure threshold. Shankapulshpi, an Ayurvedic preparation, may decrease phenytoin levels as well as diminish drug efficacy. Kava

when used with alprazolam has resulted in coma. Immunostimulants (eg, Echinacea and zinc) should not be given with immunosuppressants (eg, corticosteroids and cyclosporine). Tannic acids present in some herbs (eg, St John wort and saw palmetto) may inhibit the absorption of iron. Kelp as a source of iodine may interfere with thyroid replacement therapies. Licorice can offset the pharmacological effect of spironolactone. Numerous herbs (eg, karela and ginseng) may affect blood glucose levels and should not be used in patients with diabetes mellitus.

Mochitomi Y, Inoue A, Kawabata H, Ishida S, Kanzaki T. **Stevens-Johnson syndrome caused by a health drink (Eberu) containing ophiopogonis tuber.** J Dermatol 1998;25(10):662-5.
Stevens-Johnson syndrome is considered to be a severe type of erythema exsudativum multiforme. It is characterized by erythema with bullous and eroded lesions of skin and mucous membranes. We report a case of Steven-Johnson syndrome following consumption of a health drink containing ophiopogonis tuber. A 66-year-old female took an O.T.C. health drink for fever. The next morning, she noted erythema and swelling of her face, neck, and chest. She started to develop bullous and eroded lesions on the skin of her entire body and the mucous membranes of her oral cavity, conjunctiva, and cornea, and she became feverish. She had high degrees of corneal erosion and liver dysfunction. Skin biopsy showed diffuse necrosis of the epidermis. After admission to the hospital, steroid pulse therapy (1000 mg/day of methylprednisolone sodium succinate) was continued for 5 days. The health drink induced a positive drug lymphocyte stimulation test (DLST) and patch test. A challenge test was done with a one hundredth dose, and it was positive. We did patch tests with all components of the drink and found that Mai-Meu-Dong-Tang (ophiopogonis) alone was positive at 72 hours. There is no previous report of Stevens-Johnson syndrome caused by a health drink or Mai-Meu-Dong-Tang. Even though it is a health drink, we should be aware of the possibility of a severe reaction.

Moore DA, Moore NL. **Paediatric enema syndrome in a rural African setting.** Ann Trop Paediatr 1998;18(2):139-44.
We have observed a distinct clinical syndrome amongst acutely unwell children frequently associated with the administration of a traditional medicine enema. We describe the clinicopathological features of this 'enema syndrome' based on retrospective case note review of 50 consecutive admissions to a South African rural district hospital. Admission was frequently prompted by sudden, marked clinical deterioration following enema administration (68% seen within 24 h). Respiratory distress with tachypnoea, abdominal distension, hypotonia and loss of consciousness occurred frequently. In-hospital mortality was 28% and was higher in those receiving herbal (43%) rather than chemical (21%) enemas. Hyperkalaemia, leucocytosis (> 15,000 mm3) and respiratory distress occurred more frequently in those who died. Diagnosis of an underlying illness was established in 78%. Whilst the majority of enemas are given without incident, children struggling with an underlying illness may be unable to tolerate rectally administered traditional medicines. Toxic chemical substances in frequent use may increase complication rates.

Moss TM. **Herbal medicine in the emergency department: a primer for toxicities and treatment.** J Emerg Nurs 1998;24(6):509-13.
Herbal therapies are very safe, and side effects are uncommon. Side effects requiring ED treatment are rare and would most likely involve an allergic reaction or toxic effect from

improper administration of the herb. However, a working knowledge of possible side effects of herbal therapies can be helpful in those rare instances. Simple treatment options with herbal teas are also suggested as an adjunct to medical therapies in certain instances.

Mukhopadhyay MJ, Saha A, Dutta A, De B, Mukherjee A. **Genotoxicity of sennosides on the bone marrow cells of mice.** Food Chem Toxicol 1998;36(11):937-40.
Preparations of a number of plants which contain hydroxyanthraquinones as active constituents are used worldwide for their laxative effect. Anthraquinone glycosides of Cassia angustifolia and C. fistula were investigated for their ability to induce a clastogenic effect on the bone marrow cells of Swiss albino mice. The endpoints screened were chromosomal aberrations and frequency of aberrant cells. Oral exposure to doses of these anthraquinones and their equivalent amount in leaf and pod extracts did not induce significant numbers of chromosomal aberrations or aberrant cells. The results indicate that anthraquinone sennoside B and rhein are weakly genotoxic.

Mullins ME, Horowitz BZ. **The case of the salad shooters: intravenous injection of wild lettuce extract.** Vet Hum Toxicol 1998;40(5):290-1.
Three young adult drug users obtained wild lettuce and valerian root, prepared a crude aqueous extract of the wild lettuce, and injected the extract i.v. One also injected an alcohol extract of the valerian root. All 3 rapidly became ill with fevers, chills, abdominal pain, flank and back pain, neck stiffness, headache, leucocytosis and mild liver function abnormalities, but recovered over the next 3 d. Various literature and internet sources claim that wild lettuce has opiate properties not demonstrated in this case.

Mullins RJ. **Echinacea-associated anaphylaxis.** Med J Aust 1998;168(4):170-1.
A woman with atopy experienced anaphylaxis after taking, among other dietary supplements, a commercial extract of echinacea. Hypersensitivity was confirmed by skinprick and RAST testing. Regular ingestion of echinacea by up to 5% of surveyed patients with atopy, combined with detection of echinacea-binding IgE in atopic subjects (19% by skin testing; 20% with moderate to strong reactivity by RAST testing), raises the possibility of severe allergic reactions, even with first-time use, due to cross-reactivity with other structurally similar allergens. Patients with atopy should be cautioned about the risk of developing life-threatening reactions to complementary medicines, including echinacea.

Murphy JM. **Preoperative considerations with herbal medicines.** AORN J 1999;69(1):173-5, 177-8, 180-3.
More patients are using herbal remedies. Even though herbs are natural products, they often act like medications and may interact with or potentiate other medications. During a preoperative evaluation, nurses should ask patients about their use of herbal remedies. Certain herbs are dangerous and should never be taken, and others must be avoided before elective surgery. Today's perioperative health care professionals must become familiar with basic information about herbs to carry out thorough assessments. At times, caregivers may need to educate and counsel consumers about benefits and harmful aspects of herbal preparations.

Musk SR, Clapham P, Johnson IT. **Cytotoxicity and genotoxicity of diallyl sulfide and diallyl disulfide towards Chinese hamster ovary cells.** Food Chem Toxicol 1997;35(3-4):379-85.

Two compounds found in garlic, diallyl sulfide (DAS) and diallyl disulfide (DDS), were tested for cytotoxic and genotoxic effects in a Chinese hamster ovary cell line. DDS was found to be more cytotoxic than DAS (showing a Dq of 1.6 micrograms/ml and a D0 of 0.6 microgram/ml as opposed to values of 295 and 90 micrograms/ml, respectively). Both compounds were found to induce both chromosome aberrations and sister chromatid exchanges (SCEs) with DDS again being more active on a weight-for-weight basis, exhibiting activity at concentrations below 10 micrograms/ml compared with the levels of 300 micrograms/ml and above required for DAS to show any effect. The addition of rat liver S-9 activation fraction to the assays modified the effects of the two compounds in a non-consistent manner. It reduced the induction of SCEs by both compounds, enhanced the generation of aberrations by DDS (but not by DAS) and radically altered the parameters of both survival curves, reducing the Dq values almost to zero but increasing the D0 values.

Myers JH, Moro-Sutherland D, Shook JE. **Anticholinergic poisoning in colicky infants treated with hyoscyamine sulfate.** Am J Emerg Med 1997;15(5):532-5.
Hyoscyamine, one of the principal alkaloid components of belladonna, is a potent anticholinergic agent. Because of its anticholinergic properties, hyoscyamine sulfate drops are often prescribed for the treatment of colic in infants. Anticholinergic poisoning in infants is rare. However, five cases are reported of infants with anticholinergic toxicity following the administration of hyoscyamine drops for the treatment of colic. Common presenting symptoms included irritability, tachycardia, and erythematous flushed skin. These cases emphasize the need for a heightened awareness by emergency physicians and pediatricians of possible anticholinergic toxicity caused by the use of hyoscyamine for infant colic.

Myers SP, Wohlmuth H. **Echinacea-associated anaphylaxis [letter].** Med J Aust 1998;168(11):583-4.

Nakai T, Kioka K, Sano K, Aoki T, Moriyoshi Y, Kurai O, Nebiki H, Okawa K, Oka H, Harihara S, et al. **[A case of drug-induced liver injury by Chinese digestive medicine].** Nippon Shokakibyo Gakkai Zasshi 1998;95(12):1374-7. (Jpn)

Navarro JF, Macia ML, Garcia Perez J. **[The false illusion of medicinal herbs (letter; comment) (see comments)].** Med Clin (Barc) 1997;109(4):159. (Spa)

Nguyen B, Weytjens K, Cloutier Y, Ghezzo H, Malo JL. **Determinants of the bronchial response to high molecular weight occupational agents in a dry aerosol form.** Eur Respir J 1998;12(4):885-8.
In occupational challenge tests with isocyanate vapours, bronchial responsiveness is determined by the total dose rather than the concentration or duration of exposure. Whether the same applies for high molecular weight (HMW) agents in powder form is unknown. The aim of this study was to determine whether the total dose of HMW agents in powder form is responsible for the immediate reaction documented in specific challenge tests. Included in the study were nine subjects (seven males and two females) with a diagnosis of occupational asthma proved by specific challenge tests carried out on a preliminary visit. Two challenge tests (using a closed-circuit exposure chamber) were performed at an interval of 2 weeks; the concentrations

administered in a random order on these two visits were half and double the one that had caused a 20% fall in forced expiratory volume in one second (FEV1) on a preliminary visit. The duration of exposure was adjusted until a significant fall in FEV1 (target of 20%) occurred. The two concentrations obtained were significantly different, by 2.07+/-0.36-fold (SD). The observed durations of exposure leading to a 20% fall in FEV1 on the two visits also differed significantly by 0.46+/-0.32-fold. Consequently, the cumulative efficient doses were not significantly different between the two visits: 12+/-5.4 and 9+/-5 mg x mL(-1) x min(-1), respectively. The corresponding cumulative dose ratio was 0.96+/-0.61. The expected duration of exposure (10.8+/-24 min) was not significantly different from the observed duration (5.4+/-9 min). The mean and 95% confidence interval for the difference in concentration between the two visits was 1.83-fold (1.48-2.21). In conclusion, the total dose rather than the concentration or duration of exposure per se determines bronchial responsiveness to high molecular weight agents in powder form.

Nicolie B, Drouet M, Sabbah A. **[Chronic rhinitis, or the consequences of gluttony].** Allerg Immunol (Paris) 1997;29(1):22-3. (Fre)

Ning-Sheng L. **Renal involvement in Chinese patients with rheumatoid arthritis [letter].** Ann Rheum Dis 1998;57(9):571.

Nortier JL, Deschodt-Lanckman MM, Simon S, Thielemans NO, De Prez EG, Depierreux MF, Tielemans CL, Richard C, Lauwerys RR, Bernard AM, et al. **Proximal tubular injury in Chinese herbs nephropathy: monitoring by neutral endopeptidase enzymuria.** Kidney Int 1997;51(1):288-93.
Neutral endopeptidase (NEP) is a 94 kDa ectoenzyme of the proximal tubule brush border, physiologically released into the urine with apical membrane fragments. As proximal tubular atrophy was a histological hallmark of Chinese herbs nephropathy (CHN), this study firstly determined renal excretion of NEP in healthy control subjects (N = 31), in patients with CHN (N = 26) and in women having consumed Chinese herbs and whose renal function was normal but running the risk of developing CHN (N = 27). Another patient group consisted of female patients with glomerular diseases (N = 12). At the same time, measurements of urinary microproteins (Clara cell protein, retinol binding protein, beta 2-microglobulin and alpha 1-microglobulin) were performed, as indicators of tubular dysfunction. Cell damage was estimated by the excretion of N-acetyl-beta-D-glucosaminidase (NAG). In the control group, the physiological NEP enzymuria was 43.1 micrograms/24 hr (geometric mean). In CHN patients, levels of urinary NEP were significantly decreased in those with moderate renal failure (26.7 micrograms/24 hr; N = 21; P < 0.05) and almost abolished in end-stage renal failure patients (4.35 micrograms/24 hr; N = 5; P < 0.05). In patients at risk as well as in patients with glomerular diseases, urinary NEP levels were not statistically different from those observed in control subjects (40.68 micrograms/24 hr and 48.5 micrograms/24 hr, respectively). Several degrees of tubular dysfunction and injury were noted in patients groups, as attested by increased urinary microproteins and NAG excretions. Considering the data from control and CHN patients, NEP enzymuria positively correlated with individual creatinine clearance values (r = 0.76; P = 0.0001) and negatively correlated with urinary microproteins levels (r = -0.55; P = 0.00001). Finally, NEP was regularly quantitated in the urine of 6 CHN patients for a period ranging from six

months to two years and in 19 patients at risk during two years, respectively. In the first group, renal function progressively deteriorated in 3 patients, leading them to renal replacement therapy after 38 to 115 weeks. Stable parameters were observed in the remaining 3 patients. A direct correlation between creatinine clearance and NEP excretion was found longitudinally in each case. In the second group, no significant change of urinary NEP levels was observed (45.9 micrograms/24 hr), in parallel with stable renal function. Taken together, these results indicate that, in CHN patients, NEP enzymuria provides a rapid and noninvasive determination of the degree of structural impairment affecting the proximal tubular population and further reflecting the severity of the renal disease. The interest of this urinary marker in monitoring the progression of other tubulointerstitial diseases remains to be assessed.

O'Breasail AM, Argouarch S. **Hypomania and St John's wort [letter].** Can J Psychiatry 1998;43(7):746-7.

Oda H, Ono M, Ohashi H. **[Probable case of Chinese herbs nephropathy].** Nippon Naika Gakkai Zasshi 1998;87(11):2309-10. (Jpn)

Oertmann C, Bergmann KC. **[The increase of pollen-associated oral allergy syndrome: The marker of a change in pollen allergy].** Allergologie 1997;20(12):611-9. (Ger)
BIOSIS COPYRIGHT: BIOL ABS. The histories of pollen-associated food intolerance were obtained from questionnaires of patients with pollinosis at a hospital for allergies and diseases of the airways. The comparisons were made between 300 consecutive individual cases examined between 1979-1983 and again 300 cases between 1995-1996. The prevalence of oral allergy syndrome (OAS), particularly that produced by apples, nuts, stone and kernel fruits was 17.3% 15 years ago as opposed to 58.3% for todays figures. Almost no difference was to be observed in non-pollen-associated food intolerances. The pollen skin test showed the same frequency of tree pollen sensitization in both groups (267:264). Whilst particularly trivalent sensitizations to trees, herbs and grasses were found (238) 15 years ago, this was evident in only 133 cases for 1995-1996. However, the monovalent sensitization to trees alone increased from 2 to 55 (0,6% to 18,5%) and bivalent sensitization to trees and grasses showed an increase from 5,7% to 22.1%. Additionally, a high percentage of those patients with mono and bivalent sensitizations to trees also suffered from OAS, caused by the high identity of Bet v1 and the major allergens in apples and nuts. Thus the observed increase of OAS conforms with a higher potency of tree pollen allergy manifesting itself in mono and bivalent form - even in patients less disposed to allergies. This assumption is backed by the fact that a higher percentage of older patients had monovalent pollen allergy, grown "forced" over years whereas the younger patients of extreme allergic disposition more frequently showed a trivalent sensitization. In 1995-1996 the PRIST value was determined in 167 patients with pollinosis. This demonstrates that the level of total IgE is not significant for OAS. A heightened exposure to sensitizing tree pollen is probably of more significance today. Thus OAS is a marker syndrome indicating a change in pollinosis today more often due to tree pollen allergy whereas sensitization to grassesand herbs almost remained the same within the time period of comparison.

Oka K, Saito F, Yasuhara T, Sugimoto A. **The allergens of Dendropanax trifidus Makino and Fatsia japonica Decne. et Planch. and evaluation of cross-reactions with other plants of the**

Araliaceae family. Contact Dermatitis 1999;40(4):209-13.
cis-9,17-Octadecadiene-12,14-diyne-1,16-diol (I), an analog of falcarinol has been identified in our previous report as an active component of Dendropanax trifidus and a strong sensitizer. In this report, 16-hydroxy-cis-9,17-octadecadiene-12,14-diynoic acid (II) and cis-9,trans-16-octadecadiene-12,14-diynoic acid (III) were elucidated as 2 other active components of the plant. Compound I, however, presented with the highest concentration and showed a stronger reaction on patch testing. The leaves of Fatsia japonica Decne. et Planch. were also found to contain compound I, but the amount was found to be 7x more in Dendropanax trifidus than in Fatsia japonica. 5 subjects with hypersensitivity to Dendropanax trifidus and compound I showed positive reactions when patch tested with the leaves of Hedera helix L. and Schefflera arboricola. 1 of these also showed a positive reaction to the extract of Panax ginseng root powder diluted 1% in ethanol. There was cross-reaction among these plants, which all belong to the Araliaceae family.

Ondrizek RR, Chan PJ, Patton WC, King A. **An alternative medicine study of herbal effects on the penetration of zona-free hamster oocytes and the integrity of sperm deoxyribonucleic acid.** Fertil Steril 1999;71(3):517-22.
OBJECTIVE: To analyze the effects of certain herbs on sperm DNA and on the fertilization process. DESIGN: Prospective comparative study. SETTING: Clinical and academic research environment. PATIENT(S): Donor sperm specimens. INTERVENTION(S): Zona-free hamster oocytes were incubated for 1 hour in saw palmetto (Serenoa repens), echinacea purpura, ginkgo biloba, St. John's wort (Hypericum perforatum), or control medium before sperm-oocyte interaction. The DNA of herb-treated sperm was analyzed with denaturing gradient gel electrophoresis. MAIN OUTCOME MEASURE(S): Oocyte penetration and integrity of the sperm BRCAI exon 11 gene. RESULT(S): Pretreatment of oocytes with 0.6 mg/mL of St. John's wort resulted in zero penetration. A lower concentration (0.06 mg/mL) had no effect. High concentrations of echinacea and ginkgo also resulted in reduced oocyte penetration. Exposure of sperm to echinacea purpura and St. John's wort resulted in DNA denaturation. In contrast, saw palmetto and ginkgo had no effect. Sperm exposed to 0.6 mg/mL of St. John's wort showed mutation of the BRCA1 exon 11 gene. CONCLUSION(S): High concentrations of St. John's wort, echinacea, and ginkgo had adverse effects on oocytes. Saw palmetto had no effect. The data suggested that St. John's wort, ginkgo, and echinacea at high concentrations damage reproductive cells. St. John's wort was mutagenic to sperm cells.

Ono T, Eri M, Honda G, Kuwahara T. **Valvular heart disease and Chinese-herb nephropathy [letter; comment].** Lancet 1998;351(9107):991-2.

Paulsen E. **Occupational dermatitis in Danish gardeners and greenhouse workers (II). Etiological factors.** Contact Dermatitis 1998;38(1):14-9.
The aim of the study was to assess the distribution of different types of occupational eczema among employees in floristry and detect the allergens most commonly involved. Based on a postal questionnaire, 253 gardeners and greenhouse workers with occupational skin symptoms and 52 randomly-selected without symptoms were examined and patch tested. Routine tests comprised the standard series, the Compositae mix, feverfew and 3 fungicides, with additional testing based on case records. 184 persons from the symptom group and 1 from the random

group had occupational eczema. Irritant occupational contact eczema was suspected in 150 persons (59%). Nevertheless, 48% of the 250 persons patch tested had at least 1 positive reaction, most frequently to nickel, followed by Compositae which were positive in 25 cases (10%), of whom 24 were possibly occupationally sensitized. 13 persons from symptom group had positive reactions to fungicides. Occupational allergic eczema was suspected in 43 persons (17%), most often caused by plants belonging to the Compositae, Geraniaceae and Liliaceae families. New plant sensitizers were Exacum affine and Begonia lorraine. Exposure to specific plant species seemed to be the most important eliciting factors in both allergic and irritant occupational dermatitis in floristry, and preventive measures should include reduction of contact with plants.

Paulsen E, Sogaard J, Andersen KE. **Occupational dermatitis in Danish gardeners and greenhouse workers (III). Compositae-related symptoms.** Contact Dermatitis 1998;38(3):140-6.
The clinical part of the study aimed at describing epidemiological and diagnostic aspects of occupational Compositae dermatitis. Patch testing with the sesquiterpene lactone (SL) and Compositae mixes, feverfew extract and supplementary allergens in 250 selected gardeners showed Compositae allergy in 25, 17 females and 8 males. 24 were possibly occupationally sensitized. The mean age was lower and the preponderance of women higher compared to classical Compositae dermatitis, and the distribution and course of the dermatitis most often did not differ from other occupational plant dermatoses. The Compositae mix detected 2x as many as the SL mix, and the overall detection rate with both was 76%, making aimed patch testing necessary. Chrysanthemum (Dendranthema), marguerite daisy (Argyranthemum frutescens) and lettuce (Lactuca sativa) were frequent sensitizers. Occupational type I allergy to Compositae comprised sensitization to Gerbera, chrysanthemum, lettuce, Senecio cruentus and Aster. Among 1657 respondents in the questionnaire part of the study, 824 had worked with Compositae, and 160 (19%) reported occupational Compositae-related symptoms of skin and mucous membranes. Possible risk factors for the development of these were assessed in a stepwise logistic regression model and a history of childhood eczema, hay fever and duration of exposure were significantly associated with Compositae-related irritant and allergic symptoms in both sexes.

Pfutzner W, Thomas P, Rueff F, Przybilla B. **Anaphylactic reaction elicited by condurango bark in a patient allergic to natural rubber latex.** J Allergol Clin Immunol 1887;101(2 Pt 1):281-2.
BIOSIS COPYRIGHT: BIOL ABS. RRM CASE STUDY MARSDENIA-CONDURANGO HUMAN ADULT MALE NURSE PATIENT NATURAL RUBBER LATEX NATURAL RUBBER LATEX ALLERGY CUNDURANGO BARK ANAPHYLACTIC REACTION HERBAL TEA ALLERGY ALLERGEN IMMUNE SYSTEM DISEASE TEA.

Phan TG, Estell J, Duggin G, Beer I, Smith D, Ferson MJ. **Lead poisoning from drinking Kombucha tea brewed in a ceramic pot.** Med J Aust 1998;169(11-12):644-6.
Kombucha tea is an alternative therapy that is gaining popularity as a remedy for a diverse range of ailments. We report two cases of symptomatic lead poisoning requiring chelation therapy in a married couple who had been drinking Kombucha tea for six months, brewing the tea in a

ceramic pot. We postulate that acids in the tea eluted lead from the glaze pigment used in the ceramic pot, in a manner analogous to elution of lead from crystal decanters by wine and spirits.

Picciotto A, Campo N, Brizzolara R, Giusto R, Guido G, Sinelli N, Lapertosa G, Celle G. **Chronic hepatitis induced by Jin Bu Huan.** J Hepatol 1998;28(1):165-7.
BACKGROUND/AIMS: Jin Bu Huan and other Chinese herbal products are widely taken remedies. They have been developed as a natural alternative to traditional drugs in the treatment of various ailments. Their ability to induce several side effects such as acute hepatitis has already been described. We report a case of chronic hepatic damage following administration of Jin Bu Huan Anodyne tablets. METHODS: The patient, a 49-year-old man, developed biochemical signs of liver damage 2 months after beginning Jin Bu Huan intake (3 tablets/daily) including biopsy-proven chronic hepatitis with moderate fibrosis. Virological, autoimmune, metabolic or other hepatotoxic causes were excluded. Liver function impairment was resolved by discontinuing Jin Bu Huan intake. CONCLUSIONS: This case reinforces the already known hepatotoxicity of this product and should make us think more about the uncontrolled use of alternative products.

Powell T, Hsu FF, Turk J, Hruska K. **Ma-huang strikes again: ephedrine nephrolithiasis.** Am J Kidney Dis 1998;32(1):153-9.
Ephedrine and its metabolites are naturally occurring alkaloids that can be derived from evergreens worldwide and have been used as medicinals for hundreds of years. Because they have "real" pharmacological alpha and beta catecholamine effects and are "natural" products, the alternative medicine industry has popularized them for multiple uses, including asthma, weight loss, energy and sexual enhancement, and euphoria. Several recent reviews have documented the dangerous nature of using these "drugs" unsupervised, including multiple deaths, and the FDA is currently reviewing ephedrine's use in the alternative medicine industry. We report a new toxicity, ephedrine nephrolithiasis, in a patient using an energy supplement, Ma-Huang extract, which contains ephedrine. Although previously not reported, the Louis C. Herring and Company kidney stone database show that this is an endemic complication of ephedrine with hundreds of previous episodes. Using gas chromatography (GC) mass spectrometry, we were able to positively identify the chemical structure of our patient's stone, as well as other similar stones from Louis Herring, as containing ephedrine, norephedrine, and pseudoephedrine.

Reginster F, Jadoul M, Van Ypersele De Strihou C. **Chinese herbs nephropathy presentation, natural history and fate after transplantation.** Nephrol Dial Transplant 1997;12(1):81-6.
BACKGROUND: Chinese herbs nephropathy is a new type of subacute interstitial nephropathy reported in women who had followed a slimming regimen including Chinese herbs. METHODS: We report the clinical presentation and follow-up of 15 cases and compare them with a control group of 15 women with interstitial nephropathies of other origins, matched for age, sex, and initial serum creatinine (mean 3 mg/dl). RESULTS: At presentation the Chinese herbs nephropathy group differed from the control group by a lower proteinuria ($P = 0.009$), a more severe anaemia ($P = 0.002$), and a higher prevalence of aortic insufficiency (42% vs 0%, $P < 0.05$). It was further characterized by mild hypertension in 80%, glycosuria and leukocyturia in 40% and asymmetric kidneys in 54% of the cases. During follow-up, deterioration of renal function was faster in the Chinese herbs nephropathy than in the control group ($P < 0.05$). It was

influenced by the duration of Chinese herbs treatment (P = 0.037) and the delay between the end of Chinese herbs ingestion and diagnosis of the disease (P = 0.013). In three cases, renal failure developed 3 years after Chinese herbs ingestion. Complications included severe aortic regurgitation requiring surgery (n = 1), urothelial carcinoma (n = 2), bilateral ureterohydronephrosis due to periureteral fibrosis (n = 1). Five patients with Chinese herbs nephropathy were successfully transplanted, without evidence of recurrence of the disease. CONCLUSIONS: Chinese herbs nephropathy is characterized by a lower proteinuria, more severe anaemia, and a faster progression to renal failure than other interstitial nephropathies. The duration of Chinese herbs treatment and interval between withdrawal of Chinese herbs and diagnosis are correlated with the rate of progression. Severe, unusual extrarenal complications may affect Chinese herbs nephropathy patients.

Rodriguez-Serna M, Sanchez-Motilla JM, Ramon R, Aliaga A. **Allergic and systemic contact dermatitis from Matricaria chamomilla tea.** Contact Dermatitis 1998;39(4):192-3.

Rudzki E, Rebandel P. **Positive patch test with Kamillosan in a patient with hypersensitivity to camomile.** Contact Dermatitis 1998;38(3):164.

Ryu JC, Kim KR, Kim HJ, Youn JY, Myung SW, Kim GH, Lee MJ, Chang IM. **Genotoxicity study of bojungchisup-tang, an oriental herbal decoction-in vitro chromosome aberration assay in Chinese hamster lung cells and in vivo supravital-staining micronucleus assay with mouse peripheral reticulocytes.** Arch Pharm Res 1998;21(4):391-7.
The toxicity evaluation of oriental herbal drugs is of great concern at present. Bojungchisuptang (BCST, in Korean), a decocted medicine of oriental herbal mixture, is now well used in clinic at oriental hospitals for the treatment of edema of several diseases in practice. However, the toxicity of the oriental herbal decocted medicines such as genetic toxicity is not well defined until now. In this respect, to clarify the genetic toxicity of BCST, in vitro chromosome aberration assay with Chinese hamster lung (CHL) fibroblasts and in vivo supravital micronucleus assay with mouse peripheral reticulocytes were performed in this study. In the chromosome aberration assay, we used 5,000 micrograms/ml BCST as maximum concentration because no remarkable cytotoxicity in CHL cells was observed both in the presence and absence of S-9 metabolic activation system. No statistical significant differences of chromosome aberrations were observed in CHL cells treated with 5,000, 2,500 and 1,250 micrograms/ml BCST for 6 hour both in the presence and absence of S-9 metabolic activation. However, very weak positive result (6.5-8.0% aberration) of BCST was obtained in the absence of S-9 metabolic activation system at 5,000 micrograms/ml BCST when treated for 24 hour, i.e. 1.5 normal cell cycle time. And also, in vivo clastogenicity of BCST was studied by acridine orange-supravital staining micronucleus assay using mouse peripheral reticulocytes. We used 2,000 mg/kg as the highest oral dose in this micronucleus assay because no acute oral toxicity of BCST was observed in mice. The optimum induction time of micronucleated reticulocytes (MNRETs) was determined as 36 hours after oral administration of 2,000 mg/kg BCST. No significant differences of MNRETs between control and BCST treatment groups were observed in vivo micronucleus assay. From these results, BCST revealed very weak positive result in chromosome aberration assay in vitro with CHL cells and no clastogenicity in micronucleus assay in vivo.

Sadjadi J. **Cutaneous anthrax associated with the Kombucha "mushroom" in Iran [letter].** JAMA 1998;280(18):1567-8.

Santa Maria A, Lopez A, Diaz MM, Munoz-Mingarro D, Pozuelo JM. **Evaluation of the toxicity of guarana with in vitro bioassays.** Ecotoxicol Environ Saf 1998;39(3):164-7.
A natural stimulant, Paullinia cupana, commonly called guarana, was tested for its ability to induce in vitro toxicity in Chinese hamster ovary (CHO) cells and bacterial cells (Photobacterium phosphoreum). The cytotoxic effects of aqueous guarana extracts were evaluated by three endpoint systems: neutral red (NR) uptake assay, total protein content [kenacid blue (KB)] assay, and tetrazolium (MTT) assay. The Microtox test was also used. Results indicated that the lowest concentration of guarana tested was not toxic and that the IC50 values calculated with the NR, KB, and MTT assays were lower than the highest concentration tested (40 mg/ml). There was no significant difference in cytotoxicity between the three test systems. The EC50 values obtained with the Microtox assay were consistent with these data. The present in vitro analysis suggests that the concentration of guarana is of critical importance in its cytotoxic activity and high doses could be harmful to human health.

Schilcher H, Leuschner F. **[Studies of potential nephrotoxic effects of essential juniper oil].** Arzneimittelforschung 1997;47(7):855-8. (Ger)
BIOSIS COPYRIGHT: BIOL ABS. The nephrotoxicity of juniper oil (CAS 73049-62-4), a phytomedicine with diuretic resp. aquaretic activity, was evaluated in male Sprague-Dawley rats after oral administration. Two chemically slightly different oil batches were tested for 28 days with 100, 333 or 1000 mg (series 1, batch 1) resp. 100, 300 or 900 mg (series 2, batch 2) juniper oil/kg. Additionally terpinene-4-ol, a compound with postulated aquaretic activity, which can be found in essential juniper oil up to an amount of 10 mg% was tested in a dosage of 400 mg/kg. Neither of the tested substances induced changes in function or morphology of the kidneys at the tested doses, and they were revealed to be nontoxic.

Schwartz HJ, Jones RT, Rojas AR, Squillace DL, Yunginger JW. **Occupational allergic rhinoconjunctivitis and asthma due to fennel seed.** Ann Allergy Asthma Immunol 1997;78(1):37-40.
BACKGROUND: A patient with complaints of rhinitis and asthma occurring at work presented for consultation. OBJECTIVES: To evaluate the role of the foods and spices with which he worked, in the causation of his complaints, and to evaluate his immune reactivity to these materials. METHODS: Allergy skin testing and in vitro RAST assays were carried out. After demonstrating specific reactivity to fennel, SDS-PAGE electrophoreses was carried out. RESULTS: Positive skin tests to grass, ragweed, and freshly prepared fennel seed were found. Serum IgE antibodies to fennel were quite high. Immunoblotting studies showed reactions to two components in fennel extract as well as to components in mugwort, paprika, short ragweed and black pepper. CONCLUSION: This case of occupational rhinitis and asthma in an atopic individual involves sensitivity to unique allergens in fennel, with molecular weights of 67 to 75 KD.

See DM, Broumand N, Sahl L, Tilles JG. **In vitro effects of echinacea and ginseng on natural killer and antibody-dependent cell cytotoxicity in healthy subjects and chronic fatigue**

syndrome or acquired immunodeficiency syndrome patients. Immunopharmacology 1997;35(3):229-35.
Extracts of Echinacea purpurea and Panax ginseng were evaluated for their capacity to stimulate cellular immune function by peripheral blood mononuclear cells (PBMC) from normal individuals and patients with either the chronic fatigue syndrome or the acquired immunodeficiency syndrome. PBMC isolated on a Ficoll-hypaque density gradient were tested in the presence or absence of varying concentrations of each extract for natural killer (NK) cell activity versus K562 cells and antibody-dependent cellular cytotoxicity (ADCC) against human herpesvirus 6 infected H9 cells. Both echinacea and ginseng, at concentrations > or = 0.1 or 10 micrograms/kg, respectively, significantly enhanced NK-function of all groups. Similarly, the addition of either herb significantly increased ADCC of PBMC from all subject groups. Thus, extracts of Echinacea purpurea and Panax ginseng enhance cellular immune function of PBMC both from normal individuals and patients with depressed cellular immunity.

Seong YH, Kim HS. **Inhibitory effects of ginseng total saponins on hypoxia-induced dysfunction and injuries of cultured astrocytes.** Arch Pharmacal Res 1997;20(2):103-9.

Shaw D, Leon C, Kolev S, Murray V. **Traditional remedies and food supplements. A 5-year toxicological study (1991-1995).** Drug Saf 1997;17(5):342-56.
Since 1991, the Medical Toxicology Unit (MTU) at Guys' Hospital, London, has been assessing the toxicological problems associated with the use of traditional and herbal remedies and dietary supplements. This assessment was carried out by evaluating reports to the National Poisons Information Service (London) [NPIS(L)] which provides emergency information to medical professionals. Relevant telephone enquiries to NPIS(L) were identified. Further case details were obtained by follow-up questionnaire, clinical consultation, toxicological analysis of samples from patients and/or products and botanical identification of plant material. Of 1297 symptomatic enquiries evaluated there was a possible/confirmed association in 785 cases. Case series have been identified which substantiate previous reports, including liver problems following the use of Chinese herbal medicine for skin disorders, allergic reactions to royal jelly and propolis and heavy metal poisoning caused by remedies from the Indian subcontinent. Although the overall risk to public health appears to be low, certain groups of traditional remedies have been associated with a number of potentially serious adverse effects. Considering the extent of use of herbal remedies and food supplements a comprehensive surveillance system for monitoring the adverse health effects of these products is essential. Surveillance of a large population is needed for the complex task of identifying the uncommon and unpredictable adverse effects which are potentially serious. In the UK, the Medicines Control Agency responded to the MTU report by recognising the need for vigilance and by incorporating adverse reactions reporting on unlicensed herbal remedies into their drug reaction monitoring function. As a further step to safeguard the patients/consumers an effective single regulatory system is required which would ensure the safety and quality of all herbal remedies and food supplements available in the UK.

Shaw D, Murray V, Volans G. **Adverse effects of herbal remedies and OTC medicines [letter].** Br J Clin Pharmacol 1999;47(2):227-8; Discusion 229-30.

Sheehan DM. **Herbal medicines, phytoestrogens and toxicity: risk:benefit considerations.** Proc Soc Exp Biol Med 1998;217(3):379-85.
There are several suggested health benefits of phytoestrogens, particularly those found in soy products. Herbal medicines are also widely thought to confer health benefits. Additionally, drugs are prescribed to improve human health, but unlike phytoestrogens and herbal medicines, toxicities are defined in experimental animals and monitored in humans before and after marketing. Knowledge of toxicity is crucial to decrease the risk:benefit ratio; this knowledge defines appropriate conditions for use and strategies for development of safer products. However, our awareness of the toxicity of herbal medicines and phytoestrogen-containing foods is dramatically limited compared to drugs. Some aspects of the toxicity of herbal medicines are briefly reviewed; it is concluded that virtually all of our knowledge is derived from human exposures leading to acute toxicities. Importantly, detection of toxicity is sporadic, and little information is available from prior animal experimentation. Additionally, well-organized monitoring of human populations (as occurs for drugs) is virtually nonexistent. Important toxicities with long latencies are particularly difficult to associate with a causative agent during or even after large scale exposures, as exemplified by tobacco smoking and lung cancer; estrogen replacement therapy and endometrial cancer; diethylstilbestrol and reproductive tract cancers; and fetal alcohol exposure and birth defects. These considerations suggest that much closer study in experimental animals and human populations exposed to phytoestrogen-containing products, and particularly soy-based foods, is necessary. Among human exposures, infant soy formula exposure appears to provide the highest of all phytoestrogen doses, and this occurs during development, often the most sensitive life-stage for induction of toxicity. Large, carefully controlled studies in this exposed infant population are a high priority.

Sheikh NM, Philen RM, Love LA. **Chaparral-associated hepatotoxicity.** Arch Intern Med 1997;157(8):913-9.
BACKGROUND: Personal health care practices that may include the use of dietary supplements are common in the United States. Products marketed as dietary supplements are diverse and may include botanicals, vitamins, and/or minerals. Chaparral (Larrea tridentata) is a botanical dietary supplement made from a desert shrub and used for its antioxidant properties. Several reports of chaparral-associated hepatitis have been published since 1990, but a complete picture of the clinical presentation is still unclear. MATERIALS AND METHODS: We reviewed the 18 case reports of adverse events associated with the ingestion of chaparral reported to the Food and Drug Administration between 1992 and 1994. These reports were from health care professionals, state health departments, and individual consumers. RESULTS: Of 18 reports of illnesses associated with the ingestion of chaparral, there was evidence of hepatotoxicity in 13 cases. Clinical presentation, characterized as jaundice with a marked increase in serum liver chemistry values, occurred 3 to 52 weeks after the ingestion of chaparral, and it resolved 1 to 17 weeks after most individuals stopped their intake of chaparral. The predominant pattern of liver injury was characterized as toxic or drug-induced cholestatic hepatitis; in 4 individuals, there was progression to cirrhosis; and in 2 individuals, there was acute fulminant liver failure that required liver transplants. CONCLUSIONS: These data indicate that the use of chaparral may be associated with acute to chronic irreversible liver damage with fulminant hepatic failure, and they underscore the potential for certain dietary supplement ingredients to cause toxic effects on the liver. Health professionals should be encouraged to inquire routinely about the use of dietary

supplements and other products, to be alert to potential adverse effects that may be associated with these products, and, finally, to report any serious adverse events associated with these products through the MEDWatch Program of the Food and Drug Administration.

Shulman LM, Minagar A, Weiner WJ. **Perdiem causing esophageal obstruction in Parkinson's disease.** Neurology 1999;52(3):670-1.

Slifman NR, Obermeyer WR, Aloi BK, Musser SM, Correll WA Jr, Cichowicz SM, Betz JM, Love LA. **Contamination of botanical dietary supplements by Digitalis lanata [see comments].** N Engl J Med 1998;339(12):806-11.

Spillane PK, Fisher DA, Currie BJ. **Neurological manifestations of kava intoxication [letter] [see comments].** Med J Aust 1997;167(3):172-3.

Srinivasan R, Smolinske S, Greenbaum D. **Probable gastrointestinal toxicity of Kombucha tea: is this beverage healthy or harmful?** J Gen Intern Med 1997;12(10):643-4.
Kombucha tea is a health beverage made by incubating the Kombucha "mushroom" in tea and sugar. Although therapeutic benefits have been attributed to the drink, neither its beneficial effects nor adverse side effects have been reported widely in the scientific literature. Side effects probably related to consumption of Kombucha tea are reported in four patients. Two presented with symptoms of allergic reaction, the third with jaundice, and the fourth with nausea, vomiting, and head and neck pain. In all four, use of Kombucha tea in proximity to onset of symptoms and symptom resolution on cessation of tea drinking suggest a probable etiologic association.

Steinmann A, Schatzle M, Agathos M, Breit R. **Allergic contact dermatitis from black cumin (Nigella sativa) oil after topical use.** Contact Dermatitis 1997;36(5):268-9.

Stewart MJ, Steenkamp V, Zuckerman M. **The toxicology of African herbal remedies.** Ther Drug Monit 1998;20(5):510-6.
Toxicity related to traditional medicines is becoming more widely recognized as these remedies become popular in developed countries. Accidental herbal toxicity occurs not only as a result of a lack of pharmaceutic quality control in harvesting and preparation but also because herbal remedies are believed to be harmless. Although there is a huge amount of data available documenting the pharmacologically active ingredients of many plants, it is seldom helpful to the toxicologist in an acute situation. Current analytic methods such as high-performance liquid chromatography, gas chromatography--mass spectrometry, and immunoassays can provide identification of the toxin in those few cases in which the history or symptoms give a clear lead, but broad screening methods remain to be developed. In most cases of plant poisoning, treatment continues to be only of symptoms, with few specific antidotes available. It is important that toxicologists in the West be alert to the possibility of encountering poisoning in patients due to traditional African remedies.

Takei A, Nagashima G, Suzuki R, Hokaku H, Takahashi M, Miyo T, Asai J, Sanada Y, Fujimoto T. **Meningoencephalocele associated with Tripterygium wilfordii treatment.** Pediatr Neurosurg 1997;27(1):45-8.

We treated a male infant with occipital meningoencephalocele associated with the taking of Tripterygium wilfordii. The infant was delivered normally at 38 weeks of gestation with a huge cystic mass protruding from the occiput. He was diagnosed with occipital meningoencephalocele and cerebellar agenesis. His mother had taken T. wilfordii for rheumatoid arthritis early in her pregnancy. T. wilfordii is a herbal medicine used for rheumatoid arthritis and male contraception. Since its toxicity is high and its use during pregnancy is restricted, it is the most likely cause of this infant's anomalies.

Tan PH, Chou AK, Perng JS. **Accidental shock during epidural anesthesia in a patient with NSAID-induced hyporeninemic hypoaldosteronism.** J Clin Anesth 1997;9(5):424-7.
An obese man suffered cardiac arrest twenty minutes after receiving epidural anesthesia for incision and debridement of wound over the right leg. The patient's condition stabilized after emergent cardiopulmonary resuscitation. It was found that the patient had been self-administering an herbal drug continuously for a year and a half, and that this drug contained ethoxybenzamide, which is a nonsteroidal anti-inflammatory drug (NSAID). Low plasma renin and aldosterone levels were noted from the blood sample taken at the time of the cardiac arrest. The cardiac arrest was believed to be related to NSAID-induced hyporeninemic hypoaldosteronism, superimposed with epidural anesthesia-induced sympathectomy.

Tanaka I. **[Case of chronic renal tubular interstitial nephritis with syndrome of disappearing bile ducts (letter)].** Nippon Naika Gakkai Zasshi 1998;87(8):1601. (Jpn)

Tateno S, Kobayashi Y. [Balkan nephropathy, Balkan endemic nephropathy]. Ryoikibetsu Shokogun Shirizu 1997;(17 Pt 2):716-9. (Jpn)

Thompson CA. **Adverse reactions to alternative medicine.** Am J Health Syst Pharm 1997 Aug 1;54:1707.
IPA COPYRIGHT: ASHP The lack of data regarding adverse reactions to vitamins, minerals, and herbs marketed as alternative medical products due to a 1994 federal law that declassified these products as food is discussed, including the role of manufacturers in quality control of these products, current U.S. Food and Drug Administration (FDA) activities regarding new regulations and Good Manufacturing Practices for the dietary supplements industry, and the role of pharmacists in monitoring patients who use these supplements and reporting any adverse reactions to them.

Tomas ME, Garfia C, Marcos MS, Casis B, Perez-Carreras M, Manzano ML, Yela C. **[Intense cholestasis associated with medicinal herbs (letter].** Rev Esp Enferm Dig 1998;90(7):529-30. (Spa)

Tsiodras S, Shin RK, Christian M, Shaw LM, Sass DA. **Anticholinergic toxicity associated with lupine seeds as a home remedy for diabetes mellitus.** Ann Emerg Med 1999;33(6):715-7.
We describe a case of sparteine intoxication associated with using a preparation from lupine seeds. A female patient of Portuguese origin presented to the emergency department with classic anticholinergic signs after ingestion of a lupine seed extract. She took the preparation with the belief it represented a cure for her recently diagnosed diabetes. Analysis of the patient's lupine

bean extract identified the preponderant compound as oxo-sparteine by gas chromatography/mass spectrometry. Intoxication by lupine seeds rarely occurs in human beings. To our knowledge, no medical or toxicologic evidence supports a belief that lupine extract could lower serum glucose levels. This case highlights the need for emergency care providers to be aware of the health hazards that can be associated with the use of such home remedies.

Van Ypersele De Strihou C. **Chinese herbs nephropathy or the evils of nature.** Am J Kidney Dis 1998;32(3):l-Lii.

Van Ypersele De Strihou C. **Chinese herbs nephropathy or the evils of nature [letter].** Am J Kidney Dis 1999;33(2):412.

Van Ypersele De Strihou C. **[Gentle medicine, harmless medicine? (editorial)].** Nephrologie 1998;19(1):5-6. (Fre)

Van Ypersele De Strihou C. **Valvular heart disease and Chinese-herb nephropathy [letter; comment].** Lancet 1998;351(9107):991-2.

Vanherweghem JL. **Association of valvular heart disease with Chinese-herb nephropathy [letter; comment] [see comments].** Lancet 1997;350(9094):1858.

Vanherweghem JL. **Nephrotoxicitiy of herbal remedies and trace elements used as food additives. In: De Broe, M. E., Et Al., Editors. Clinical Nephrotoxins: Renal Injury From Drugs And Chemicals.** Dordrecht(Netherlands), Norwell(MA): Kluwer Academic Publishers; 1998. P. 19-423.
BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK CHAPTER HUMAN FOOD ADDITIVES TOXICITY HERBAL REMEDIES TRACE ELEMENTS ACUTE RENAL FAILURE FUMARIC ACID GERMANIUM NEPHROPATHY ANALGESICS TOXICOLOGY NEPHROLOGY EPIDEMIOLOGY CHINESE HERBS UROLOGIC DISEASE DRUG INDUCED AFRICA ETHIOPIAN REGION.

Vanherweghem LJ. **Misuse of herbal remedies: the case of an outbreak of terminal renal failure in Belgium (Chinese herbs nephropathy) [see comments].** J Altern Complement Med 1998;4(1):9-13.
At least 100 cases of extensive interstitial fibrosis of the kidneys were observed in Belgium in women who had followed a weight-loss regimen that included the use of Chinese herbs. The possible relation between the renal disease and these Chinese herbs was investigated. It was shown that the prescribed Chinese herb called Stephania tetrandra was, in fact, inadvertently replaced by another Chinese herb, namely Aristolochia fangchi in the powdered extracts delivered in Belgium and in France. The development of renal disease in about 100 patients exposed to the so-called Stephania tetrandra stresses the need for more stringent control of herbal medicine.

Vila L, Sanchez G, Sanz ML, Dieguez I, Martinez A, Palacios R, Martinez J. **Study of a case of hypersensitivity to lettuce (Lactuca sativa).** Clin Exp Allergy 1998;28(8):1031-5.

BACKGROUND: Allergic reactions to lettuce (Lactuca sativa) are not too frequent and few cases of systemic adverse reactions after its ingestion have been described. OBJECTIVE: We report a case of clinical sensitization to lettuce on a patient who presented mucocutaneous manifestations after its ingestion, with positive skin tests, histamine release test and serum specific-IgE to lettuce. The allergens responsible for this sensitization were also characterized by means of SDS-PAGE immunoblotting. MATERIALS AND METHODS: We performed skin tests, histamine release test, serum specific IgE determination and CAP inhibition with lettuce and mugwort (Artemisia vulgaris) extracts. An aqueous and enriched lettuce (from loose leaf type) extract was subjected to SDS-PAGE immunoblotting for determination of its IgE-binding components. RESULTS AND CONCLUSIONS: CAP inhibition showed antigenic community between lettuce and mugwort. Four protein bands from the lettuce extracts with molecular weights of 50, 43, 39 and 16 kDa exhibited IgE-binding properties.

Violon C. **Belgian (Chinese herb) nephropathy: why?** J Pharm Belg 1997;52(1):7-27.
During the last years several patients with renal failure were admitted in Brussels hospitals. The progressive interstitial fibrosis with tubular atrophy seen in these patients has been ascribed to the slimming therapy preceding the pathology. The nephropathy was remarkable with regard to its extensive fibrotic process and the rapidity of its evolution. The ingestion of Aristolochia fangchi instead of the prescribed Stephania tetrandra, one of the components of the slimming therapy, was put forward as hypothesis for the etiology of the nephropathies in the literature. Questions however remain unanswered: Why have certain persons, among thousands similarly treated including ingestion of Aristolochic acids, not withstood the treatment? Why is there no correlation between the length of treatment and the occurrence nor the degree of illness? Last but not least: Is it in the actual conditions possible to be confident again in slimming treatments as the concerned one? We made an overview of the pharmacological action and possible (nephro) toxicity of the known components of the concerned therapy. Concerning the Chinese plants we have described and commented on the procedures for quality control actually at disposal and the difficulties in differentiation between resembling species and possible substitute herbs. We have described largely the traditional and medicinal use of the involved Chinese plants as to evaluate their implication in the nephrotoxicity. The elements of the therapy possibly relevant in the etiology of the disease are mentioned. The overview shows that different elements of the therapy are hazardous. Attention is caught to the danger of the use of (Chinese) herbs of unknown origin when nor the indications nor the form of preparation--in this case decoctions--are respected and when the quality cannot be assured, due to lack of (official) operating procedures. Medicinal plants as those implied contain secondary metabolites (bis)-benzylisoquinoline-alkaloids, dihydroxy-diallyl-biphenyls, aristolochic acids) with strong pharmacological (and possibly toxic) actions. Attention is caught to the danger of alternative therapies as mesotherapy. Products are injected which are not proved safe for this administration way. The administration during long periods of cocktails with anorectics (fenfluramine and diethylpropion) in association with a diuretic, a tranquilizer, plants with laxative and atropinergic action are alike to be at the origin of susceptibility in the excretion system. Under these circumstances exposure to any toxic product might cause renal failure. Several years have passed after the scientific reports of the first nephropathy cases in Belgium. We are afraid that prohibiting (temporarily) three Chinese herbs (Stephania tetrandra, Aristolochia fangchi and Magnolia officinalis) does not provide enough safety in order to assume responsibilities for common health care. Keeping in mind that these

treatments were not meant to cure any disease but only for slimming, we ask Belgian authorities to regulate strictly the use of (Chinese) herbal medicines, the products and practices in alternative practices as mesotherapy and cocktail-treatments.

Weber KT. **Herbs, seeds, oil and eggs: a vasotoxic salad.** Cardiovasc Res 1997;34(2):266-7.

Weisbord SD, Soule JB, Kimmel PL. **Poison on line--acute renal failure caused by oil of wormwood purchased through the Internet [published erratum appears in N Engl J Med 1997 Nov 13;337(20):1483].** N Engl J Med 1997;337(12):825-7.

Wong ST, Chan HL, Teo SK. **The spectrum of cutaneous and internal malignancies in chronic arsenic toxicity.** Singapore Med J 1998;39(4):171-3.
We report 3 patients of chronic arsenic poisoning with characteristic skin changes. All 3 patients had a past history of asthma and were treated with Traditional Chinese Medication. We believe that the Chinese medications were the source of arsenic poisoning. Two of the 3 patients also had internal malignancy. The association of arsenic with internal malignancy is reviewed.

Wood B, Rademaker M, Oakley A, Wallace J. **Pellagra in a woman using alternative remedies [see comments].** Australas J Dermatol 1998;39(1):42-4.
A young woman presented with pellagra. Dietary intake of niacin was in excess of recommended guidelines. She had a low body mass index and was taking a number of alternative remedies. Resolution was rapid with oral nicotinic acid and discontinuation of the remedies.

Woolley BH. **Frequently asked questions about the serotonin syndrome.** Utah Pharm Dig 1997 Apr;107:14-5.
IPA COPYRIGHT: ASHP A brief overview of the serotonin syndrome, an iatrogenic condition caused by the additive interaction of multiple serotonergic agonists, is presented, including the symptoms; the foods, drugs, and herbs that are implicated in the syndrome are briefly discussed.

Wright IM. **Neonatal effects of maternal consumption of blue cohosh [letter].** J Pediatr 1999;134(3):384-5.

Wu CL, Hsu WH, Chiang CD, Kao CH, Hung DZ, King SL, Deng JF.

Lung injury related to consuming Sauropus androgynus vegetable.

J Toxicol Clin Toxicol 1997;35(3):241-8.
BACKGROUND: Taking Sauropus androgynus, a Malaysian food, to reduce weight began as a fad in Taiwan in 1994. Some advocates of this fad developed pulmonary dysfunction. The aim of this study is to report the lung injury in patients taking Sauropus androgynus. METHODS: From July 1995 to November 1995, we investigated 104 nonsmoking patients (one male and 103 females) with chest roentgenography, pulmonary function, test, and Technetium 99m-labeled diethylene triamine penta-acetate (Tc-99m DTPA) radioaerosol inhalation lung scintigraphy. RESULTS: Among the 90 patients receiving Tc-99m DTPA inhalation lung scan, 46 (51.1%) patients had increased clearance of Tc-99m DTPA from lung and 20 (22.2%) patients had

inhomogeneous deposition of the submicronic radioaerosol. Eighteen (18/100) patients had obstructive ventilatory impairment in pulmonary function test. Analyzing the results, we found that the patients with respiratory symptoms (n = 42) took more vegetables (p = 0.016), had increased clearance of Tc-99m DTPA (p = 0.010) and had lower FEV1 (p = 0.001), FEV1/FVC (p < 0.001), FEF25-75 (p = 0.001), VC (p = 0.002) and DLCO (p = 0.009) than the patients without respiratory symptoms (n = 62). FEV1 and FEV1/FVC were significantly reduced in patients with severe impairment of alveolar permeability. The cumulative dosage and duration of exposure were significantly associated with the reduction of FEV1 and FEV1/FVC. CONCLUSION: The lung injury after taking Sauropus androgynus involves alveoli and/or small airways and is manifest as obstructive ventilatory impairment with inhomogeneous aerosol distribution and increased lung epithelial permeability.

Wuthrich B, Schmid-Grendelmeyer P, Lundberg M. **Anaphylaxis to saffron.** Allergy 1997;52(4):476-7.
BIOSIS COPYRIGHT: BIOL ABS. RRM CASE STUDY CROCUS-SATIVA HUMAN ADULT PATIENT MALE SAFFRON ANAPHYLAXIS FOOD ALLERGY SCRATCH TEST RAST INHIBITION RADIOALLERGOSORBENT TEST INHIBITION ALLERGY HERBS AND SPICES IMMUNE SYSTEM DISEASE DIAGNOSTIC METHOD.

Yamada Y, Sakoda H, Inoue T, Kubo M, Fushimi H, Minami T, Kaneyama M. **[Lead poisoning due to Chinese herbal medication in two patients with non-insulin-dependent diabetes mellitus].** J Jpn Diabetes Soc 1998;41(10):933-6. (Jpn)
BIOSIS COPYRIGHT: BIOL ABS. Lead poisoning due to a side effect of Chinese herbal medication in two patients with non-insulin-dependent diabetes mellitus is reported here. Both patients complained of abdominal pain, severe constipation and insomnia. Laboratory data showed normocytic anemia with reticulocytosis, basophilic stippling in erythrocytes, elevated hemoglobin F level and increased excretion of urinary porphyrin, indicating abnormalities of hemoglobin synthesis. Blood lead level and urinary lead excretion were increased by their own judgement, both patients had taken several non-autorized drugs, one of which, "Zhen qi jiang tang," was thought to be the causative drug containing a high level of lead. Since lead contents in the capsules were distributed over a wide range, and another patient had taken the same drug but did not show symptoms of lead poisoning, it was suggested that some capsules were contaminated with lead. Patients were treated by dimercaprol intramuscularly, and gradually symptoms and data have improved.

Yamashiki M, Nishimura A, Nobori T, Nakabayashi S, Takagi T, Inoue K, Ito M, Matsushita K, Ohtaki H, Kosaka Y. **In vitro effects of sho-saiko-to on production of granulocyte colony-stimulating factor by mononuclear cells from patients with chronic hepatitis C.** Int J Immunopharmacol 1997;19(7):381-5.
During the past 2 years, drug-induced interstitial pneumonia was reported in 66 Japanese patients, mainly among chronic hepatitis C patients, undergoing treatment with the Japanese herbal medicine "Sho-saiko-to" (TJ-9). As interstitial pneumonia is also induced by granulocyte colony-stimulating factor (G-CSF), we examined the effects of TJ-9 on G-CSF production in peripheral blood mononuclear cells. In patients with hepatitis B or C, G-CSF production in the absence of any stimulation was significantly lower than healthy controls (p < 0.01). G-CSF

production increased along with the increase of TJ-9 levels, and this could induce excessive production of G-CSF in hepatitis C patients, and this may be a cause of interstitial pneumonia.

Yang HY, Chen CF. **Pharmacology and toxicology of herbal medicine: subacute toxicity of commonly used Chinese drugs.** J Toxicol Sci 1998;23(Suppl 2):229-33.

Yang Jiong, Hu Suping, Zhong Lihou, et al . **[An investigation into the major allergic pollens in Wuchang district].** Acta Acad Med Hubei 1998;19(1):37-9. (Chi)
BIOSIS COPYRIGHT: BIOL ABS. An preliminary investigation on airborne pollens in Wuchang district showed that platanus, pinus, artemisia is the major pollen. Inraderimed skin test against 13 pollens was done among 210 allergic patients. The results were:positive rate of artemisia is the highest of all, ambrosia next to it. From high to low., the positive rate is humulus, platanus, broussoretia, etc. Pollens allerge concentrated from March to May and August to October especially in the latter. It is suggested that platanus is the main allergic pollen, artemisia, ambrosia, humulus is the main allergic pollen in Summer and Autumn in Wuchang district.

Yeung CY. **Changing pattern of neonatal jaundice and kernicterus in Chinese neonates.** Chin Med J (Engl) 1997;110(6):448-54.

Yokoi T. **[Chinese herbs nephropathy in the Kansai area: a warning report (letter)].** Nippon Jinzo Gakkai Shi 1998;40(5):364-5. (Jpn)

Yoshikubo S, Kimura K, Mizutari K, Kamo S, Maeda K. **[A case of drug-induced liver injury due to bukuryo-in-go-hange-koboku-to].** Nippon Shokakibyo Gakkai Zasshi 1997;94(8):564-8. (Jpn)

Yu CM, Chan JC, Sanderson JE. **Chinese herbs and warfarin potentiation by 'danshen'.** J Intern Med 1997;241(4):337-9.
Drug interactions with warfarin can be dangerous and although common drug interactions are now well recognized those with Chinese herbs are not widely appreciated. 'Danshen' is a herbal medicine often used for various complaints, particularly cardiovascular, in the Chinese community. We report a case of danshen-induced overcoagulation with severe and dangerous abnormalities of clotting in a patient with rheumatic heart disease.

Zahn KA, Li RL, Purssell RA. **Cardiovascular toxicity after ingestion of "herbal ecstacy".** J Emerg Med 1999;17(2):289-91.
"Herbal Ecstacy" (sic) is an alternative drug of abuse usually containing both ephedrine and caffeine. Our literature search did not reveal any other reported cases of cardiovascular toxicity related to herbal "drugs of abuse." A case of cardiovascular toxicity following the ingestion of herbal ecstacy is presented. A 21-year-old male presented to the emergency department with an initial blood pressure of 220/110 mmHg and ventricular dysrhythmias after ingesting four capsules of herbal ecstacy. He was treated with lidocaine and sodium nitroprusside, and his symptoms resolved in 9 h. The pathophysiology and clinical course of ephedrine toxicity are discussed. Emergency physicians should consider ephedrine preparations in the differential

diagnosis of patients presenting with a sympathomimetic toxidrome. Drugs of abuse containing "herbal" products can produce serious morbidity and mortality.

Mechanisms/Pharmacology

Adegoke GO, Kumar MV, Sambaiah K, Lokesh BR. **Inhibitory effect of Garcinia kola on lipid peroxidation in rat liver homogenate.** Indian J Exp Biol 1998;36(9):907-10.
Garcinia kola, (a herb grown in Nigeria; calorific value 358.54 k.cal/100 g) inhibited in vitro lipid peroxidation of rat liver homogenate in a dose dependent manner. The inhibitory activity of G.kola was not affected by heating (100 degrees C/10 min). The antioxidant component of G.kola was soluble in aqueous and ethanolic media. The active component(s) in G. kola responsible for its inhibitory activity on lipid peroxidation is tentatively identified as isoflavones.

Ahn YJ, Lee CO, Kweon JH, Ahn JW, Park JH. **Growth-inhibitory effects of Galla Rhois-derived tannins on intestinal bacteria.** J Appl Microbiol 1998;84(3):439-43.
The growth-inhibitory activity of Galla Rhois-derived materials towards 17 intestinal bacteria was evaluated using an impregnated paper disc method. The biologically active components of Galla Rhois were characterized as the tannins methyl gallate (MG) and gallic acid (GA) by spectral analysis. The growth responses varied with bacterial strain tested. In the test using 10 mg disc-1, MG and GA produced a clear inhibitory effect on harmful bacteria such as Clostridium perfringens, Cl. paraputrificum, Eubacterium limosum, Bacteroides fragilis, Staphylococcus aureus and Escherichia coli. Methyl gallate showed no growth-inhibitory activity towards Bifidobacterium adolescentis or B. longum whereas the growth of B. bifidum, B. breve, B. infantis, B. animalis, B. thermophilum, Lactobacillus acidophilus, Lact. plantarum and Streptococcus faecalis was slightly affected. However, GA did not adversely affect the growth of the bifidobacteria and lactobacilli. At 5 mg disc-1, MG significantly inhibited the growth of Cl. perfringens and Cl. paraputrificum but did not affect the growth of the bifidobacteria and lactobacilli. At 1 mg disc-1, MG greatly inhibited the growth of Cl. perfringens alone. These results may be an indication of at least one of the pharmacological actions of Galla Rhois.

Akamatsu H, Asada Y, Horio T. **Effect of keigai-rengyo-to, a Japanese kampo medicine, on neutrophil functions: a possible mechanism of action of keigai-rengyo-to in acne.** J Int Med Res 1997;25(5):255-65.
On the basis of recent reports that keigai-rengyo-to (TJ-50), an oral Japanese Kampo (herb) medicine, is clinically effective in treating acne, and that tetracyclines are effective against acne by acting directly as an antioxidant on infiltrated neutrophils, we investigated the effect of TJ-50 on the generation of reactive oxygen species (ROS), using human neutrophils and a cell-free, xanthine-xanthine oxidase system. The species investigated were superoxide radical anion (O2-), hydrogen peroxide (H2O2), and hydroxyl radical (OH.). In addition, neutrophil chemotaxis, phagocytosis and calcium concentration, [Ca2+]i in neutrophils were also assessed. TJ-50 significantly decreased neutrophil-generated O2-, H2O2 and OH. in a dose-dependent manner. Three kinds of ROS generated in the cell-free system were also reduced in the presence of TJ-50. On the other hand, the medicine did not markedly affect neutrophil chemotaxis, phagocytosis or

[Ca2+]i in neutrophils. Our results indicate that the clinical effectiveness of TJ-50 in the treatment of acne may be due partly to its antioxidant action on infiltrated neutrophils.

Arai I, Komatsu Y, Hirai Y, Shingu K, Ida Y, Yamaura H, Yamamoto T, Kuroiwa Y, Sasaki K, Taguchi S. **Stimulative effects of saponin from kikyo-to, a Japanese herbal medicine, on pancreatic exocrine secretion of conscious rats.** Planta Med 1997;63(5):419-24.
Our previous report stated that kikyo-to, a Japanese herbal medicine, consisting of the roots of Platycodon grandiflorum and Glycyrrhiza sp., stimulates the pancreatic exocrine secretion of conscious rats. The present study focused on the effective components of kikyo-to and the mechanism of stimuli to pancreatic secretion of rats. When 10 to 100 mg of platycodin D, a saponin from the root of Platycodon grandiflorum, was intragastrically administered, the pancreatic secretion of rats was stimulated. At the same time, the plasma CCK concentration increased. On the other hand, the stimulative effects of glycyrrhizin, a saponin from the root of Glycyrrhiza sp. were weak compared to platycodin D. The effects of 10 mg/kg of platycodin D on pancreatic secretion were inhibited by loxiglumide (50 mg/kg, i.g.), a CCK receptor antagonist. In contrast, the suppressive effect of atropine (300 micrograms/kg/h, i.v.) on pancreatic secretion was reduced by administering 10 mg/kg of platycodin D. In addition, up to 1 mM of platycodin D did not inhibit the trypsin activities in vitro. In conclusion, kikyo-to serves to stimulate pancreatic exocrine secretion mainly because platycodin D causes gastrointestinal hormones, particularly, CCK to be released from the duodenum.

Asano K, Matsuishi J, Yu Y, Nemoto K, Nakazawa M, Kasahara T, Hisamitsu T. **Suppressive activity of the chloroform extract of Tripterygium wilfordii Hook f on effector T cell activation during Hymenolepis nana infection in mice.** Am J Chin Med 1998;26(2):181-9.
The chloroform extract of Tripterygium wilfordii Hook f (TWH extract) administered into mice daily at doses of 80.0 to 200.0 micrograms/kg (but not 40.0 micrograms/kg) caused suppression of protective immunity to Hymenolepis nana when the extract was injected subcutaneously during the induction phase of protective immunity. Daily administration of 200.0 micrograms/kg TWH extract, during the course of larval development from challenge, also suppressed protective immunity. Inhibition of protective immunity was only observed in mice that received TWH extract for 6 days at a daily dose of 200.0 micrograms/kg and were challenged 24 h after the final injection. TWH extract did not inhibit formation of effector cells that mediate delayed type hypersensitivity (DTH) to H. nana egg antigen when the extract was administered subcutaneously at a dose of 200.0 micrograms/kg/day for 5 days before cell preparation. However, TWH extract did inhibit DTH effector cell activation when cells prepared from infected, PBS-injected mice were transferred into 200.0 micrograms/kg TWH extract-treated recipient mice. These results strongly indicate that TWH extract cannot inhibit the generation of effector cells but will suppress their function in vivo.

Bae EA, Han MJ, Kim NJ, Kim DH. **Anti-Helicobacter pylori activity of herbal medicines.** Biol Pharm Bull 1998;219(9):990-2.

Bennett DA Jr, Phun L, Polk JF, Voglino SA, Zlotnik V, Raffa RB. **Neuropharmacology of St. John's Wort (Hypericum).** Ann Pharmacother 1998;32(11):1201-8.
OBJECTIVE: To review preclinical information related to possible antidepressant mechanism(s)

of action of St. John's wort in order to address the issue of whether its purported clinical effectiveness has a rational pharmacologic basis. DATA SOURCES: Primary and review articles were identified by a MEDLINE search (1966-January 1998) and through secondary sources. Many of the original German articles had English abstracts, but where necessary, German articles were translated into English. The results of a new screen of hypericin activity at receptor and uptake sites are summarized. STUDY SELECTION AND DATA EXTRACTION: All of the articles identified from the data sources were evaluated and all information deemed relevant was included in this review. DATA SYNTHESIS: The neuropharmacology of St. John's wort has been examined in only a few studies. A mechanism similar to that of the synthetic antidepressants, such as the selective serotonin-reuptake inhibitors or monoamine oxidase (MAO) inhibitors, might play a role, but other mechanisms are possible. CONCLUSIONS: Hypericum extracts have only weak activity in assays related to mechanisms of the synthetic antidepressants, that is, inhibition of MAO, catechol O-methyltransferase, or serotonin reuptake. It has been postulated that the clinical efficacy of St. John's wort could be attributable to the combined contribution of several mechanisms, each one too weak by itself to account for the overall effect. The recent demonstration of a significant affinity of hypericin for sigma receptors presents new possibilities for consideration.

Bork PM, Schmitz ML, Kuhnt M, Escher C, Heinrich M. **Sesquiterpene lactone containing Mexican Indian medicinal plants and pure sesquiterpene lactones as potent inhibitors of transcription factor NF-kappaB.** FEBS Lett 1997;402(1):85-90.
The potential inhibitory effect of 54 Mexican Indian medicinal plants on the activation of transcription factor NF-kappaB was studied. Band-shift experiments identified the ethanolic leaf extracts of Artemisia ludoviciana ssp. mexicana, Calea zacatechichi, and Polymnia maculata (all rich in sesquiterpene lactones) as inhibitors of NF-kappaB down to a concentration of 25 microg/ml. The sesquiterpene lactones isohelenin and parthenolide prevented NF-kappaB activation completely as low as 5 microM. Treatment of HeLa cells with leaf extract of A. ludoviciana ssp. mexicana, isohelenin and parthenolide prevented the induction of transcription on the IL-6 promoter. These experiments identify the eudesmanolide and germacranolide type of sesquiterpene lactones as potent non-antioxidant inhibitors of NF-kappaB. All plants active in the NF-kappaB assay also showed a delay in the onset of capillary reactions of the allantois membrane in a physiological model for anti-inflammatory activity - the HET-CAM assay.

Burger RA, Torres AR, Warren RP, Caldwell VD, Hughes BG. **Echinacea-induced cytokine production by human macrophages.** Int J Immunopharmacol 1997;19(7):371-9.
Echinacea purpurea, a plant originally used by native Americans to treat respiratory infections, was evaluated for its ability to stimulate the production of cytokines by normal human peripheral blood macrophages in vitro. Commercial preparations of echinacea fresh pressed juice and dried juice were tested at concentrations ranging from 10 micrograms/ml to 0.012 microgram/ml and compared to endotoxin stimulated and unstimulated controls. Cytokine production was measured by ELISA after 18 h of incubation for IL-1 and 36 and 72 h for TNF-alpha, IL-6, and IL-10. Macrophages cultured in concentrations of echinacea as low as 0.012 microgram/ml produced significantly higher levels of IL-1, TNF-alpha, IL-6 and IL-10 ($P < 0.05$) than unstimulated cells. The high levels of IL-1, TNF-alpha, and IL-10 induced by very low levels of echinacea are consistent with an immune activated antiviral effect. Echinacea induced lower levels of IL-6 in

comparison to the other cytokines measured. These results demonstrate the immune stimulatory ability of the unpurified fresh pressed juice of Echinacea purpurea and offer some insight into the nature of the resulting immune response as compared to endotoxin.

Caballero T, Pascual C, Garcia-Ara MC, Ojeda JA, Martin-Esteban M. **IgE crossreactivity between mugwort pollen (Artemisia vulgaris) and hazelnut (Abellana nux) in sera from patients with sensitivity to both extracts.** Clin Exper Allergy 1997;27(10):1203-11. BIOSIS COPYRIGHT: BIOL ABS. Background. An association between sensitization to Compositae pollens and hypersensitivity to hazelnut has been previously described. There is no previous in vitro study about crossreactivity between mugwort pollen and hazelnut. Objectives. To study mugwort pollen and hazelnut allergens and to assess if there is IgE crossreactivity between mugwort pollen and hazelnut. Methods. A serum pool formed by 28 individual sera with specific IgE to mugwort pollen and hazelnut was used to investigate IgE crossreactivity. RAST-inhibition, SDS-PAGE/IEF immunoblotting inhibition assays were performed by preincubation of the sera with mugwort pollen and hazelnut. Results. RAST to hazelnut was inhibited up to 63% by mugwort pollen, but the mugwort pollen RAST was only inhibited up to 36% by hazelnut. In SDS-PAGE immunoblotting mugwort pollen showed nine allergens ranging from

Carlson M, Thompson RD. **Liquid chromatographic determination of methylxanthines and catechins in herbal preparations containing guarana.** J AOAC Int 1998;81(4):691-701. Herbal preparations derived from the dried seeds of guarana (Paullinia cupana) have become a popular nutritional supplement used for stimulatory purposes. Once considered a drug substance in the United States, guarana currently is classified as a food additive and dietary supplement. The pharmacological activity of guarana-containing products is primarily due to methylxanthine alkaloids. For guarana preparations, methylxanthine levels and, more significantly, the presence of several polyphenol compounds (i.e., catechins) provide phytochemical markers of authenticity. Methylxanthines and polyphenols are extracted from sample matrix with a heated phosphate buffer-methanol solution, the cooled extract is filtered, and the extract is injected into the liquid chromatographic (LC) system. A Nova-Pak C18 column eluted with phosphate buffer-methanol mobile phase (pH = 3.50) and monitored at 272 nm gave satisfactory resolution for the methylxanthines theobromine, theophylline, caffeine and the polyphenols (+)-catechin and (-)-epicatechin. Twenty-four products including dried seeds, dried paste, seed powders, tablets, and capsule formulations were assayed and conclusions were drawn about their authenticity. The LC system responded linearly to methylxanthines over the 100-fold range in concentration from 0.043 to 4.30 micrograms/mL for theobromine and caffeine and from 0.041 to 4.10 micrograms/mL for theophylline. Precision data for the 3 methylxanthines obtained from 10 different products (n = 5) gave relative standard deviation (RSD) values of 1.18-15.52% within a concentration range of 0.01-52.28 mg/g. Recoveries of methylxanthines from fortified products varied from 87.5 to 120.0%. The response for catechins was linear over a 200-fold range in concentration of 0.05-10.0 micrograms/mL. Precision data from 5 products (n = 5) gave RSD values of 1.08-5.54% within a concentration range of 0.34-32.65 mg/g. Recoveries from these products ranged from 87.7 to 109.7%. Results and chromatographic profiles for 14 commercial products in solid dosage form indicate that a number of these products may not contain authentic

guarana as an active ingredient or contain less than the declared quantity of guarana. The proposed procedure also was applied to 2 carbonated soft drinks and a sample of mate.

Chaumontet C, Droumaguet C, Bex V, Heberden C, Gaillard-Sanchez I, Martel P. **Flavonoids (apigenin, tangeretin) counteract tumor promoter-induced inhibition of intercellular communication of rat liver epithelial cells.** Cancer Lett 1997;114(1-2):207-10.
We have shown previously that two flavonoids, apigenin and tangeretin, enhance gap junctional intercellular communication (GJIC) in rat liver epithelial cells, named REL cells. Here, we show that these two flavones also antagonize the inhibition of GJIC induced by tumor promoters like 12-O-tetradecanoyl-phorbol-acetate (TPA) and 3,5,di-tertio-butyl-4-hydroxytoluene (BHT). Their preventive effect is rapid. It does not seem to involve any change of the amount of the connexin expressed in REL cells, connexin 43 (Cx 43), and in its phosphorylation state. Other flavonoids tested including naringenin, myricetin, catechin and chrysin did not enhance GJIC nor counteract TPA-induced inhibition of GJIC.

Chavali SR, Weeks CE, Zhong WW, Forse RA. **Increased production of TNF-alpha and decreased levels of dienoic eicosanoids, IL-6 and IL-10 in mice fed menhaden oil and juniper oil diets in response to an intraperitoneal lethal dose of LPS.** Prostaglandins Leukot Essent Fatty Acids 1998;59(2):89-93.
Eicosapentaenoic acid (EPA) and the non-methylene interrupted fatty acids (NMIFA) displace arachidonic acid (AA: 20:4omega6 -5,8,11,14) in the membrane phospholipids. Unlike EPA (20:5omega3 -5,8,11,14,17), the NMIFA (20:3omega6 -5,11,14 and 20:4omega3 -5,11,14,17) lacking the delta-8 double bond are not substrates for the formation of eicosanoids. For 20 days, the mice were fed diets containing 5wt% dietary fats from various sources. The magnitudes in the production of eicosanoids and cytokines produced in response to an intraperitoneal injection of endotoxin in mice fed menhaden fish oil (MO) diets enriched with EPA were compared with those maintained on juniper oil (JO) containing NMIFA or on safflower oil (SO), a major source of the AA precursor, linoleic acid. The levels of PGE2, 6-keto-PGF1alpha and TXB2 were markedly lower ($P < 0.01$) in animals fed either MO or JO diets compared to the controls. The plasma levels of tumor necrosis factor (TNF)-alpha were significantly higher ($P < 0.05$) with a concomitant decrease of interleukin (IL)-6 and of IL-10 in mice fed MO or JO diets ($P < 0.01$) compared to those fed SO diet. These data suggest that the effects of consuming NMIFA of JO despite their inability to form eicosanoids are similar to those of feeding EPA which forms biologically active alternate metabolites.

Chen L, Hong JY, So E, Hussin AH, Cheng WF, Yang CS. **Decrease of hepatic catalase level by treatment with diallyl sulfide and garlic homogenates in rats and mice.** J Biochem Mol Toxicol 1999;13(3-4):127-34.
Diallyl sulfide (DAS) is a flavor compound derived from garlic and is active in the inhibition of chemically induced cytotoxicity and carcinogenicity in animal models. This study was conducted to examine the effects of the treatment of DAS and garlic homogenates on the activities of catalase, glutathione peroxidase, and superoxide dismutase. Male Sprague-Dawley rats were treated with DAS i.g. at daily doses of 50 or 200 mg/kg for 8 days, causing the hepatic catalase activity to decrease by 55 and 95%, respectively. Such a decrease in hepatic catalase activity was also observed when the DAS treatment was extended to 29 days. Western blot analysis showed

that the DAS treatments resulted in corresponding decreases in the liver catalase protein level. No significant change in the catalase activity in the kidney, lung, and brain was observed with the treatments, but a slight decrease in heart catalase activity was observed. These treatments did not cause significant changes in superoxide dismutase and glutathione peroxidase activities in these tissues. Treatment with DAS at a daily dose of 200 mg/kg for 1-7 days resulted in a gradual decrease in the liver catalase activity to 5% of the control level, but it did not decrease the erythrocyte catalase activity. Treatment of rats with fresh garlic homogenates (2 or 4 g/kg, i.g., daily for 7 days) caused a 35% decrease in liver catalase activity. A/J mice treated with DAS and garlic homogenates also showed a decrease in the liver catalase activity. Diallyl sulfone (DASO2), a DAS metabolite, however, did not effectively decrease catalase activity in mice. The catalase activity was not inhibited by either DAS or DASO2 in vitro. The present results demonstrate that treatment with DAS and garlic homogenates decrease the hepatic catalase level in rats and mice.

Chiu KW, Fung AY. **The cardiovascular effects of green beans (Phaseolus aureus), common rue (Ruta graveolens), and kelp (Laminaria japonica) in rats.** Gen Pharmacol 1997;29(5):859-62.
1. The hypotensive effect of green beans, common rue and kelp was recently shown in normotensive rats in vivo. A number of mechanisms of action of these aqueous extracts was identified. The present study examined these actions at the tissue level in vitro with possible interactions of these extracts. 2. Rue showed positive chronotropic and inotropic effects on isolated right atria. Green beans and kelp alone showed negative chronotropic effects on isolated right atria but no effect on atrial tension (AT). A combination of green beans and kelp showed no additive effect on the decrease in atrial rate (AR) nor any negative inotropic responses. Combinations of rue and green beans and of rue and kelp showed responses that were either positive or negative chronotropically, were not dose dependent and were less than the sum total of their individual responses (i.e., subtractive). A combination of all three showed subtractive effects on the decrease in AR that were dose related. No change in AT was observed upon treatment with a combination of the three plant extracts in spite of the positive inotropic effect of true. 3. Rue and kelp alone relaxed KCl preconstricted rat tail artery strips probably by a direct effect of vascular smooth muscle. Green beans had no effect. The combination of rue and kelp exerted a subtractive relaxation effect. These plants therefore contained cardiovascular active substances that had a direct effect on the cardiovascular system. These substances further interacted to modify their cardiovascular effects. 4. Data explained why herbs, as in herbal medicine, should be used together therapeutically.

Choudhury AR, Das T, Sharma A. **Mustard oil and garlic extract as inhibitors of sodium arsenite-induced chromosomal breaks in vivo.** Cancer Lett 1997;121(1):45-52.
Arsenic, a well-known human carcinogen present as a contaminant in ground water poses a serious threat to public health in various countries. The anticlastogenic properties of two dietary supplements, garlic and mustard oil, were screened against the clastogenic activity of sodium arsenite, since diet may contain factors which affect the process of mutagenesis and carcinogenesis. Aqueous extract of garlic (100 mg/kg b.w.) and mustard oil (0.643 mg/kg b.w.) were fed to Mus musculus for 30 consecutive days either singly or simultaneously. Sodium arsenite (0.1 mg/kg b.w.) was injected subcutaneously on days 7, 14, 21 and 30 of the

experiment, singly and together with the dietary supplements. The animals were sacrificed 24 h after the last exposure to sodium arsenite and clastogenic effects were observed in the bone marrow cells. The degree of modulation of sodium arsenite-induced chromosomal aberrations was more pronounced in mustard oil than in garlic extract and simultaneous administration of both the dietary supplements reduced the clastogenic effects of sodium arsenite closer to the level of the negative control. The greater efficacy could be due to the interaction of the two dietary supplements and its radical scavenging property.

Choudhury AR, Das T, Sharma A, Talukder G. **Inhibition of clastogenic effects of arsenic through continued oral administration of garlic extract in mice in vivo.** Mutat Res 1997;392(3):237-42.
Crude aqueous extract of garlic bulbs (Allium sativum L. single clove variety) was administered by gavage to mice of both sexes daily for up to 30 and 60 days, in doses corresponding to 6 g for a 60 kg human body. Sodium arsenite (at 1/50 of LD50 dose) was injected subcutaneously to mice on every 7th day of the experiment. Chromosome preparations made from bone marrow following flame drying Giemsa schedule were screened for chromosomal aberrations. The clastogenic affects of prolonged exposure to sodium arsenite --a strong clastogen-- was reduced by a highly significant amount when crude garlic extract, in the dose used, was given daily to the mice by intubation for the same period.

Chu TC, Han P, Han G, Potter DE. **Intraocular pressure lowering by S-allylmercaptocysteine in rabbits.** J Ocul Pharmacol Ther 1999;15(1):9-17.
The purpose of this study was to examine the actions of a garlic-derived compound, S-allylmercaptocysteine (SAMC) on intraocular pressure (IOP) and to determine the possible involvement of sulfhydryl reactivity, sympathetic neuronal activity and atrial natriuretic peptide (ANP) in the IOP response. Topical, unilateral application of SAMC (20, 100, 200 microg) elicited dose-dependent decreases in IOP. The magnitude of the IOP-lowering effect induced by SAMC was between four to six mmHg. The ocular hypotensive responses were unilateral, peaked at one to three hours and lasted from two to four hours. The IOP-lowering effect by SAMC (100 microg) was enhanced modestly by topical, bilateral pretreatment with a reducing agent, tris(2-carboxyethyl) phosphine (100 microg) which itself produced no change in IOP. No alteration of pupil diameter was observed following topical application of either SAMC or tris(2-carboxyethyl) phosphine. Thus, alteration of sulfhydryl reactivity does not seem to be a major mechanism of action for SAMC. SAMC caused no change of basal and electrically stimulated norepinephrine release in rabbit iris-ciliary bodies, ruling out a prejunctional effect on sympathetic nerve activity. However, SAMC increased the ANP levels in aqueous humor by five-fold. It is concluded that the ocular hypotensive response induced by SAMC in rabbits could involve the elevation of ANP levels in aqueous humor.

Chung E, Lee KY, Lee YJ, Lee YH, Lee SK. **Ginsenoside Rg1 down-regulates glucocorticoid receptor and displays synergistic effects with cAMP.** Steroids 1998;63(7-8):421-4.
Ginsenoside-Rg1 (G-Rg1) from the roots of Panax ginseng C. A. Meyer has been shown to bind to the glucocorticoid receptor (GR). To further explore the effect of G-Rg1 binding to GR, a luciferase reporter gene containing two copies of a glucocorticoid response element was constructed and transiently transfected into FTO2B rat hepatoma cells. A dose-dependent

induction of the reporter gene was observed in response to G-Rg1, and the inductive effect was blocked by treatment with the antiglucocorticoid RU486. In addition, both G-Rg1- and dexamethasone (Dex)-induced transcription was synergistically enhanced by the treatment of dibutyryl cAMP (Bt2-cAMP). G-Rg1 treatment also led to the down-regulation of intracellular GR content, which was similar to the effect of Dex. By showing that G-Rg1 down-regulates GR and induces GR-mediated transcription synergistically with cAMP, we conclude that G-Rg1 is a functional GR ligand in FTO2B cells.

Coulombe RA Jr, Drew GL, Stermitz FR. **Pyrrolizidine alkaloids crosslink DNA with actin.** Toxicol Appl Pharmacol 1999;154(2):198-202.
Pyrrolizidine alkaloids (PAs) are toxic constituents of hundreds of plant species, some of which people are exposed to in herbal products and traditional remedies. The bioactivity of PAs are related, at least in part, to their ability to form DNA-protein complexes (DPC). Previous studies from our laboratory indicated a possible role for actin in PA-induced DPCs. Nuclei prepared from Madin-Darby bovine kidney (MDBK) and human breast carcinoma (MCF-7) cells were treated with the pyrrolic PAs dehydrosenecionine (DHSN) and dehydromonocrotaline (DHMO). DPCs were purified and then analyzed by Western immunoblotting. Actin was found in DPCs induced by both DHSN and DHMO, but not in those from control nuclei. Actin was also present in DPCs induced by cisplatinum and mitomycin C, two bifunctional cross-linkers. In separate experiments, DHSN and DHMO were crosslinked to a mixture of HindIII digested lambda phage with varying amounts of glutathione (GSH), cysteine, or methionine to identify the stoichiometry of competition between DNA and alternate nucleophiles for crosslink formation with pyrroles. GSH and cysteine, but not methionine, competed with lambda phage for DNA crosslinking, indicating that reduced thiols may have a role in nucleophilic reactions with pyrroles in the cell. While actin involvement in cisplatinum-induced DPCs is documented, the discovery of actin crosslinking in PA or mitomycin C-treated cells or nuclei is, to our knowledge, novel. Pyrrole-induced DPC formation with actin, a protein with structural and/or regulatory importance proteins, may be a significant mechanism for PA toxicity and bioactivity. Copyright 1999 Academic Press.

Cullen WJ, Dulchavsky SA, Devasagayam TP, Venkataraman BV, Dutta S. **Effect of Maharishi AK-4 on H2O2 induced oxidative stress in isolated rat hearts.** J Ethnopharmacol 1997;56(3):215-22.
IPA COPYRIGHT: ASHP The ability of the Ayurvedic herbal food supplement Maharishi Amrit Kalash (MAK-4) to decrease oxidative damage in potassium-arrested isolated rat hearts was examined, using hydrogen peroxide as a model pro-oxidant to induce oxidative stress. MAK-4 decreased oxidative stress in terms of release of lactate dehydrogenase and glutathione and as assessed by measuring developed contractile tension. In vitro studies showed that MAK-4 contains hydrogen peroxide binding activity that resulted in the decreased availability of hydrogen peroxide itself. It was concluded that the food supplement MAK-4 may have potential benefits in reducing oxidative stress.

Cupp MJ. **Herbal remedies: adverse effects and drug interactions.** Am Fam Physician 1999;59(5):1239-45.
A growing number of Americans are using herbal products for preventive and therapeutic

purposes. The manufacturers of these products are not required to submit proof of safety and efficacy to the U.S. Food and Drug Administration before marketing. For this reason, the adverse effects and drug interactions associated with herbal remedies are largely unknown. Ginkgo biloba extract, advertised as improving cognitive functioning, has been reported to cause spontaneous bleeding, and it may interact with anticoagulants and antiplatelet agents. St. John's wort, promoted as a treatment for depression, may have monoamine oxidase-inhibiting effects or may cause increased levels of serotonin, dopamine and norepinephrine. Although St. John's wort probably does not interact with foods that contain tyramine, it should not be used with prescription antidepressants. Ephedrine-containing herbal products have been associated with adverse cardiovascular events, seizures and even death. Ginseng, widely used for its purported physical and mental effects, is generally well tolerated, but it has been implicated as a cause of decreased response to warfarin. Physicians must be alert for adverse effects and drug interactions associated with herbal remedies, and they should ask all patients about the use of these products.

Denke A, Schneider W, Elstner EF. **Biochemical activities of extracts from Hypericum perforatum L. 2nd Communication: inhibition of metenkephaline- and tyrosine-dimerization.** Arzneimittelforschung 1999;49(2):109-14.
Extracts from the herb "St. John's wort" (Hypericum perforatum L.), besides other activities such as wound healing, antigout, antirheumatic and diuretic properties, are widely used to counteract neurological disorders such as depressive situations, nervousness and sleeplessness. The characteristic and leading component in these extracts, the dianthraquinone hypericin, is very likely not to represent the main active principle mediating the desirable effects. Thus, standardization of the drug is no longer based on the quantification of total hypericin and since several years simply the determination of dry matter content is in use instead. As biochemical background of depression the lack of catecholamine neurotransmitters or decreased beta-endorphins such as methionine- or leucine-enkephalins have to be envisaged. This communication reports on the inhibition of myeloperoxidase-catalyzed dimerization of enkephalins by Hypericum extracts. The substitution for enkephalins by tyrosine and for myeloperoxidase by horseradish peroxidase may represent a simple and inexpensive biochemical model reaction of pathological events during the manifestation of depressive events suitable for drug standardization.

Dhuley JN. **Effect of some Indian herbs on macrophage functions in ochratoxin A treated mice.** J Ethnopharmacol 1997;58(1):15-20.
The effect of Indian herbs namely, Asparagus racemosus, Tinospora cordifolia, Withania somnifera and Picrorhiza kurrooa on the functions of macrophages obtained from mice treated with the carcinogen ochratoxin A (OTA) was investigated. The chemotactic activity of murine macrophages was significantly decreased by 17 weeks of treatment with OTA compared with controls. Production of interleukin-1 (IL-1) and tumor necrosis factor (TNF) was also markedly reduced. Treatment with Asparagus racemosus, Tinospora cordifolia, Withania somnifera and Picrorhiza kurrooa significantly inhibited OTA-induced suppression of chemotactic activity and production of IL-1 and TNF-alpha by macropahges. Moreover, we found that Withania somnifera treated macrophage chemotaxis and that Asparagus racemosus induced excess production of TNF-alpha when compared with controls.

Diel F, Detscher M, Borck H, Schrimpf D, Diel E, Hoppe HW. **Effects of permethrin on human basophils and lymphocytes in vitro.** Inflamm Res 1998;47(Suppl 1):11-2.

Dimpfel W, Schober F, Mannel M. **Effects of a methanolic extract and a hyperforin-enriched CO2 extract of St. John's Wort (Hypericum perforatum) on intracerebral field potentials in the freely moving rat (Tele-Stereo-EEG).** Pharmacopsychiatry 1998;31(Suppl 1):30-5.
Two extracts of St. John's Wort (Hypericum perforatum) were investigated in the animal model "Tele-Stereo-EEG" which consisted of continuous recording of intracerebral field potentials in the freely moving rat. One was a CO2 extract for research purposes containing 30.14% hyperforin, a phloroglucine derivative known to occur within the reproductive parts of the plant, and lacking other major constituents like naphtodianthrones and flavonoids according to HPLC fingerprint. The other extract was the methanolic extract LI 160S (4.67% hyperforin). The dosage schedule was elaborated for the application of identical amounts of hyperforin in both extracts in each dosing group. Both extracts produced nearly identical patterns of electrical power changes during the first two hours of recording. These changes mainly consisted of reproducible power increases within the alpha1 band of the striatum. Comparison with earlier data obtained by identical protocols revealed that the early action was very similar to that following the application of serotonin reuptake inhibitors, thus matching biochemical in vitro data previously reported. These changes might be due to the presence of hyperforin. Only LI 160S developed a late action not seen with the CO2 extract, consisting in increases in delta activity. This late action of LI 160S matched data obtained by analysis of the action of NMDA-antagonists like MK 801 or memantine. Again, these results support previously reported biochemical findings of the interaction of hypericum extract with the glutamatergic system. In all probability, this action stems from substances only present in LI 160S, not in the CO2 extract. Which of the components contained within hypericum extracts are responsible for the clinical efficacy of St. John's wort in depression remains to be determined.

Dong Y, Yang MM, Kwan CY. **In vitro inhibition of proliferation of HL-60 cells by tetrandrine and coriolus versicolor peptide derived from Chinese medicinal herbs.** Life Sci 1997;60(8):135-40.
Coriolus versicolor polysaccharide peptide (CVP) and the bis-benzylisoquinoline alkaloids, tetrandrine (TET) and berbamine (BER), the active ingredients isolated from Chinese medicinal herbs known to possess antitumor activities, concentration-dependently inhibited the proliferation of human leukemic HL-60 cells. CVP did not affect the growth of normal human peripheral blood lymphocytes (PBL), whereas TET elicited concentration-dependent cytotoxic effects. Morphological observation and DNA analysis revealed that CVP elicited no effect on the morphological features of HL-60 cells and did not cause DNA fragmentation, but TET and BER caused cell shrinkage with the formation of apoptotic bodies, and showed clear evidence of DNA fragmentation. These findings indicate that TET and BER, but not CVP, inhibited the proliferation of HL-60 cells via induction of apoptosis.

Dres C, Johnson C, Lods L, Scholz D, Brooks G. **Enzymes and erythema reduction.** Soap Perfum Cosmet 1998 Mar;71:31, 33.
IPA COPYRIGHT: ASHP In vitro and in vivo studies of the effects of a stabilized copper and zinc yeast derived superoxide dismutase with antioxidant properties and peroxidase extracted

from Foeniculum vulgare (fennel) on UV induced erythema are described. It was noted that the studies indicated that superoxide dismutase prevents the synthesis of prostaglandin E2 and thus decreases visible erythema levels. A study conducted in 12 subjects (ages 24-40 yr) who applied various antioxidants showed an overall 47.9% reduction in UV B induced erythema with superoxide dismutase. The efficacy of the peroxidase extract was demonstrated in 2 studies. The first study showed the ability of fennel extract to consistently inhibit lipid peroxidation. It also reduced UV induced erythema. The results of the second study showed a 65% reduction in UV induced erythema.

Dwivedi C, John LM, Schmidt DS, Engineer FN. **Effects of oil-soluble organosulfur compounds from garlic on doxorubicin-induced lipid peroxidation.** Anticancer Drugs 1998;9(3):291-4.
Clinical efficacy of doxorubicin is compromised due to free radical generation leading to cardiac toxicity. Oil-soluble organosulfur compounds, diallyl sulfide (DAS), diallyl disulfide (DADS), dipropyl sulfide (DPS) and dipropyl disulfide (DPDS), present in garlic were examined for their antiperoxidant effects. DADS inhibited liver microsomal lipid peroxidation induced by NADPH, ascorbate and doxorubicin. DAS, DPS and DPDS were ineffective inhibitors of liver microsomal lipid peroxidation. DADS could be used in combination with doxorubicin to protect oxidative injuries to improve the clinical efficacy of doxorubicin.

Espinola EB, Dias RF, Mattei R, Carlini EA. **Pharmacological activity of Guarana (Paullinia cupana Mart.) in laboratory animals.** J Ethnopharmacol 1997;55(3):223-9.
Mice that ingested a suspension of guarana (Paullinia cupana, Sapindaceae) in a dose of 0.3 mg/ml showed a significant increase in physical capacity when subjected to a stressful situation such as forced swimming after 100 and 200 days of treatment. Such an effect, however, was not obtained with a concentration of 3.0 mg/ml, nor with the ingestion of a suspension of ginseng 5.0 mg/ml, nor of a solution of caffeine 0.1 mg/ml. Guarana, both after a single (3.0 and 30 mg/kg) or chronic administrations (0.3 mg/ml), was able to partially reverse the amnesic effect of scopolamine as measured through a passive avoidance test in mice and rats, indicating a positive effect on memory acquisition. However, no effect was observed when an active avoidance task was used in rats, even after 20 days of guarana administration. There was also a tendency of rats treated with 0.3 mg/ml of guarana to better maintain the memory of a Lashley III maze path. The animals had the same average lifespan, indicating a low toxicity of guarana, even after 23 months of treatment.

Fan YC, Lu R, Lu YZ. **[Effect of xinfukang on lipid peroxidation and membrane fluidity in myocardial cells of suckling mice incubated in vitro].** Chin Tradit Herb Drugs 1997 Sep;28:545-7. (Chi)
IPA COPYRIGHT: ASHP The effect of xinfukang, a Chinese herbal preparation, on lipid peroxidation and membrane fluidity in myocardial cells of suckling mice incubated in vitro was investigated. Xinfukang decreased lipid peroxidation and improved membrane fluidity in mouse hypoxic myocardial cells.

Fejes S, Kery A, Blazovics A, Lugasi A, Szoke E, et al . **[Investigation of the in vitro antioxidant effect of Petroselinum crispum (Mill.) Nym. ex A. W. Hill].** Acta Pharm Hung 1998;68(3):150-6. (Hun)

Geng Z, Rong Y, Lau BH. **S-allyl cysteine inhibits activation of nuclear factor kappa B in human T cells.** Free Radic Biol Med 1997;23(2):345-50.
Reactive oxygen species are involved in signal transduction pathways leading to nuclear factor kappa B (NF-kappa B) activation which has been implicated in the regulation of gene transcription. We recently reported that a garlic compound, S-allyl cysteine (SAC), protects bovine pulmonary artery endothelial cells from oxidant injury induced by hydrogen peroxide (H2O2). In this study we determined the effects of SAC on NF-kappa B activation in human T lymphocytes (Jurkat cells) induced by tumor necrosis factor alpha (TNF- alpha) and H2O2. Activated NF-kappa B in nuclear extracts was measured by an electrophoretic mobility shift assay using 32P-labeled probe. SAC consistently exhibited a dose-dependent inhibition of NF-kappa B activation induced by both TNF-alpha and H2O2. Supershift with specific antibodies to NF-kappa B subunits confirmed that the inducible retarded bands observed in the EMSA and p65-p50 heterodimer of the NF-kappa B/Rel protein. Our data suggest that SAC may act via antioxidant mechanisms to block NF-kappa B activation in Jurkat cells.

Gleitz J, Beile A, Wilkens P, Ameri A, Peters T. **Antithrombotic action of the kava pyrone (+)-kavain prepared from Piper methysticum on human platelets.** Planta Med 1997;63(1):27-30.
(+)-Kavain, a 4-methoxy-alpha-pyrone prepared from Piper methysticum Forst. (Piperaceae), was investigated regarding its assumed antithrombotic action on human platelets which was deduced from its ability to suppress arachidonic acid (AA)-induced aggregation, exocytosis of ATP, and inhibition of cyclooxygenase (COX) and thromboxane synthase (TXS) activity, the latter two effects being estimated from the generation of prostaglandin E2 (PGE2) and thromboxane A2 (TXA2), respectively. Exogenously applied AA (100 mumol/l) provoked a 90% aggregation of platelets, the release of 14 pmol ATP, and the formation of either 220 pg TXA2 or 43 pg PGE2, each parameter being related to 10(6) platelets. An application of (+)-kavain 5 min before AA, dose-dependently diminished aggregation, ATP-release, and the synthesis of TXA2 and PGE2 with IC50 values of 78, 115, 71, and 86 mumol/l, respectively. The similarity of the IC50 values suggest an inhibition of COX by (+)-kavain as primary target, thus suppressing the generation of TXA2 which induces aggregation of platelets and exocytosis of ATP by its binding on TXA2-receptors.

Gutser UT, Friese J, Heubach JF, Matthiesen T, Selve N, Wilffert B, Gleitz J. **Mode of antinociceptive and toxic action of alkaloids of Aconitum spec..** Naunyn Schmiedebergs Arch Pharmacol 1998;357(1):39-48.
Extracts of the plant Aconitum spec. are used in traditional Chinese medicine predominantly as anti-inflammatory and analgesic agents, the latter allegedly equally potent as morphine but without any habit-forming potential. As the only pharmacologically active compounds, the C19 diterpenoid alkaloid aconitine, and some of its derivatives, have been proven to be antinociceptive in different analgesic assays, but the mode of action is unknown. To elucidate the mode of action, ten aconitine-like derivatives were investigated with respect to their affinity for

voltage-dependent Na+ channels, the action on synaptosomal Na+ and Ca2+ homoeostasis and their antinociceptive, arrhythmogenic and acute toxic properties. Since aconitine is known to bind to site II of Na+ channels, we determined the affinity of the aconitine-like derivatives in vitro to synaptosomal membranes by the [3H]-batrachotoxinin-binding assay and their properties on intrasynaptosomal concentrations of free Na+ and Ca2+ ([Na+]i and [Ca2+]i), both the latter determined fluorometrically with SBFI and Fura-2 respectively. Furthermore, the alkaloids' arrhythmogenic potential was investigated in guinea-pig isolated atria and the antinociceptive action on formalin-induced hyperalgesia and the acute toxic action estimated in mice. The results show that the alkaloids could be divided into at least three groups. The first is characterized by a high affinity to the site II of Na+ channels (Ki about 1.2 microM), the ability to enhance [Na+]i and [Ca2+]i (EC50 about 3 microM), a strong arrhythmogenic action that starts at about 30 nM, an antinociceptive effect (ED50 about 0.06 mg/kg) and high acute toxicity (LD50 values about 0.15 mg/kg). To this group belong aconitine, 3-acetylaconitine and hypaconitine. The second group, with lappaconitine as the only member, has an affinity to Na+ channels an order of magnitude lower (Ki = 11.5 microM), less acute toxicity (LD50 about 5 mg/kg), and a two orders of magnitude lower antinociceptive action (ED50 about 2.8 mg/kg) and lower cardiotoxicity (bradycardia observed at 3 microM). Additionally, lappaconitine suppresses the increase in [Ca2+]i of aconitine-stimulated synaptosomes and increases the excitation threshold of left atria, indicating an inhibition of Na+ channels. The other derivatives, i.e. delcorine, desoxydelcorine, karakoline, lappaconidine, lappaconine and lycoctonine, belong to the third group, which has hardly any effects. They have a low affinity to Na+ channels with Ki values in the millimolar range, show no effect on synaptosomal [Na+]i and [Ca2+]i, no arrhythmogenic potential up to 100 microM, no antinociceptive activity and low toxicity with LD50 values greater than 50 mg/kg. For the investigated alkaloids we suggest two different antinociceptive-like modes of action. Aconitine, hypaconitine and 3-acetylaconitine may induce a block of neuronal conduction by a permanent cell depolarisation, whereas lappaconitine might act like local anaesthetics. However, because of the low LD50/ED30 quotients of 2-6, the antinociceptive-like action of the Aconitum alkaloids seems to reflect severe intoxication rather than a specific antinociceptive action. The structure/activity relationship shows that alkaloids that activate or block Na+ channels have a benzoyl ester side chain in the C-14 or C-4 positions respectively, whereas the other compounds lack this group.

Hamasaki Y, Kobayashi I, Hayasaki R, Zaitu M, Muro E, Yamamoto S, Ichimaru T, Miyazaki S. **The Chinese herbal medicine, shinpi-to, inhibits IgE-mediated leukotriene synthesis in rat basophilic leukemia-2H3 cells.** J Ethnopharmacol 1997;56(2):123-31.
We examined the action of Shinpi-To (Formula divinita; TJ-85), a granular extract of seven Chinese medicinal herbs that is used in treating childhood asthma, on the leukotriene synthesis in rat basophilic leukemia-2H3 cells (RBL-2H3 cells). IgE-loaded cells were stimulated with anti-IgE serum in the presence or absence of Shinpi-To. Released LTC4 and LTB4 were measured by radioimmunoassay (RIA). Shinpi-To significantly inhibited IgE-mediated synthesis of leukotriene (LT)C4 and LTB4. To identify the inhibitory sites, we investigated the action of this extract on four synthetic enzymes, phospholipase A2 (PLA2), 5-lipoxygenase (5-LO). LTC4 synthase, and LTA4 hydrolase. Shinpi-To inhibited the A23187-stimulated release of [3H]arachidonic acid (AA) from the cell membrane, reflecting an effect on PLA2 activity. It also suppressed production of LTC4 and LTB4 when cell lysates were incubated with AA as

substrate. It did not inhibit the production of LTC4 and LTB4 when LTA4-free acid was used as the substrate. Shinpi-To did not inhibit the IgE-mediated increase of intracellular Ca2+ ([Ca2+]i) concentration. Results indicate that Shinpi-To inhibits LT synthesis by inhibiting PLA2 and 5-LO activities without affecting the mobilization of [Ca2+]i.

Hong YS. **Effect of diallyl sulfide on tetrachlorodibenzo-P-dioxin-induced cytochrome P-450 1A1 gene in mouse lung.** Biochem Arch 1997;13(3):179-87.
BIOSIS COPYRIGHT: BIOL ABS. Cytochrome P-450 (CYP) 1A1 plays a key role in the metabolic activation of procarcinogen, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The present study was conducted to investigate inhibitory effect of diallyl sulfide and garlic extract on CYP1A1 induced by TCDD in mouse lung. CYP1A1 was induced by a single oral gavage of TCDD (100 ng/kg) to mouse and the induction was confirmed by the increase of its enzyme activity and of immunoprecipitable protein as well as that of mRNA for CYP1A1. When dially sulfide (200 mg/kg) or garlic extract (50 mg/kg) were given 4 days prior to TCDD administration, CYP1A1 activity measured by benzo(a)pyrene hydroxylase or 7-ethoxyresorufin-O-deethylase and the expression detected by Northern blot analysis using CYP1A1 cDNA decreased significantly in the lung compared to the TCDD-induced activities. On the other hand, those activities in the liver decreased moderately, indicating tissue specificity of the CYP gene expression. These results together with poor correlation of CYP1A2 activity under the same experimental condition indicate that the reduction of CYP1A1 gene expression by diallyl sulfide or garlic extract is selective in mouse lung induced by TCDD.

Hood B. **Paclitaxel (Taxol): newly identified source of alcohol intoxication.** Miss Pharm 1998;24(4):13.
IPA COPYRIGHT: ASHP The case of a 57-yr-old woman who developed symptoms of acute ethyl alcohol (ethanol) intoxication, with a blood alcohol concentration of 0.098%, during treatment with 200-348 mg/sq m paclitaxel (Taxol) per cycle is described. Concomitant therapy included diphenhydramine, belladonna alkaloids, phenobarbital, ergotamine tartrate, terfenadine, metoclopramide, morphine, amitriptyline, and hydrocodone.

Huber WW, Mcdaniel LP, Kaderlik KR, Teitel CH, Lang NP, Kadlubar FF. **Chemoprotection against the formation of colon DNA adducts from the food-borne carcinogen 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) in the rat [see comments].** Mutat Res 1997;376(1-2):115-22.
The mutagenic heterocyclic aromatic amine, 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP), is a pyrolysis product in cooked foods that has been shown to be a rat colon carcinogen and has been implicated in the etiology of human colon cancer. In order to identify chemoprotection strategies that could be carried out in humans, a pilot study was conducted in which PhIP-DNA-adduct levels were quantified in the colons of male F344 rats that had been subjected to 16 different putative chemoprotection regimens, followed by a gavage of PhIP (50 mg/kg) and sacrifice 24 h later. The 16 treatments (Oltipraz, benzylisothiocyanate, diallyl sulfide, garlic powder, ethoxyquin, butylated hydroxyanisole, glutathione, indole-3-carbinol, alpha-angelicalactone, kahweol/cafestol palmitates, quercetin, green tea, black tea, tannic acid, amylase-resistant starch, and physical exercise) comprised sulfur-containing compounds, antioxidants, flavonoids, diterpenes, polyphenols, high dietary fiber, etc. The strongest inhibition

of PhIP-DNA adduct formation in the colon was observed upon pretreatment with black tea, benzylisothiocyanate, and a mixture (1:1) of kahweol:cafestol palmitates, which resulted in 67, 66, and 54% decreases in colon PhIP-DNA adduct levels, as compared with controls. Preliminary studies on their mechanism of action indicated that only kahweol:cafestol caused a substantial induction of glutathione S-transferase isozymes (GSTs) that are thought to be important in the detoxification of PhIP. Notably, this induction occurred in the liver rather than in the colon.

Huong NT, Matsumoto K, Kasai R, Yamasaki K, Watanabe H. **In vitro antioxidant activity of Vietnamese ginseng saponin and its components.** Biol Pharm Bull 1998;21(9):978-81.
To elucidate the antioxidant action of Vietnamese ginseng saponin against free radial-mediated cellular damage, we examined the effect of Vietnamese ginseng saponin on lipid peroxidation in the mouse brain, liver, and liver microsomes by using two in vitro free radical generating systems (iron ferrous+ascorbic acid and iron ferrous+hydrogen peroxide). Free radical-mediated lipid peroxidation was determined by measuring the endogenous and stimulated accumulation of thiobarbituric acid reactive substance (TBA-RS). Vietnamese ginseng saponin (0.05-0.5 mg/ml), as well as vitamin E, significantly inhibited the formation of TBA-RS in tissue homogenates. Panax ginseng saponin, at the same concentration range as Vietnamese ginseng saponin, also had inhibitory action on free radical-mediated lipid peroxidation. However, majonoside-R2, ginsenoside-Rg1 and ginsenoside-Rb1, the main saponin components of Vietnamese ginseng saponin fraction, had no effect on lipid peroxidation. These results suggest that Vietnamese ginseng exerts a protective action against free radical-induced tissue injury and that this effect is attributable to minor components rather than the main saponin components tested.

Ikeda Y, Iijima OT, Iizuka A, Ishige A, Amagaya S, Komatsu Y, Okada M, Abe C, Fujihira E. **Anti-inflammatory effects of mao-bushi-saishin-to in mice and rats.** Am J Chin Med 1998;26(2):171-9.
Effects of Mao-Bushi-Saishin-to (MBS) on anti-inflammatory activities were examined in mice and rats. MBS significantly inhibited the increase in vascular permeability induced by acetic acid, the ear edema induced by arachidonic acid and phorbol ester, and the cutaneous extravasation induced by bradykinin and histamine. MBS, however, was not effective against the serotonin-induced cutaneous permeability increase in mice. MBS significantly inhibited carrageenin-induced hind foot edema and cotton pellet-induced granulation tissue growth in rats. These results show that MBS may exert anti-inflammatory effects through the underlying mechanism(s) of preventing mediator release from mast cells and macrophages.

Imoto K, Takemura H, Kwan CY, Sakano S, Kaneko M, Ohshika H. **Inhibitory effects of tetrandrine and hernandezine on Ca2+ mobilization in rat glioma C6 cells.** Res Commun Mol Pathol Pharmacol 1997;95(2):129-46.
The effects of tetrandrine (TET), a Ca2+ antagonist of Chinese herbal origin, and hernandezine (HER), a structural analogue of TET, on Ca2+ mobilization were studied in rat glioma C6 cells. TET and HER alone did not affect the resting cytoplasmic Ca2+ concentration ([Ca2+]i). TET and HER inhibited the peak and sustained elevation of [Ca2+]i induced by bombesin and thapsigargin (TG), a microsomal Ca2+ ATPase inhibitor, in a dose-dependent manner. The doses of TET or HER needed to abolish the sustained and peak increase in [Ca2+]i induced by

bombesin and TG were 30 microM and 300 microM, respectively. TET and HER did not increase inositol 1,4,5-trisphosphate (IP3) accumulation by themselves but inhibited IP3 accumulation elevated by bombesin. In permeabilized C6 cells, the addition of IP3 and TG released Ca2+ from intracellular stores. Pretreatment with TET or HER abolished Ca2+ release from intracellular stores induced by bombesin and TG. In the absence of extracellular Ca2+, the addition of 3 mM Ca2+ to extracellular medium slightly increased [Ca2+]i, which indicated Ca2+ entry due to leakage of Ca2+ at the plasma membrane but not Ca2+ influx through Ca2+ channels. TET and HER did not affect this leakage entry of Ca2+. The present results suggest that TET and HER inhibit Ca2+ release from intracellular stores as well as Ca2+ entry from extracellular medium evoked by bombesin and TG. In addition, TET and HER inhibit IP3 accumulation induced by bombesin in rat glioma C6 cells.

Ip C, Lisk DJ. **Modulation of phase I and phase II xenobiotic-metabolizing enzymes by selenium-enriched garlic in rats.** Nutr Cancer 1997;28(2):184-8.
Previous research showed that treatment with selenium-enriched garlic (Se-garlic) was able to inhibit the initiation phase of mammary carcinogenesis in the dimethyl-benz[a]anthracene (DMBA) model in rats. The present study was designed to investigate the following parameters: 1) DMBA-DNA adduct formation in liver and mammary gland, 2) urinary excretion of DMBA metabolites, 3) phase I and phase II xenobiotic-metabolizing enzymes, and 4) tissue selenium levels as a function of Se-garlic supplementation. Prior feeding with an Se-garlic-containing diet (at 3 ppm Se) for two weeks resulted in a consistent reduction of all DMBA adducts in liver and mammary gland. This was accompanied by a 40% increase in urinary excretion of DMBA metabolites over a two-day period. Several liver P-450 enzymes were examined in rats fed a diet supplemented with 1, 2, or 3 ppm Se. Compared with controls receiving 0.1 ppm Se, no significant alteration in activity was detected with respect to P-450 1A1 (responsible for DMBA activation), 1A2, 2B1, 2E1, and 3A4. In contrast, glutathione S-transferase and uridine 5'-diphosphate-glucuronyltransferase activities were elevated to a maximum of 2- to 2.5-fold in liver and kidney. As expected, there was a dose-dependent elevation of selenium concentrations in liver, kidney, mammary gland, and plasma as a function of the level of Se-garlic supplementation. Our data seem to suggest that an increased detoxification of carcinogen via the phase II conjugating enzymes might represent a mechanism of tumor suppression by Se-garlic.

Ip SP, Ma CY, Che CT, Ko KM. **Methylenedioxy group as determinant of schisandrin in enhancing hepatic mitochondrial glutathione in carbon tetrachloride-intoxicated mice.** Biochem Pharmacol 1997;54(2):317-9.
As a preliminary approach to exploring whether the methylenedioxy group of the dibenzocyclooctadiene skeleton of schisandrins plays an important role in hepatic mitochondrial-reduced glutathione (GSH) stimulatory activity, we examined the effects of three schisandrins, namely schisandrin A (Sch A), schisandrin B (Sch B), and schisandrin C (Sch C), on carbon tetrachloride (CCl4) hepatotoxicity and hepatic mitochondrial GSH status in mice. Pretreating mice with Sch A at a daily oral dose of 1 mmol/kg for 3 days did not protect against CCl4 hepatotoxicity, whereas pretreatment with Sch B or Sch C at the same dosage regimen produced almost complete protection. The hepatoprotection afforded by Sch B or Sch C pretreatment was associated with significant increases in the hepatic mitochondrial GSH level and glutathione reductase (EC 1.6.4.2) activity. Our results indicate that the methylenedioxy group of the

dibenzocyclooctadiene skeleton of schisandrin is an important structural determinant in the stimulation of hepatic mitochondrial GSH, particularly under conditions of CCl4 intoxication.

Iqbal M, Athar M. **Attenuation of iron-nitrilotriacetate (Fe-NTA)-mediated renal oxidative stress, toxicity and hyperproliferative response by the prophylactic treatment of rats with garlic oil.** Food Chem Toxicol 1998;36(6):485-95.
Iron nitrilotriacetate (Fe-NTA) is a potent nephrotoxic agent. In this communication we show that Fe-NTA-mediated nephrotoxicity is diminished by 1 wk of oral daily pretreatment of male albino Wistar rats with garlic oil given by gavage at 50 or 100 mg/kg body weight/ml corn oil. Intraperitoneal Fe-NTA treatment at a dose level of 9 mg Fe/kg body weight/10 ml enhances renal microsomal lipid peroxidation and hydrogen peroxide generation which are accompanied by a decrease in the activities of renal antioxidant enzymes (e.g. catalase, glutathione peroxidase, glutathione reductase and glutathione S-transferase), and a depletion in the level of renal glutathione. Parallel to these changes, a sharp increase in blood urea nitrogen and serum creatinine has been observed. In addition, Fe-NTA treatment also enhances renal ornithine decarboxylase (ODC) activity and increases [3H]thymidine incorporation into renal DNA. Prophylactic treatment of animals with garlic oil before the administration of Fe-NTA resulted in the diminution of Fe-NTA mediated injury. The enhancement of renal lipid peroxidation and hydrogen peroxide generation was decreased. In addition, there was recovery of glutathione depletion and inhibition of the activities of antioxidant enzymes. Similarly, in animals given the higher dose of garlic oil (100 mg/kg body weight) the enhanced blood urea nitrogen and serum creatinine levels, which are indicative of renal injury, showed a reduction of about 30% and 40%, respectively, in comparison with the group treated with Fe-NTA alone. Pretreatment with garlic oil also ameliorated the Fe-NTA-mediated induction of ODC activity and enhancement of [3H]thymidine incorporation into DNA in a dose-dependent manner. Our data suggest that garlic oil is a potent chemopreventive agent and may suppress Fe-NTA-induced nephrotoxicity.

Janetzky K, Morreale AP. **Probable interaction between warfarin and ginseng.** Am J Health Syst Pharm 1997;54(6):692-3.

Jeong HG. **Suppression of constitutive and inducible cytochrome P450 gene expression by alpha-hederin in mice.** Biochem Mol Biol Int 1998;46(5):1019-26. The effects of alpha-Hederin, a triterpenoid saponin which exists in some oriental herbs, on the expression of liver cytochrome P450s were examined in mice. The administration of alpha-Hederin to mice significantly decreased the hepatic content of P450 and the activities of microsomal ethoxyresorufin O-deethylase, methoxyresorufin O-demethylase, and aniline hydroxylase, representative activities of cytochrome-P4501A1, -P4501A2, and -P4502E1, respectively, in a dose- and time-dependent manner. However, pentoxyresorufin O-dealkylase, a representative activity of cytochrome P4502B1/2, was decreased to a lesser extent. alpha-Hederin also decreased inducible monooxygenase activities in the same manner. Suppressions of P450 isozyme expression occurred in alpha-Hederin treated hepatic microsomes, as determined by immunoblot analysis in a manner consistent with that of the enzyme activity levels. Levels of mRNA of P4501A1/2 and P4502B1/2 were also decreased by alpha-Hederin as shown by Northern blot analysis. In contrast, the level of P4502E1 mRNA in the liver of alpha-Hederin treated mice was unchanged. These results suggest that alpha-Hederin may act as a more specific

suppressor for P4501A and P4502E1 than P4502B and that the suppression involves decreases in mRNA levels except in the case of P4502E1.

Jin L, Baillie TA. **Metabolism of the chemoprotective agent diallyl sulfide to glutathione conjugates in rats.** Chem Res Toxicol 1997;10(3):318-27.
The chemoprotective effects of diallyl sulfide (DAS), a flavor component of garlic, have been attributed to its inhibitory effects on CYP2E1-mediated bioactivation of certain carcinogenic chemicals. In addition to being a competitive inhibitor of CYP2E1 in vitro, DAS is known to cause irreversible inhibition of CYP2E1 in rats in vivo. The latter property is believed to be mediated by the DAS metabolite diallyl sulfone (DASO2), which is thought to be a mechanism-based inhibitor of CYP2E1, although the underlying mechanism remains unknown. In order to investigate the nature of the reactive intermediate(s) responsible for the inactivation of CYP2E1 by DAS and its immediate metabolites, the present studies were carried out to detect and identify potential glutathione (GSH) conjugates of DAS and its metabolites diallyl sulfoxide (DASO) and DASO2. By means of ionspray LC-MS/MS, ten GSH conjugates were identified in bile collected from rats dosed with DAS, namely: S-[3-(S'-allyl-S'-dioxomercapto)-2-hydroxypropyl]glutathione (M1, M2; diastereomers), S-[3-(S'-allyl-S'-dioxomercapto)-2-hydroxypropyl]-glutathione (M5), S-[2-(S'-allyl-S'-dioxomercapto)-1-(hydroxymethyl)ethyl]glutathio- n e (M3, M4; diastereomers), S-[3-(S'-allylmercapto)-2-hydroxypropyl]glutathione (M6), S-(3-hydroxypropyl)-glutathione (M7), S-(2-carboxyethyl)glutathione (M8), allyl glutathionyl disulfide (M9), and S-allylglutathione (M10). With the exception of M6, all of the above GSH conjugates were detected in the bile of rats treated with DASO, while only M3, M4, M5, M7, M8, and M10 were found in the bile of rats treated with DASO2. Experiments conducted in vitro showed that GSH reacted spontaneously with DASO to form conjugates M9 and M10, and with DASO2 to form M10. In the presence of NADPH and GSH, incubation of DAS with cDNA-expressed rat CYP2E1 resulted in the formation of metabolites M6, M9, and M10, while incubation with DASO led to the formation of M3, M4, M5, M9, and M10. When DASO2 acted as substrate, CYP2E1 generated only conjugates M3, M4, M5, and M10. These results indicate that while DAS and DASO undergo extensive oxidation in vivo at the sulfur atom, the allylic carbon, and the terminal double bonds, CYP2E1 preferentially catalyzes oxidation of the sulfur atom to form the sulfoxide and the sulfone (DASO and DASO2). However, it appears that the end product of this sequence, namely, DASO2, undergoes further CYP2E1-mediated activation of the olefinic pi-bond, a reaction which transforms many terminal olefins to potent mechanism-based P450 inhibitors. We hypothesize, therefore, that it is this final metabolic event with DASO2 which leads to autocatalytic destruction of CYP2E1 and which is mainly responsible for the chemoprotective effects of DAS in vivo.

Jung JH, Ha JY, Min KR, Shibata F, Nakagawa H, Kang SS, Chang IM, Kim Y. **Reynosin from Sassurea lappa as inhibitor on CINC-1 induction in LPS-stimulated NRK-52E cells [letter].** Planta Med 1998;64(5):454-5.
An inhibitor on CINC-1 (cytokine-induced neutrophil chemoattractant-1) induction in LPS-stimulated rat kidney epithelioid NRK-52E cells was purified from the roots of Sassurea lappa Clarke, a herbal medicine used in Korean traditional prescriptions for gastric intestinal diseases by a variety of column chromatographic procedures. The inhibitor was identified as reynosin, a

sesquiterpene lactone isolated and characterized previously from Ambrosia confertiflora DC., and Magnolia grandiflora L. Reynosin exhibited a dose-dependent inhibition on CINC-1 induction in LPS-stimulated NRK-52E cells, where 50% of inhibitory effect was shown at the concentration of about 1 microM.

Kaehler ST, Sinner C, Chatterjee SS, Philippu A. **Hyperforin enhances the extracellular concentrations of catecholamines, serotonin and glutamate in the rat locus coeruleus.** Neurosci Lett 1999;262(3):199-202.
Hyperforin is the main antidepressant component of hypericum perforatum (St. John's Wort). Using the push-pull superfusion technique we tested whether hyperforin influences extracellular concentrations of neurotransmitters in the rat locus coeruleus. Hyperforin (10 mg/kg, i.p.) not only enhanced the extracellular levels of the monoamines dopamine, noradrenaline and serotonin, but also that of the excitatory amino acid glutamate. The levels of the main serotonin metabolite 5-hydroxyindolacetic acid, as well as those of the amino acids GABA, taurine, aspartate, serine and arginine, were not influenced. Together with in vitro studies, our findings suggest that the antidepressant property of hyperforin is due to enhanced concentrations of monoamines and glutamate in the synaptic cleft, probably as a consequence of uptake inhibition.

Kanai S, Okano H. **Mechanism of the protective effects of sumac gall extract and gallic acid on the progression of CCl4-induced acute liver injury in rats.** Am J Chin Med 1998;26(3-4):333-41.
To examine the mechanism of the preventive effect of tannins on the progression of carbon tetrachloride (CCl4)-induced acute liver injury in rats, sumac gall (SG) extract and gallic acid (GA) were used as substitutes for crude tannins, because SG is a kind of Chinese traditional medicinal herb containing large amounts of various tannins, and GA is one of the major constituents of SG. The protective effect of oral (p.o.) and intraperitoneal (i.p.) administration of each substance on progression of CCl4-induced hepatitis was investigated in rats. Speculating that the superoxide dismutase (SOD)-like activities (O2 radical-scavenging activities) and/or protective effects of these substances on cell membranes might play a key role in the mechanism opposing the progression of CCl4-induced hepatitis, the O2 radical-scavenging activities in liver cells and serum in rats were monitored. Both substances significantly prevented the progression of acute liver injury with both p.o. and i.p. administration. These findings suggest that the mechanism for this prevention might be due mainly to the protective effect of these substances on cell membranes rather than O2 radical-scavenging activities.

Kar A, Choudhary BK, Bandyopadhyay NG. **Preliminary studies on the inorganic constituents of some indigenous hypoglycaemic herbs on oral glucose tolerance test.** J Ethnopharmacol 1999;64(2):179-84.
Medicinal herbs used in indigenous medicines in crude forms for the management of diabetes mellitus, contain both the organic and inorganic constituents. It is known that certain inorganic mineral elements (potassium, zinc, calcium, traces of chromium, etc.) play an important role in the maintenance of normal glucose-tolerance and in the release of insulin from beta cells of islets of Langerhans. In the present study, 30 hypoglycaemic herbs were selected from indigenous folk medicines, Ayurvedic, Unani and Siddha systems of medicines. Special emphasis was given to their inorganic parts by carefully preparing ash (which contains mainly mineral elements) of the

specific parts of the herbal samples under study. Next, the single dose effect on the oral glucose tolerance test (GTT) was studied using previously fasted albino rats. Similar effects were also compared with their organic parts of the concerned herbal samples in the form of 95% ethanolic extracts. In certain inorganic samples, more pronounced action (as glucose tolerance factor) were noticed than their corresponding organic parts.

Khojasteh-Bakht SC, Chen W, Koenigs LL, Peter RM, Nelson SD. **Metabolism of (R)-(+)-pulegone and (R)-(+)-menthofuran by human liver cytochrome P-450s: evidence for formation of a furan epoxide.** Drug Metab Dispos 1999;27(5):574-80.
(R)-(+)-Pulegone, a monoterpene constituent of pennyroyal oil, is a hepatotoxin that has been used in folklore medicine as an abortifacient despite its potential lethal effects. Pulegone is metabolized by human liver cytochrome P-450s to menthofuran, a proximate hepatotoxic metabolite of pulegone. Expressed human liver cytochrome (CYP) P-450s (1A2, 2A6, 2C9, 2C19, 2D6, 2E1, and 3A4) were tested for their ability to catalyze the oxidations of pulegone and menthofuran. Expressed CYP2E1, CYP1A2, and CYP2C19 oxidized pulegone to menthofuran, with respective Km and Vmax values of 29 microM and 8.4 nmol/min/nmol P-450 for CYP2E1, 94 microM and 2.4 nmol/min/nmol P-450 for CYP1A2, and 31 microM and 1.5 nmol/min/nmol P-450 for CYP2C19. The human liver P-450s involved in the metabolism of menthofuran are the same as pulegone except for the addition of CYP2A6. These P-450s were found to oxidize menthofuran to a newly identified metabolite, 2-hydroxymenthofuran, which is an intermediate in the formation of the known metabolites mintlactone and isomintlactone. Based on studies with 18O2 and H218O, 2-hydroxymenthofuran arises predominantly from a dihydrodiol formed from a furan epoxide. CYP2E1, CYP1A2, and CYP2C19 oxidized menthofuran with respective Km and Vmax values of 33 microM and 0.43 nmol/min/nmol P-450 for CYP2E1, 57 microM and 0.29 nmol/min/nmol P-450 for CYP1A2, and 62 microM and 0.26 nmol/min/nmol P-450 for CYP2C19.

Kim HS, Hong YT, Jang CG. **Effects of the ginsenosides Rg1 and Rb1 on morphine-induced hyperactivity and reinforcement in mice.** J Pharm Pharmacol 1998;50(5):555-60.
Recent studies have demonstrated that ginseng saponin inhibits the hyperactivity and conditioned place-preference response induced by psychostimulants and opiates. This seems to occur by direct or indirect modulation of dopaminergic activity. However, it is not known which components of ginseng saponin are active. These experiments were conducted to determine the effects of the ginsenosides Rb1 and Rg1, major components of the protopanaxadiol and protopanaxatriol fractions of ginseng saponin, on morphine-induced hyperactivity and conditioned place-preference. Morphine-induced hyperactivity, but not apomorphine-induced climbing behaviour, was inhibited by both Rb1 and Rg1. These findings confirm the hypothesis that ginsenosides modulate catecholaminergic activity preferentially at pre-synaptic sites. Morphine-induced conditioned place-preference was inhibited by Rg1, but not by Rb1. It has previously been shown that at low doses Rb1 and Rg1 are equally effective at inhibition of catecholamine secretion at the pre-synaptic site, but that at high doses Rg1 is a more effective inhibitor. This observation might explain our finding that morphine-induced conditioned place-preference was inhibited by Rg1 only. Our findings suggest that Rg1, a component of ginseng saponin with appropriate activity, might be a useful agent for prevention and treatment of the adverse effects of morphine.

Kim HS, Hong YT, Oh KW, Seong YH, Rheu HM, Cho DH, Oh S, Park WK, Jang CG. **Inhibition by ginsenosides Rb1 and Rg1 of methamphetamine-induced hyperactivity, conditioned place preference and postsynaptic dopamine receptor supersensitivity in mice.** Gen Pharmacol 1998;30(5):783-9.
The ginsenosides Rb1 and Rg1, the major components of ginseng saponin, inhibited not only methamphetamine-induced hyperactivity but also conditioned place preference (CPP) in mice following a single or repeated administration. Dopamine (DA) receptor supersensitivity, which developed in methamphetamine-induced CPP mice, was also inhibited by both Rb1 and Rg1. Therefore, the present results suggest that Rb1 and Rg1 may be the active components of ginseng saponin in the modulation of methamphetamine-induced dopaminergic behaviors such as hyperactivity and CPP, supporting our previous conclusion that ginseng saponin might modulate methamphetamine-induced dysfunction at both the pre- and postsynaptic DA receptors.

Kim YC, Kim SR, Markelonis GJ, Oh TH. **Ginsenosides Rb1 and Rg3 protect cultured rat cortical cells from glutamate-induced neurodegeneration [published erratum appears in J Neurosci Res 1998 Oct 1;54(1):123].** J Neurosci Res 1998;53(4):426-32.
Certain natural products and Asian herbal remedies have been used in Asia to attenuate neurodegenerative diseases, including senile dementia. We have examined derivatives of several natural products for potential neuroprotective activity in an in vitro test system. In the present study, we assayed a number of compounds that were isolated from Panax ginseng C.A. Meyer (Araliaceae) for an ability to protect rat cortical cell cultures from the deleterious effects of the neurotoxicant, glutamate. We found that ginsenosides Rb1 and Rg3 significantly attenuated glutamate-induced neurotoxicity. Brief exposure of cultures to excess glutamate caused extensive neuronal death. Glutamate-induced neuronal cell damage was reduced significantly by pretreatment with Rb1 and Rg3. Ginsenosides Rb1 and Rg3 inhibited the overproduction of nitric oxide, which routinely follows glutamate neurotoxicity, and preserved the level of superoxide dismutase in glutamate-treated cells. Furthermore, in cultures treated with glutamate, these ginsenosides inhibited the formation of malondialdehyde, a compound that is produced during lipid peroxidation, and diminished the influx of calcium. These results show that ginsenosides Rb1 and Rg3 exerted significant neuroprotective effects on cultured cortical cells. Therefore, these compounds may be efficacious in protecting neurons from oxidative damage that is produced by exposure to excess glutamate.

Kim YS, Kim DS, Kim SI. **Ginsenoside Rh2 and Rh3 induce differentiation of HL-60 cells into granulocytes: modulation of protein kinase C isoforms during differentiation by ginsenoside Rh2.** Int J Biochem Cell Biol 1998;30(3):327-38.
Ginsenoside Rh1 or Rh2 differentiated B16 melanoma or F9 teratocarnoma to phenotypic normal melanocyte-like cells or parietal endoderm-like cells. Ginsenoside Rh3 and Rh4 were recently isolated from Panax ginseng, but their biochemical and pharmacological effects remain unidentified. The present study investigated whether the ginsenoside Rh group (G-Rh1, -Rh2, -Rh3 and -Rh4) having similar structures induce differentiation of HL-60 cells and whether protein kinase C (PKC) is involved in differentiation by ginsenoside. Differentiation was assessed by Wright-Giemsa stain and nitroblue tetrazolium reduction. G-Rh2 and G-Rh3 induced differentiation of HL-60 cells into morphologically and functionally granulocytes but G-Rh1 and G-Rh4 did not. G-Rh2 and G-Rh3 arrested the cell cycle at the G1/S phase, consistent with the

ability to induce differentiation in a decreasing order of retinoic acid > G-Rh2 > G-Rh3. During differentiation by G-Rh2, Ca2+/phospholipid-dependent PKC activity was increased in both the cytosol and total cell extract and Ca2+/phospholipid-dependent phosphorylation of 38 and 200 kDa endogenous proteins increased, while phosphorylation of 60, 64, 66 and 97 kDa proteins was Ca2+/phospholipid-independent. When cytosolic PKC isoforms were analyzed by immunoblotting, no significant change was observed in the alpha level, however, the immunoreactive 60 kDa band of a similar mass to the PKC catalytic fragment appeared following treatment with G-Rh2. The beta isoform was gradually increased with prolonged treatment. The gamma isoform was not detected in the cytosol of untreated cells, whereas a small amount was detected 5 days after treatment. It is concluded that G-Rh2 and G-Rh3 can induce differentiation of HL-60 cells into granulocytes and modulation of PKC isoform levels may contribute to differentiation of HL-60 cells by G-Rh2.

Kim YW, Song DK, Kim WH, Lee KM, Cho MK, et al . **Long term oral administration of ginseng extract decreases serum gamma globulin and IgG1 isotype in mice.** J Ethnopharmacol 1997;58(1):55-8.
IPA COPYRIGHT: ASHP The effects of long term treatment with ginseng extract on the serum protein profile and immunoglobulin isotypes were studied in mice after an oral dose of 30 or 150 mg/kg/day ginseng extract for 52 days. Serum levels of gamma-globulin were decreased to 82% and 56% of control values during treatment with 30 and 150 mg/kg/day extract, respectively. Levels of total protein, albumin, alpha2- and beta-globulin fractions, and the ratio of albumin to globulin did not change significantly. However, the alpha1-globulin level increased by 24% during treatment with the extracts. Serum IgG1 was dose dependently decreased to 68% of control values at the dose of 150 mg/kg/day, without significant changes in other Ig isotypes.

Kleber E, Obry T, Hippeli S, Schneider W, Elstner EF. **Biochemical activities of extracts from Hypericum perforatum L. 1st Communication: inhibition of dopamine-beta-hydroxylase.** Arzneimittelforschung 1999;49(2):106-9.
Extracts from the herb "St. John's wort" (Hypericum perforatum L.) are used for the treatment of mental depression, nervousness, sleeplessness and for their wound healing, diuretic and antirheumatic properties. As one biochemical mechanism for depression lack of catecholamine neurotransmitters has been discussed. The results of this investigation show that alcoholic extracts from Hypericum perforatum L. on the basis of total hypericin content inhibit dopamine-beta-hydroxylase with an IC50 of 0.1 mu mol/l; pure commercial hypericin inhibits with an IC50 of 21 mu mol/l. Enzymes involved in the synthesis of dopamine from tyrosine, namely tyrosinase and tyrosine decarboxylase, are not influenced by hypericin at concentrations from 1 up to 10 mu mol/l.

Koike K, Zhang ZX, Sakamoto Y, Jikihara H, Masuhara K, Murakami K, Miyake A, Inoue M. **The herbal medicine unkei-to stimulates cytokine-induced neutrophil chemoattractant production in the pituitary folliculo-stellate-like cell line (TtT/GF).** Am J Reprod Immunol 1998;39(4):249-55.
PROBLEM: We previously reported that a cytokine-induced neutrophil chemoattractant (CINC) was produced in the pituitary gland and that it influenced anterior pituitary hormone release. In this study we investigated the effect of Unkei-to, a Japanese herbal medicine, on CINC

production in the rat anterior pituitary gland and the pituitary folliculo-stellate-like cell line (TtT/GF). METHOD OF STUDY: Dispersed normal anterior pituitary cells and the folliculo-stellate-like cell line TtT/GF were used to test the effect of Unkei-to on CINC secretion and CINC mRNA accumulation. Concentrations of CINC in the conditioned media were measured by an enzyme-linked immunosorbent assay, and levels of CINC mRNA were analyzed by Northern blot analysis. RESULTS: Unkei-to (20 micrograms/ml) significantly increased the secretion of CINC by normal anterior pituitary cells within 12 hr of incubation. Unkei-to also stimulated CINC secretion from TtT/GF cells in a time- and dose-dependent manner. Unkei-to (20 micrograms/ml) increased CINC mRNA accumulation in TtT/GF cells within 3 hr of incubation and also caused a 13-fold increase in the secretion of CINC from TtT/GF cells compared with the vehicle group within 24 hr of incubation. Finally, we found that some of the Unkei-to's ingredients, Evodiae fructus and Pinelliae tuber, markedly stimulated CINC secretion from TtT/GF cells. CONCLUSIONS: Our results will help to elucidate the mechanism behind the clinical effect of Unkei-to on the anterior pituitary gland. They also suggested the presence of special substances, which stimulate CINC secretion, within Unkei-to's ingredients such as E. fructus and P. tuber.

Kyo R, Nakahata N, Sakakibara I, Kubo M, Ohizumi Y. **Baicalin and baicalein, constituents of an important medicinal plant, inhibit intracellular Ca2+ elevation by reducing phospholipase C activity in C6 rat glioma cells.** J Pharm Pharmacol 1998;50(10):1179-82.
Glial cells have a role in maintaining the function of neural cells. This study was undertaken to clarify the effects of baicalin and baicalein, flavonoids isolated from an important medicinal plant Scutellariae Radix (the root of Scutellaria baicalensis Georgi), on glial cell function using C6 rat glioma cells. Baicalin and baicalein caused concentration-dependent inhibition of a histamine-induced increase in intracellular Ca2+ concentrations ([Ca2+]i). The potency of baicalein was significantly greater than that of baicalin. The noradrenaline- and carbachol-induced increase in [Ca2+]i was also inhibited by baicalein and both drugs inhibited histamine-induced accumulation of total [3H]inositol phosphates, consistent with their inhibition of the increase in [Ca2+]i. These results suggest that baicalin and baicalein inhibit [Ca2+]i elevation by reducing phospholipase C activity. The inhibitory effects of baicalin and baicalein on [Ca2+]i elevation might be important in the interpretation of their pharmacological action on glial cells, such as inhibition of Ca2(+)-required enzyme phospholipase A2.

Lee BH, Lee SJ, Hui JH, Lee S, Sung JH, Huh JD, Moon CK. **In vitro antigenotoxic activity of novel ginseng saponin metabolites formed by intestinal bacteria.** Planta Med 1998;64(6):500-3.
Ginseng saponin metabolites produced by human intestinal bacteria were evaluated for antigenotoxic properties by testing their effects on benzo[a]pyrene (B[a]P)-induced mutagenicity and clastogenicity. They include 20-O-(beta-D-glucopyranosyl)-20(S)-protopanaxadiol (IH-901), 20-O-(alpha-D-arabinopyranosyl(1-->6)-beta-D-glucopyranosyl]- 20(S)-protopanaxadiol (IH-902) and 20-O-[alpha-D-arabinofuranosyl(1-->6)-beta-D-glucopyranosyl]-20(S-)-protopanaxadiol (IH-903). IH-901, IH-902 and IH-903 inhibited the mutagenicity of B[a]P in a dose-dependent manner. In the chromosome aberration assay, IH-901 and IH-903 reduced the frequency of chromosome aberration induced by B[a]P. These results suggest that the ginseng saponin metabolites tested in the present study have potential as chemopreventive agents.

Lee MJ, Lee OH, Yoon SH, Lee SK, Kim KW, et al . **In vitro angiogenic activity of Aloe vera gel on calf pulmonary artery endothelial (CPAE) cells.** Arch Pharmacal Res 1998;21(3):260-5.

Leung YM, Ou YJ, Kwan CY, Loh TT. **Specific interaction between tetrandrine and Quillaja saponins in promoting permeabilization of plasma membrane in human leukemic HL-60 cells.** Biochim Biophys Acta 1997;1325(2):318-28.
Spontaneous Ni2+ entry (leak), measured as fluorescence quench in fura-2-loaded HL-60 cells at the excitation wavelength of 360 nm, was strongly inhibited by tetrandrine (TET, 100 microM), a Ca2+ antagonist of Chinese herbal origin. Exposure of the cells for 5 min to saponins from Quillaja saponaria (QS, 30 microg/ml), surfactants well known to permeabilize the plasma membrane by complexing with cholesterol, promoted Ni2+ entry without causing fura-2 leak-out. Unexpectedly, TET caused an immediate (within 2.5 min) augmentation of QS-promoted Ni2+ entry; and a 5-min treatment with both TET and QS resulted not only in an enhanced Ni2+ entry, but also a fura-2 leak-out. Ginseng saponins (100 microg/ml) alone or together with TET did not cause such a permeabilization. Permeabilization induced by 1-3 microM digitonin, another cholesterol-complexing glycoside, could not be enhanced by TET. TET did not affect permeabilization induced by Triton X-100 (0.01%), a detergent which non-specifically disrupts the hydrophobic interaction at the plasma membrane. TET also did not enhance Ni2+ entry triggered by ionomycin (0.35 microM) or SK&F 96365 (20 microM). Further, it did not augment Ni2+ entry when the plasma membrane fluidity was modulated by changes of temperature (27-47 degrees C) or treatment with 5% ethanol. This QS-promoted Ni2+ entry could not be amplified by other lipophilic Ca2+ antagonists, such as diltiazem (100 microM) and verapamil (100 microM). The results hence indicate that TET enhanced Ni2+ entry (or permeabilization) elicited by QS treatment, but not other perturbations of the plasma membrane. We suggest that pore formation at the plasma membrane, a consequence of QS-cholesterol interaction, can be specifically enhanced by TET. Also, a comparative study of the effects of TET and its very close analogues, hernandezine and berbamine, reveals that the methoxyl group at the R2 position of TET appears to be crucial in enhancing QS-promoted Ni2+ entry.

Li JQ, Zhang XG, Zhang JT. **[Study on the anti-apoptotic mechanism of ginsenoside Rg1 in cultured cortical neurons].** Yao Hsueh Hsueh Pao 1997 Jun;32:406-10. (Chi)
IPA COPYRIGHT: ASHP A study on the anti-apoptotic mechanism of ginsenoside Rg1, an active principle isolated from Panax ginseng CA Meyer, in cultured cortical neurons was performed with different concentrations of the drug. On day 14, the culture was changed to serum-free medium. On day 16, neurons were harvested and assayed microscopically; membrane fluidity was measured using fluorescence spectrophotometer in 5 groups of cultured cortical neurons. Results showed that serum withdrawal from the medium induced apoptosis in primary cultured cortical neurons. Ginsenoside Rg1 (1.10 mumol/l) was shown to inhibit apoptosis and protect neurons against injury. Findings indicated that a substantial alteration of membrane fluidity occurred with neuronal apoptosis. Changes in membrane fluidity provide an aspect of elucidating the mechanism of ginsenoside Rgl's anti-apoptosis function.

Li LL, Wang XW, Wang XF. **[Antilipid peroxidation and antiradiation of glycosides of herba Cistanches(GCs)].** Zhongguo Zhongyao Zazhi 1997;22(6):364-7. (Chi)

IPA COPYRIGHT: ASHP The effects of the oral administration of glycosides isolated from herbs of Cistanche species on red blood cells and the contents of nucleic acids in the liver, kidneys, and spleen were studied in mice. Results suggested that the protective effects of Cistanche on nucleic acid and antiradiative actions may be related to its antilipid peroxidation.

Liao JF, Huang SY, Jan YM, Yu LL, Chen CF. **Central inhibitory effects of water extract of Acori graminei rhizoma in mice.** J Ethnopharmacol 1998;61(3):185-93.
The present study evaluated in mice the central inhibitory effects of a water extract of shichangpu (Acori graminei rhizoma (AGR), the dry rhizome of Acorus gramineus Soland. (Araceae)). AGR (0.5-5.0 g/kg) dose-dependently decreased the locomotor activity and increased the pentobarbital-induced sleeping time, but had no significant effect on the treadmill performance. AGR also dose-dependently inhibited the intensity of apomorphine-induced stereotypic behavior. At the highest dose (5.0 g/kg), AGR had a weak anticonvulsant effect on the pentylenetetrazol-induced seizures. Receptor binding assays showed that AGR competed with [3H]SCH-23390 and [3H]YM-09151-2 for specific binding to striatal dopamine D1 and D2 receptors with Ki values of 5.6 and 4.2 mg/ml, respectively. AGR also competed with [3H]muscimol for specific binding to the gamma-aminobutyric acid (GABA) binding site of cortex GABA(A) receptors with a Ki value of 0.31 mg/ml. It also increased the specific binding of [3H]flunitrazepam to the benzodiazepine binding site of the GABA(A) receptors, suggesting a GABA agonist-like action. These results suggested that the central inhibitory effects of AGR were probably effected through an action on the central dopamine receptors and GABA(A) receptors. The principle of AGR acting at these ligand binding sites was not alpha-asarone, one of the important principles of AGR, since that alpha-asarone (10(-6)-10(-4) M) had no significant interactions with these binding sites.

Liao MH, Wu CC, Yen MH. **Beneficial effects of tetramethylpyrazine, an active constituent of Chinese herbs, on rats with endotoxemia.** Proc Natl Sci Counc Repub China B 1998;22(1):46-54.
Tetramethylpyrazine, an inhibitor of phosphodiesterase, has been widely used for treatment of cardiovascular diseases in China. Here, we investigate the effects of tetramethylpyrazine on hypotension, vascular hyporeactivity to norepinephrine (NE), release of tumor necrosis factor-alpha (TNF alpha) and nitric oxide (NO) in a rat model of circulatory shock induced by bacterial endotoxin (E. coli lipopolysaccharide, LPS). Male Wistar-Kyoto rats were anesthetized and instrumented for the measurement of mean arterial pressure (MAP) and heart rate (HR). Injection of LPS (10 mg/kg, i.v.) resulted in a fall in MAP and an increase of HR. In contrast, animals pretreated with tetramethylpyrazine (10 micrograms/kg, i.p. at 30 min prior to LPS) maintained a significantly higher MAP, but tachycardia was further enhanced at 60 min and 120 min when compared to rats given only LPS (LPS-rats). The pressor effect of NE (1 microgram/kg, i.v.) was also significantly reduced after treatment of rats with LPS. Similarly, the thoracic aorta obtained from rats after in vivo studies showed a significant reduction in the contractile responses elicited by NE (1 microM). Pretreatment of LPS-rats with tetramethylpyrazine partially, but significantly, prevented this LPS-induced hyporeactivity to NE in vivo and ex vivo. The injection of LPS resulted in a significant increase in the plasma TNF alpha level at 60 min, whereas the effect of LPS on the plasma nitrate (an indicator of NO formation) level increased in a time-dependent manner. This increment of both TNF alpha and nitrate levels induced by LPS

was significantly reduced in LPS-rats pretreated with tetramethylpyrazine. The early hypotension caused by LPS was slightly, but significantly, prevented by pretreatment with tetramethylpyrazine, suggesting that tetramethylpyrazine affects the endothelial constitutive NOS (eNOS). This was examined by the effect of tetramethylpyrazine on acetylcholine (ACh, 1 microM)-induced relaxation in rats treated with tetramethylpyrazine for 4 h. However, tetramethylpyrazine had no significant effects on the ACh-induced relaxation, indicating that tetramethylpyrazine does not affect the activity of eNOS. Thus, tetramethylpyrazine attenuates the early hypotension and the delayed circulatory failure caused by endotoxin in the rat. These effects may be due to inhibition of the release of circulation factors and TNF alpha, which usually reveal synergism upon the induction of iNOS.

Lin HL, Liu TY, Lui WY, Chi CW. **Up-regulation of multidrug resistance transporter expression by berberine in human and murine hepatoma cells.** Cancer 1999;85(9):1937-42.
BACKGROUND: Berberine, one of the major constitutents of alkaloids of Coptis chinensis is frequently utilized in the treatment of inflammation and liver-related diseases. In Chinese herbal medicine, Coptis chinensis is used as a prophylactic drug to treat gastrointestinal disorders. In a previous study, the authors found that berberine reduced cell proliferation and alpha-fetoprotein expression in human hepatoma HepG2 cells. Multidrug resistance transporter (pgp-170) is known to be overexpressed in HepG2 cells. Whether berberine regulates the expression of pgp-170 in HepG2 and other hepatoma cell lines is unknown and worthy of investigation. METHODS: Human and murine hepatoma cells were treated with berberine (0.32, 3.2, 32, and 320 microM), tamoxifen (1 microM), or verapamil (10 microM) for 24 hours. Flow cytometry was used to measure retention of a fluorescence dye, rhodamine 123, and the level of immunoreactive pgp-170 in berberine-treated hepatoma cells. RESULTS: Berberine up-regulated the expression of pgp-170 in three human hepatoma cell lines. The function of pgp-170 was blocked by tamoxifen and verapamil, resulting in increased retention of rhodamine 123. Retention of rhodamine 123 was significantly reduced in berberine-treated hepatoma cells. CONCLUSIONS: Berberine modulates the expression and function of pgp-170 in hepatoma cells. These results suggest that treatment of tumor cells with berberine may result in reduced retention of chemotherapeutic agents.

Lin JK, Chen YC, Huang YT, Lin-Shiau SY. **Suppression of protein kinase C and nuclear oncogene expression as possible molecular mechanisms of cancer chemoprevention by apigenin and curcumin.** J Cell Biochem Suppl 1997;28-29:39-48.
Apigenin, a less-toxic and non-mutagenic flavonoid, suppressed 12-0-tetradecanoyl-phorbol-13-acetate-(TPA)-mediated tumor promotion of mouse skin. TPA had the ability to activate protein kinase C (PKC) and induced nuclear proto-oncogene expression. Our study indicates that apigenin inhibited PKC by competing with adenosine triphosphate (ATP). Apigenin also reduced the level of TPA-stimulated phosphorylation of cellular proteins and inhibited TPA-induced c-jun and c-fos expression. Curcumin, a dietary pigment phytopolyphenol, is also a potent inhibitor of tumor promotion induced by TPA in mouse skin. When mouse fibroblast cells were treated with TPA alone, PKC translocated from the cytosolic fraction to the particulate fraction. Treatment with 15 or 20 microM curcumin for 15 min inhibited TPA-induced PKC activity in the particulate fraction by 26-60%. Curcumin also inhibited PKC activity in vitro by competing with phosphatidylserine. Curcumin (10 microM) suppressed the expression of c-jun in TPA-

treated cells. Fifteen flavonoids were examined for their effects on morphological changes in soft agar and cellular growth in v-H-ras transformed NIH3T3 cells. The results demonstrated that only apigenin, kaempferol, and genistein exhibited the reverting effect on the transformed morphology of these cells. Based on these findings, it is suggested that the suppression of PKC activity and nuclear oncogene expression might contribute to the molecular mechanisms of inhibition of TPA-induced tumor promotion by apigenin and curcumin.

Lis-Balchin M, Hart S. **A preliminary study of the effect of essential oils on skeletal and smooth muscle in vitro.** J Ethnopharmacol 1997;58(3):183-7.
The pharmacological activity of nine commercial essential oils was studied on the rat isolated phrenic nerve diaphragm preparation and compared with activity on field-stimulated guinea-pig ileum preparations. The essential oils at final bath concentrations of 2 x 10(-5) and 2 x 10(-4) g/ml produced four different effects on skeletal muscle, whilst only a contracture with or without a decrease in response to field stimulation in smooth muscle. The first type of effect on skeletal muscle involved a contracture and inhibition of the twitch response to nerve stimulation shown by a sample of clary sage, dill, fennel, frankincense and nutmeg; a second, shown by thyme produced a contracture without a change in the twitch response; a third, shown by lavender reduced the twitch response alone and the fourth, shown by camphor, increased the size of the twitch response. Angelica root oil at the highest concentration studied showed no response on skeletal muscle.

Liu W, Xiao K, Zhou J, He M, Sun H, Tang J. **Study on the protective effects of compound blood-activating soup on bone marrow hematopoietic cells in acute radiation injured mice.** J Tongji Med Univ 1997;17(4):225-8.
After irradiation with 8 Gy 60Co gamma-ray, mice were immediately given intraperitoneal injection of 200 mg 100% compound blood-activating soup twice a day. On the 3rd and 7th day, the P53 gene expression of bone marrow hematopoietic cells in Chinese drug group was found to be higher than that in normal group, and it was also significantly higher than that in control group. The expression level of GADD153 gene which was not expressed in normal group was much lower in Chinese drug group than that in control group. On the 7th day after irradiation, the P53 and GADD153 gene expression levels of splenic mononuclear cells were consistent with those of bone marrow hematopoietic cells both in Chinese drug group and control group. On the 3rd and 7th day, the bone marrow hematopoietic tissue volume in Chinese drug group was higher than that in control group, with no difference found between the two groups. While on the 14th day, the difference became significant ($P < 0.01$). The results showed that commonly used blood-activating and stasis-eliminating drugs may strengthen the viability of hematopoietic cells and promote the rehabilitation of hematopoiesis by inducing wt-P53 expression to block the bone marrow hematopoietic cells in G1 phase, during which DNA could be repaired.

Liu YP, Liu J. **Effect of alpha-hederin on hepatic detoxifying systems in mice.** Chung Kuo Yao Li Hsueh Pao 1997;18(1):33-6.
AIM: To examine whether alpha-hederin (Hed) modulates hepatic detoxifying systems as a means of hepatoprotection. METHODS: Mice were injected Hed 10 and 30 mumol.kg-1 sc for 3 d, and liver cytosols were prepared 24 h after the last dose to study antioxidant enzymes and nonenzymatic defense components. RESULTS: Hed increased liver glutathione (GSH) content

(20%), but had no effect on GSH peroxidase, GSH reductase, and GSH S-transferase. The activities of superoxide dismutase and quinone reductase were unaffected by Hed treatment. At the high dose of Hed, catalase activity was decreased by 20%. Hepatic content of metallothionein was dramatically increased (50-fold), along with elevations of hepatic Zn and Cu concentrations (25%-80%). Hed also increased ascorbic acid concentration (20%), but no effect on alpha-tocopherol in liver. CONCLUSION: Hed enhanced some nonenzymatic antioxidant components in liver, which play a partial role in Hed protection against hepatotoxicity produced by some chemicals.

Loew D. **Is the biopharmaceutical quality of extracts adequate for clinical pharmacology?** Int J Clin Pharmacol Ther 1997 Jul;35:302-6.
IPA COPYRIGHT: ASHP Guidelines for the scientific proof of equivalence and interchangeability of chemical/synthetic substances are described, including instances in which chemical and/or synthetic substances are considered equivalent, equivalence standards for phytopharmaceuticals, classification of the active ingredients of phytopharmaceuticals with drug examples, the definition of pharmaceutical equivalence, biopharmaceutical and therapeutical equivalence of phytopharmaceuticals, criteria for deciding on bioequivalence trials, and problems in demonstrating the bioequivalence of phytopharmaceuticals.

Madyastha KM, Gaikwad NW. **Metabolic fate of S-(-)-pulegone in rat.** Xenobiotica 1998;28(8):723-34.
1. S-(-)-pulegone was administered orally to rat (250 mg/kg) and the nature of the urinary metabolites was investigated. Eleven metabolites, namely S-(-)-menthofuran, piperitone, piperitenone, p-cresol, 5-hydroxypulegone, 4-methylcyclohexenone, 3-methylcyclohexanone, isopulegone, pulegol, 7-hydroxypiperitone and benzoic acid, have been isolated from rat urine. It is assumed that menthofuran, isopulegone and 4-methylcyclohexenone retain the stereochemistry of the parent compound, whereas in other metabolites the stereochemistry at the asymmetric centres is not known. 2. The relative amounts of various major metabolites present in the total urine extracts from the R-(+) and S-(-)-pulegone-treated rat were established by glc analyses. Urine samples of rats treated with R-(+)-pulegone contained higher levels of p-cresol and piperitenone than in similar experiment carried out with S-(-)-pulegone, whereas the levels of unmetabolized pulegone, piperitone and benzoic acid were considerably higher in the urine of rat treated with S-(-)-pulegone than in a corresponding experiment with R-(+)-pulegone. 3. Phenobarbital-induced rat liver microsomes converted S-(-)-pulegone to S-(-)-menthofuran (VII) and piperitenone (III) in the presence of NADPH and O2. The levels of VII and III were significantly higher in similar experiments carried out with R-(+)-pulegone. 4. Based on these studies, metabolic pathways for the biotransformation of S-(-)-pulegone in rat have been proposed and possible reasons for the observed difference in the toxicity mediated by these two enantiomers are discussed.

Madyastha KM, Gaikwad NW. **Metabolism disposition of a monoterpene ketone, piperitenone, in rats: Evidence for the formation of a known toxin, p-cresol.** Drug Metab Dispos 1999;27(1):74-80.
BIOSIS COPYRIGHT: BIOL ABS. It was shown earlier that the monoterpene ketone, piperitenone (I) is one of the major metabolites of R-(+)-pulegone, a potent hepatotoxin. In the

present studies, the metabolic disposition of piperitenone (1) was examined in rats. Piperitenone (1) was administered orally (400 mg/kg of the b. wt./day) to rats for 5 days. The following urinary metabolites were isolated and identified by various spectral analyses: p-cresol (VI), 6,7-dehydromenthofuran (III), p-mentha-1,3,5,8-tetraen-3-ol (IX), p-mentha-1, 3,5-triene-3, 8-diol (X), 5-hydroxypiperitenone (VIII), 7-hydroxypiperitenone (XI), 10-hydroxypiperitenone (XII), and 4-hydroxypiperitenone (VII). Incubation of piperitenone (1) with phenobarbital-induced rat liver microsomes in the presence of NADPH resulted in the formation of five metabolites which have been tentatively identified as metabolites III, VII, VIll, XI, XII, on the basis of gas chromatography retention time and gas chromatography-mass spectrometry analysis. Based on these results, a probable mechanism for the formation of p-cresol from piperitenone (I) via the intermediacy of metabolite III has been proposed.

Manson MM, Ball HW, Barrett MC, Clark HL, Judah DJ, Williamson G, Neal GE. **Mechanism of action of dietary chemoprotective agents in rat liver: induction of phase I and II drug metabolizing enzymes and aflatoxin B1 metabolism.** Carcinogenesis 1997;18(9):1729-38.
A range of potential chemoprotective agents, most of them natural dietary constituents, has been examined for ability to modulate both phase I (cytochrome P450 1A1, 1A2, 2B1/2, 2C11, 2E1, 3A, 4A) and phase II drug metabolizing enzymes (glutathione S-transferases, in particular subunits Yc2 and P, aflatoxin B1-aldehyde reductase and quinone reductase) in rat liver. In addition to assays of total enzyme activity and Western blots for individual isozymes, the ability of microsomes to metabolize aflatoxin B1, and of cytosols to conjugate aflatoxin B1 (AFB1)-epoxide to GSH and to produce AFB1-dialcohol, were measured. Induction of gamma-glutamyl transpeptidase activity was examined by histochemistry. Differing patterns of induction were observed, reflecting differences in the control of expression of the individual enzymes studied. Of the compounds examined, butylated hydroxytoluene, ethoxyquin, indole-3-carbinol and phenethyl isothiocyanate were the most potent bifunctional agents (inducing both phase I and II activities). Oltipraz, while only weakly inducing CYP1A2 and 2B1/2, was a potent inducer of phase II enzymes. Caffeic acid, garlic oil, sinigrin and propyl gallate all showed some ability to induce phase II enzymes. 4-Methyl catechol, alpha-tocopherol and red wine decreased certain phase I enzyme activities, while inducing total GST activity. Butylated hydroxytoluene, ethoxyquin, garlic oil and indole-3-carbinol induced gamma glutamyltranspeptidase in periportal hepatocytes. Particularly because of their ability to induce the detoxifying activities of glutathione S-transferase Yc2 and aldehyde reductase, butylated hydroxytoluene, ethoxyquin, indole-3-carbinol, oltipraz, phenethyl isothiocyanate and sinigrin will be effective blocking agents in rodents, if administered prior to AFB1. While these studies indicate the relative contributions of phase I and II metabolism in the overall protective effect in rat, care should be taken that a similar balance is achieved in man, and that relevant enzymes or iso forms a e induced.

Martin N, Bardisa L, Pantoja C, Barra E, Demetrio C, Valenzuela J, Barrios M, Sepulveda MJ. **Involvement of calcium in the cardiac depressant actions of a garlic dialysate.** J Ethnopharmacol 1997;55(2):113-8.
In order to elucidate a possible role for calcium on the negative cardiotropic effects of a garlic (Allium sativum L., Liliaceae) dialysate in rat atria we studied: (a) the effects of our extract 15 min after preincubation with high and low concentrations of extracellular calcium ([Ca2+]o) on

left and right activity of rat atria. The negative inotropism of garlic dialysate increased with calcium 0.75 mM; in contrast, high level of calcium (4.5 mM) induced a significant reduction of this depressant effect. None of these treatments modified the negative chronotropism of garlic; (b) nifedipine (10(-9) to 10(-7) M, verapamil (10(-9) to 10(-7) M) and diltiazem (10(-9) to 10(-7) M) induced a concentration-dependent synergism of the log concentration-effect of garlic dialysate on left atria. Verapamil and diltiazem (10(-7)M), but not nifedipine increased the inhibitory chronotropism of garlic in right atria; (c) negative inotropic and chronotropic effects demonstrated by nifedipine (1 x 10(-10) to 1.1 x 10(-6) M) were antagonized as expected by preincubation with Bay K-8644. Depressant actions of garlic were not modified with this pretreatment. These results suggest that the negative inotropic effect of our garlic dialysate is related to [Ca2+]o availability. It is possible that a restriction of intracellular calcium contributes to this effect. However, the negative chronotropic effect of garlic is scarcely affected by these modifications.

Matsuda H, Dai Y, Ido Y, Ko S, Yoshikawa M, Kubo M. **Studies on kochiae fructus. III. Antinociceptive and antiinflammatory effects of 70% ethanol extract and its component, momordin Ic from dried fruits of Kochia scoparia L.** Biol Pharm Bull 1997;20(10):1086-91.
The 70% ethanol extract (KS-ext) from Kochiae Fructus (dried fruits of Kochia scoparia L.) was screened for its activity on nociceptive and inflammatory responses in experimental animals. Although KS-ext at an oral administration of 500 mg/kg had an antinociceptive effect on writhing responses induced by acetic acid, it was ineffective on nociceptive response in the hot plate test. Oleanolic acid oligoglycoside, momordin Ic isolated from Kochiae Fructus significantly decreased the frequency of licking behavior within a unit of time at the late phase without affecting that of the early phase in the formalin test. Also, KS-ext inhibited the rise of vascular permeability induced by acetic acid, the increase of paw edema induced by carrageenin, histamine, serotonin or bradykinin and ear swelling induced by arachidonic acid. Momordin Ic also exhibited an inhibitory effect on carrageenin-induced edema. These results indicated that Kochiae Fructus has a peripheral antinociceptive effect mediated by antiinflammatory action, and that its active component can be partially attributed to momordin Ic.

Matsuda H, Dai Y, Ido Y, Murakami T, Matsuda H, Yoshikawa M, Kubo M. **Studies on Kochiae Fructus. V. Antipruritic effects of oleanolic acid glycosides and the structure-requirement.** Biol Pharm Bull 1998;21(11):1231-3.
We examined the antipruritic effects of various oleanolic acid glycosides from natural medicines such as Kochiae Fructus (the fruit of Kochia scoparia SCHRAD.) and Momordicae Radix (the roots of Momordica cochinchinensis SPRENG.) using a compound 48/80-induced pruritic model in mice. Oleanolic acid 3-O-monodesmosides showed an antipruritic effect, while oleanolic acid 3,28-O-bisdesmosides and their common sapogenol oleanolic acid lacked the activity. This evidence indicated that the 3-O-glycoside moiety and the 28-carboxyl group in oleanolic acid glycosides were essential for exhibiting the antipruritic effect. Furthermore, it was found that the 3-O-glucuronides showed more potent activity than the corresponding 3-O-glucosides.

Matsuda H, Li Y, Murakami T, Yamahara J, Yoshikawa M. **Protective effects of oleanolic acid oligoglycosides on ethanol- or indomethacin-induced gastric mucosal lesions in rats.** Life Sci 1998;63(17):L245-50.

We examined the effects of various oleanolic acid oligoglycosides obtained from traditional herbs on ethanol- or indomethacin-induced gastric mucosal lesions in rats and on gastric secretion in pylorus-ligated rats. Test samples were given orally to fasted rats 1 h before absolute ethanol (1.5 ml/rat, p.o.) or indomethacin (30 mg/kg, s.c.) treatment, or ligation of the pylorus. Oleanolic acid 3-O-monodesmosides [oleanolic acid 3-O-glucuronide (1, 20-50 mg/kg), momordin Ic (2, 5-50 mg/kg), and 28-O-deglucosyl-chikusetsusaponins IV (5, 10-50 mg/kg) and V (7, 10-50 mg/kg)] were found to show protective effects on ethanol-induced gastric mucosal lesions, whereas oleanolic acid 3,28-O-bisdesmosides [momordin IIc (3), chikusetsusaponins IV (4) and V (6)], oleanolic acid 28-O-monodesmoside [compound O (8)], and their common aglycon [oleanolic acid (9)] showed no such effects. Oleanolic acid 3-O-monodesmosides (1, 2, and 5) also showed protective effects on indomethacin-induced gastric mucosal lesions. 28-O-Deglucosyl-chikusetsusaponin V (7) did not inhibit the indomethacin-induced lesions, while chikusetsusaponins V (6, 50 mg/kg) had the gastroprotective effect. These active saponins (1, 2, 4-7, 10-50 mg/kg) did not decrease the gastric secretion by oral administration in pylorus-ligated rats.

Matsuda H, Tomohiro N, Yoshikawa M, Kubo M. **Studies on Alismatis Rhizoma. II. Anti-complementary activities of methanol extract and terpene components from Alismatis Rhizoma (dried rhizome of Alisma orientale).** Biol Pharm Bull 1998;21(12):1317-21.
A methanol extract (TMe-ext) from the dried rhizome of Alisma orientale was screened for anti-complementary activity in experimental models. In the animal models, it was found that TMe-ext inhibits zymosan-induced hind paw edema in rats and zymosan-activated rat serum (ZAS)-induced vascular permeability in mice. TMe-ext showed an inhibitory effect on complement-induced hemolysis through both the classical pathway and the alternative pathway. And TMe-ext inhibited hypotonic shock-induced hemolysis, but this effect was weak compared with the anti-complementary activities of TMe-ext. Four triterpenes (alisol A, alisol A monoacetate, alisol B and alisol B monoacetate) isolated from the rhizome also inhibited the complement-induced hemolysis through the classical pathway, but two sesquiterpenes (alismol and alismoxide) were ineffective. These results indicate that Alismatis Rhizoma shows anti-complementary activity, and its anti-complementary components are partially attributable to the terpene components mentioned above.

Matsumoto Y, Kato M, Tamada Y, Mori H, Ohashi M. **Enhancement of interleukin-1 alpha mediated autocrine growth of cultured human keratinocytes by sho-saiko-to.** Jpn J Pharmacol 1997;73(4):333-6.
We investigated the effects of Sho-saiko-to, the most commonly used herbal medicine in Japan, on the production of interleukin (IL)-1 alpha by cultured human epidermal keratinocytes. IL-1 alpha production was significantly promoted by treatment with 100 or 500 micrograms/ml Sho-saiko-to for 24 or 48 hr. Expression of IL-1 alpha receptors was the most markedly upregulated after treatment with 500 micrograms/ml Sho-saiko-to for 24 hr and with 100 or 500 micrograms/ml for 48 hr; these cells showed the characteristics of multilayered differentiated keratinocytes. The presence of an anti-IL-1 alpha antibody during the treatment with 500 micrograms/ml of Sho-saiko-to for 24 or 48 hr or with 100 micrograms/ml for 48 hr significantly down-regulated the synthesis by the keratinocytes and induced damages in them. Keratinocytes treated with Sho-saiko-to might produce IL-1 alpha and express IL-1 alpha receptors. IL-1 alpha

may regulate the proliferation and differentiation of keratinocytes after Sho-saiko-to treatment. These findings suggest that Sho-saiko-to enhances the autocrine growth mediated by IL-1 alpha.

Matsuo K, Kobayashi M, Takuno Y, Kuwajima H, Yoshida T, et al . **[Anti-tyrosinase activity of constituents of Arctostaphylos uva-ursi].** Yakugaku Zasshi 1997 Dec;117:1028-32. (Jpn)
IPA COPYRIGHT: ASHP The inhibitory effect on the activity of tyrosinase of different constituents, including 1,2,3,6-tetragalloylglucose (1,2,3,6-tetra-O-galloyl-beta-D-glucose), 1,2,3,4,6-pentagalloylglucose (1,2,3,4,6-penta-O-galloyl-beta-D-glucose), methyl gallate, gallic acid, and hydroquinone, of a methanolic extract of the leaves of Arctostaphylos uva-ursi was studied.

Mattei R, Dias RF, Espinola EB, Carlini EA, Barros SB. **Guarana (Paullinia cupana): toxic behavioral effects in laboratory animals and antioxidants activity in vitro.** J Ethnopharmacol 1998;60(2):111-6.
The effects on toxic and behavioral levels of guarana (Paullinia cupana) were assessed in rats and mice subsequent to acute and chronic administrations and were compared to those produced by Ginseng (Panax ginseng). Experimental parameters included tests for antioxidant capacity in vitro and measured in vivo, toxicological screening, progress in weight, motor activity, death rate, and histopathological examination of the viscera. Guarana showed an antioxidant effect because, even at low concentrations (1.2 microg/ml), it inhibited the process of lipid peroxidation. In high doses of 1000-2000 mg/kg (i.p. and p.o.) it did not induce significant alterations in parameters for toxicological screening. No effects on motor activity were observed, neither did guarana alter the hypnotic effect of pentobarbital. Ginseng (250-1000 mg/kg i.p.), however, elicited reductions in motor activity, eyelid ptosis and bristling fur. Consumption of liquids containing guarana or ginseng and progress in weight of the animals remained at levels similar to the controls, even after prolonged administration. The percentage mortality was equivalent in control and in treated groups. The absence of toxicity of guarana was also demonstrated by histopathological examination, with no alteration being detected in heart, lungs, stomach, small and large intestine, liver, pancreas, kidneys, bladder and spleen.

Maulik G, Maulik N, Bhandari V, Kagan VE, Pakrashi S, Das DK. **Evaluation of antioxidant effectiveness of a few herbal plants.** Free Radic Res 19997;27(2):221-8.
We have screened a number of plants from the Indian soil for potential antioxidant properties out of which fifteen extracts were found to be positive. Leaves/bulk from the plants were crushed and extracted with organic solvents by three different ways. The first group of plants were extracted with CHCL3:CH3OH (2:1), evaporated, partitioned between petroleum ether and methanol (9:1), aqueous methanolic part re-partitioned between methanol:H2O (4:1) and dichloromethane. Methanol was evaporated from the aqueous methanolic part and extracted with n-butanol. The second group of plants were extracted with methanol followed by partitioning between petroleum ether and CH3OH. The rest of the extraction procedure was the same as above. A third extraction procedure was used for Ocimum sanctum which after extraction with CHCL3:CH3OH (2:1), partitioned between CCL4 and CH3OH:H2O (9:1). Aqueous methanolic part was repartitioned between CH3OH:H2O (4:1) and CHCl3 and CHCl3 soluble part was used for the study. Free radical scavenging activities of the plant extracts were examined by chemiluminescence method. Peroxyl radical was generated from 2,2'-azobis(2-amidinopropane)

dihydrochloride (AAPH), superoxide radical (O2-) from xanthine/xanthine oxidase (XO) and hydroxyl radical (OH) from Xanthine/XO/FeCl3/ EDTA. In addition, O2- and OH. scavenging activities were also determined by cytochrome C reduction and deoxyribose oxidation methods, respectively. The results of this study demonstrate that these plant extracts possess potent antioxidant activities.

Molck AM, Poulsen M, Tindgard Lauridsen S, Olsen P. **Lack of histological cerebellar changes in Wistar rats given pulegone for 28 days. Comparison of immersion and perfusion tissue fixation.** Toxicol Lett 1998;95(2):117-22.
Pulegone was given orally by gavage to groups of 28 SPF Wistar rats at dosage levels of 0 or 160 mg/kg body weight per day for 28 days. Clinically treated animals showed slackness, depression, decreased food consumption, and body weight. The loss of body weight was accompanied by a marked decrease in plasma creatinine. In contrast to earlier results, this study did not reveal occurrence of cyst-like spaces in the white matter of cerebellum using either perfusion or immersion tissue fixation techniques. Pulegone increased plasma alkaline phosphatase and relative liver weight indicating an adverse effect on the liver.

Moon A, Kim SH. **Effect of Glycyrrhiza glabra roots and glycyrrhizin on the glucuronidation in rats.** Planta Med 1997;63(2):115-9.
As an approach to elucidate the possible in vivo interaction of synthetic drugs and herbs which are frequently used in combination in Asia, the effect of Glycyrrhiza glabra on the metabolism of acetaminophen (AAP) was examined in male Sprague-Dawley rats. The pretreatment of the methanol extract of Glycyrrhiza glabra roots (Glycyrrhizae Radix, GR, 1 g/kg, p.o.) for 6 days significantly increased the cumulative biliary (156%) and urinary (132%) excretions of AAP-glucuronide conjugate within 120 min after the administration of AAP (150 mg/kg, i.v.) without affecting thioether and sulfate conjugates. These findings suggest that GR might enhance the glucuronidation pathway of AAP. In order to study the effect of GR on the glucuronidation in rat liver, we examined enzymatic activity of p-nitrophenol UDP-glucuronosyltransferase (UGT), which is also called UGT1A, and intracellular concentrations of hepatic UDP-glucuronic acid, upon the administration of GR (1 g/kg, p.o.) or glycyrrhizin (23 mg/kg, p.o.), a major component of GR, for 6 days. GR and glycyrrhizin caused increases in specific activities of UGT1A by 111% and 96%, respectively. Concentration of UDP-glucuronic acid was increased 257% by GR and 484% by glycyrrhizin. These data indicate that GR and glycyrrhizin activated glucuronidation and thus suggest the possibility that GR may influence detoxification of xenobiotics in rat liver. Using the p-nitrophenol UGT1A1 cDNA as a probe, we found that the activation of UGT1A by GR was not due to the induction of mRNAs for the enzyme.

Moreno L, Bello R, Beltran B, Calatayud S, Primo-Yufera E, Esplugues J. **Pharmacological screening of different Juniperus oxycedrus L. extracts.** Pharmacol Toxicol 1998;82(2):108-12.
Methanol and dichloromethanol extracts of leaves and stems of Juniperus oxycedrus have been tested for their toxicity, analgesic, antiinflammatory and central effects. Both extracts showed low acute toxicity and decreased spontaneous motility. The methanol extract exhibited an analgesic effect in models of chemical, mechanical and thermal stimulation whereas dichloromethanol extract showed only a significant effect in models of pain induced by chemical

stimulation. Both extracts showed a significant antiinflammatory activity and inhibition of the rat paw oedema induced by carrageenin.

Motoyashiki T, Miyake M, Morita T, Mizutani K, Masuda H, Ueki H. **Enhancement of the vanadate-stimulated release of lipoprotein lipase activity by astilbin from the leaves of Engelhardtia chrysolepis.** Biol Pharm Bull 1998;21(5):517-9.
Astilbin, a dihydroflavonol rhamnoside isolated from the leaves of Engelhardtia chrysolepis, enhanced the vanadate-stimulated release of lipoprotein lipase (LPL) activity from rat isolated fat pads. N-[2-(Methyl-amino)ethyl]-5-isoquinolinesulfonamide (H-8), a potent inhibitor of cAMP-dependent protein kinase (PKA), markedly inhibited the enhancement by astilbin. Lipolysis in the fat pads was stimulated by astilbin alone in a dose-dependent manner and this stimulation was suppressed in the presence of vanadate, probably due to its antilipolytic action. A significant enhancement by astilbin was observed with increasing effects of vanadate on cAMP content in the fat pads and on cAMP phosphodiesterase (PDE) activity in the particulate fraction although astilbin alone showed only a slight increase in the cellular cAMP content and PDE activity. Astilbin may enhance the vanadate-stimulated release of LPL activity through a synergistic effect on an increase in the cellular cAMP content produced by vanadate accompanied by more potent activation of PKA.

Mukherjee S, Sur A, Maiti BR. **Hepatoprotective effect of Swertia chirata on rat.** Indian J Exp Biol 1997;35(4):384-8.
Present work was undertaken to ascertain the hepatoprotective effect of Swertia chirata in albino rats. Intraperitoneal injection of CCl4 (1 ml/kg body wt on every 72 hr. for 16 days) significantly increased serum aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), and alkaline phosphatase (ALP) activities and bilirubin level in rat, but liver glycogen and serum cholesterol levels were decreased. Histologically it produced hepatocytic necrosis especially in the centrilobular region. Simultaneous treatments with S. Chirata (in different doses, viz, 20, 50 and 100 mg/kg body wt daily) and CCl4 (similar dose to that mentioned earlier) caused improvement at both biochemical and histopathological parameters compared to that of CCl4 treatment alone but it was most effective when S. chirata was administered in a moderate dose (50 mg/kg body wt).

Neary JT, Bu Y. **Hypericum LI 160 inhibits uptake of serotonin and norepinephrine in astrocytes.** Brain Res 1999;816(2):358-63.
Extracts of Hypericum perforatum, commonly known as St. John's wort, are frequently used in Germany and other European countries to treat mild to moderately severe depression, but the mechanism of antidepressant activity of Hypericum is not understood. Because known mechanisms of antidepressant activity include inhibition of serotonin and/or norepinephrine uptake, we investigated the effects of standardized extracts of Hypericum LI 160 on the transport of these monoamine neurotransmitters into astrocytes, cells which surround synaptic terminals and regulate neurotransmission by means of their uptake systems. We found that LI 160 inhibited both serotonin and norepinephrine uptake in a dose-dependent manner. The two monoamine transport systems were affected differently by LI 160: for serotonin, the main effect was a 50% decrease in the rate of maximal transport, whereas for norepinephrine, the main effect was a 4.5 fold reduction in the apparent affinity of norepinephrine for its uptake sites. Upon

removal of LI 160, uptake was restored, thereby indicating that the inhibition was not due to a toxic effect of Hypericum on the cells. These findings suggest that the ability of LI 160 to inhibit serotonin and norepinephrine uptake may underlie the antidepressant activity of this Hypericum extract. Copyright 1999 Elsevier Science B.V.

Nijs PM. **[Bio-active substances from nutrition and herbs: influence on the brain activity in children, elderly people and sportsmen].** Farm Tijdschr Belg 1997 Dec;74:16-29. (Dut)
IPA COPYRIGHT: ASHP An overview of secondary plant extracts, such as antihypoxidotics (Ginkgo biloba), adaptogenes (ginseng), phytosterols (in certain seeds and nuts), immunostimulators (Echinacea species), terpenes, organic fruity acids, and omega-3 fatty acids, that seem to exert an activity on the human brain function, is presented.

Nishimura N, Naora K, Hirano H, Iwamoto K. **Effects of Sho-saiko-to on the pharmacokinetics and pharmacodynamics of tolbutamide in rats.** J Pharm Pharmacol 1998;50(2):231-6.
Although Sho-saiko-to (Xiao Chai Hu Tang), a major Chinese traditional medicine, is frequently prescribed with other synthetic or biotechnological drugs for the treatment of various chronic diseases, there is a dearth of information about interactions between sho-saiko-to and co-administered drugs. This paper reports the effects of Sho-saiko-to on the pharmacokinetics and glucose responses of a sulphonylurea hypoglycaemic agent, tolbutamide, after their oral administration in rats. After oral administration of tolbutamide (50 mg kg(-1)) with or without Sho-saiko-to extract powder (300 mg kg(-1)) to male Sprague-Dawley rats cannulated in the jugular vein, plasma tolbutamide and glucose levels were periodically measured. Co-administration of Sho-saiko-to tended to elevate the plasma tolbutamide concentration in the absorption phase. A two-compartment lag-time model was found to describe the plasma tolbutamide concentration-time data. The maximum concentration of tolbutamide was significantly increased and time to reach the maximum concentration was reduced to about 70% by co-administration with Sho-saiko-to. There was no significant change in area under the curve or in the elimination half-life of tolbutamide. The extent of the lowering effect of tolbutamide on plasma glucose levels was increased up to 0.75 h and decreased after 5 h after co-administration of Sho-saiko-to. In conclusion, these studies suggest that sho-saiko-to slightly hastens the gastrointestinal absorption of tolbutamide. Furthermore, it is considered that elevation of the gastrointestinal absorption rate by Sho-saiko-to might potentiate the hypoglycaemic effect of this sulphonylurea in the early period after oral administration.

O'Brien LW. **Interactions and toxicities of drugs for HIV disease.** Drug Ben Trends 1998 Jul 10;10:44-52.
IPA COPYRIGHT: ASHP An overview of the physiologic, genetic, and immunologic issues affecting the pharmacokinetics and pharmacodynamics of drugs prescribed for treating human immunodeficiency virus (HIV) and its related complications is presented, including toxicities associated with drugs frequently administered for HIV disease, drug interactions of commonly used agents to treat HIV disease, and medicinal herbs used by HIV-infected patients.

Oh KW, Kim HS, Wagner GC. **Inhibitory effects of ginseng total saponin on methamphetamine-induced striatal dopamine increase in mice.** Arch Pharmacal Res 1997;20(5):516-8.

Ohdo S, Ogawa N, Song JG, Higuchi S. **Chronopharmacological study of KE-SI-TO components in mice.** Life Sci 1998;62(22):2057-64.
Influence of dosing time on pharmacological effects and toxicity of KE-SI-TO (KST) components, as well as the role of each component in the circadian rhythms of KST, was investigated in ICR male mice under an LD (12:12) cycle. The mice given Cinnamomi Cortex (258 mg/kg, i.p.) or Paeoniae Radix (258 mg/kg, i.p.) showed a significant circadian rhythm in the time spent on the hot plate with the shortest latency at 0900 and the longest one at 0100 (p

Ohta Y, Sasaki E, Nishida K, Kongo M, Hayashi T, Nagata M, Ishiguro I. **Inhibitory effect of Oren-gedoku-to (Huanglian-Jie-Du-Tang) extract on hepatic triglyceride accumulation with the progression of carbon tetrachloride-induced acute liver injury in rats.** J Ethnopharmacol 1998;61(1):75-80.
The inhibitory effect of Oren-gedoku-to (Huanglian-Jie-Du-Tang) extract (TJ-15) on hepatic triglyceride (TG) accumulation with the progression of acute liver injury was examined in rats intoxicated with carbon tetrachloride (CCl4). TJ-15 at a dose of 100, 250 or 500 mg/kg body weight (BW) was orally administered to male Wistar rats aged 7 weeks, 6 h after the intraperitoneal injection of CCl4 (1.0 ml/kg BW) at which time apparent liver injury and hepatic TG accumulation occurred. TJ-15 significantly prevented not only the progression of liver injury but also inhibited hepatic TG accumulation with the progression of the injury in a dose-dependent manner when these effects were examined 24 h after CCl4 injection. In CCl4-untreated rats with oral administration of TJ-15 at a dose of 100, 250 or 500 mg/kg BW, liver and serum TG concentrations decreased depending on the dose of the herbal medicine. These results indicate that in rats intoxicated once with CCl4, orally administered TJ-15 can inhibit hepatic TG accumulation with the progression of acute liver injury by its decreasing action on serum and liver TG levels, leading to a prevention of the progression of the liver injury.

Panossian AG, Oganessian AS, Ambartsumian M, Gabrielian ES, Wagner H, Wikman G. **Effects of heavy physical exercise and adaptogens on nitric oxide content in human saliva.** Phytomedicine 1999;6(1):17-26.
Since heavy physical exercise increases the content of nitric oxide and cortisol in blood and saliva, standardized extracts of the adaptogen herbal drugs Schizandra chinensis and Bryonia alba roots were applied to several groups of athletes in a placebo controlled double blind study. In the beginning of a test with athletes Schizandra chinensis and Bryonia alba extracts increased the concentration of NO and cortisol in blood plasma and saliva similar to athletes with heavy physical exercise. These results correlate with an increased physical performance in athletes taking adaptogens versus athletes taking placebo. In contrast after treatment with the adaptogen heavy physical exercise does not increase salivary NO and cortisol in athletes, whereas athletes treated with placebo heavy physical exercise increased salivary NO. These results show that the salivary NO test can be used both for evaluation of physical loading and stress protective effect of an adaptogen.

Park JA, Kim KW, Kim SI, Lee SK. **Caspase 3 specifically cleaves p21WAF1/CIP1 in the earlier stage of apoptosis in SK-HEP-1 human hepatoma cells.** Eur J Biochem 1998;257(1):242-8.
We report here that p21WAF1/CIP1, an inhibitor of cyclin kinases, underwent proteolytic processing into a smaller fragment, p14, in the early stage of apoptosis in SK-HEP-1 cells. Apoptosis was induced by either staurosporine or ginsenoside Rh2, a ginseng saponin with a dammarane skeleton. Proteolytic processing was the result of caspase-3 activity, which accompanied the early changes in cell morphology and DNA fragmentation. p21WAF1/CIP1 translated in vitro was cleaved into a p14 fragment when incubated with cell extracts obtained from either ginsenoside Rh2-treated or staurosporine-treated cells. Cleavage was equally inhibited in both cases by adding Ac-DEVD-CHO, a specific caspase-3 inhibitor, but not by Ac-YVAD-CHO, a specific caspase-1 inhibitor. Similarly, p21WAF1/CIP1 was efficiently cleaved by recombinant caspase-3, overexpressed in Escherichia coli. Moreover, the endogenous p21WAF1/CIP1 of untreated cell extracts was also cleaved by recombinant caspase 3, as measured by immunoblotting. Mutation analysis allowed identification of two caspase-3 cleavage sites, DHVD112/L and SMTD149/F, which are located within or near the interaction domains for cyclins, Cdks, and proliferating cell nuclear antigen (PCNA). Taken together, these results show that ginsenoside Rh2 and staurosporine increase caspase-3 activity, which in turn directly cleaves p21WAF1/CIP1 during the early stages of apoptosis. We propose that proteolytic cleavage of p21WAF1/CIP1 is a functionally relevant event that allows release of the cyclin/Cdk complex from the p21WAF1/CIP1 inhibitor, resulting in the elevated levels of cyclin/Cdk kinase activity seen in the earlier stage of apoptosis.

Park JA, Lee KY, Oh YJ, Kim KW, Lee SK. **Activation of caspase-3 protease via a Bcl-2-insensitive pathway during the process of ginsenoside Rh2-induced apoptosis.** Cancer Lett 1997;121(1):73-81.
We have demonstrated that ginsenoside Rh2 (G-Rh2), a ginseng saponin with a dammarane skeleton, induces apoptosis of human hepatoma SK-HEP-1 cells as evidenced by analyses of DNA fragmentation, flow cytometry and changes in cell morphology. Ac-YVAD-CMK or Ac-DEVD-CHO effectively prevented G-Rh2-induced DNA fragmentation, indicating the involvement of caspase-like proteases in the process of apoptosis. In addition, G-Rh2 induced the processing of caspase-3 to an active form, p17. In stable Bcl-2 transfectants, G-Rh2 also induced DNA fragmentation, while staurosporine-induced DNA fragmentation was totally blocked. As it did in wild-type cells, G-Rh2 induced the proteolytic activation of caspase-3 protease and subsequent cleavage of PARP in the bcl-2 transfectants. In summary, G-Rh2 contains an apoptotic inducing activity in SK-HEP-1 cells which functions via Bcl-2-insensitive activation of caspase-3, followed by proteolytic cleavage of PARP.

Premalatha B, Sujatha V, Sachdanandam P. **Modulating effect of Semecarpus anacardium Linn. nut extract on glucose metabolizing enzymes in aflatoxin B1-induced experimental hepatocellular carcinoma.** Pharmacol Res 1997;36(3):187-92.
The herbal remedy extended by Semecarpus anacardium nut extract against Aflatoxin B1 mediated hepatocellular carcinoma was established by studies on carbohydrate metabolizing enzymes. Since some definite correlation exists between tumour progression and the activities of glycolytic and gluconeogenic enzymes, assessment of alterations in their activity can be used as

successful markers of diagnosis and prognosis. The present work compares the activities of glycolytic and gluconeogenic enzymes in hepatocellular carcinoma bearing rats with drug-treated animals. An overall increase in glycolytic enzymes namely hexokinase, phosphoglucoisomerase, and aldolase with a subsequent reduction in gluconeogenic enzymes, glucose-6-phosphatase and fructose-1,6-biphosphatase was observed in plasma and liver homogenates of hepatocellular carcinoma bearing rats. The administration of Semecarpus anacardium nut extract caused a significant decrease in the activity of glycolytic enzymes and an increase in gluconeogenic enzymes' activities to near normal values in drug-treated animals. Copyright 1997 The Italian Pharmacological Society.

Preuss HG, Jarrell ST, Scheckenbach R, Lieberman S, Anderson RA. **Comparative effects of chromium, vanadium and gymnema sylvestre on sugar-induced blood pressure elevations in SHR.** J Am Coll Nutr 1998;17(2):116-23.
OBJECTIVE: Effects on systolic blood pressure (SBP) of ingesting three agents reported to influence insulin metabolism, i.e., chromium polynicotinate, bis(maltolato)oxovanadium (BMOV), and the herb, Gymnema sylvestre, were assessed simultaneously in spontaneously hypertensive rats (SHR). METHODS: In the first study, SHR were fed either a starch, sugar, or sugar diet containing chromium polynicotinate, bis(maltolato)oxovanadium (BMOV), or G. sylvestre. Tail SBP was estimated indirectly and various blood chemistries were measured. TBARS formation was determined in hepatic and renal tissue. In a second study, tail SBP was measured in SHR ingesting diets containing different concentrations of BMOV. RESULTS: Compared to starch, SHR consuming sucrose showed a significant elevation of SBP within days that was maintained for the duration of study. Addition of chromium polynicotinate to the sucrose diet at the beginning of study prevented the sucrose-induced elevation of SBP for 2 weeks, but SBP rose significantly after that. BMOV at high concentrations overcame the sucrose-induced rise in SBP and even decreased SBP below values seen in SHR eating the starch diet, but marked weight loss was noted. A second study examined different concentrations of BMOV. At 0.01% w/w concentration of BMOV, SBP was still significantly decreased, even though SHR did not lose body weight (BW) early on. SHR consuming G. sylvestre showed no change or even elevated SBP. Hepatic thiobarbituric acid reacting substances (TBARS) formation, an estimate of lipid peroxidation, was decreased by chromium polynicotinate and BMOV, and renal TBARS by chromium polynicotinate. Circulating cholesterol concentrations were decreased in the SHR consuming G. sylvestre. CONCLUSIONS: Chromium decreases the portion of SBP elevated by high sucrose intake as shown previously, but high levels of sucrose ingestion can eventually overcome this. BMOV overcame sucrose-induced elevation of SBP as well as some of the "genetic hypertension." Different from chromium, this decrease was not overcome by high levels of dietary sucrose. The significant lowering of cholesterol with G. sylvestre ingestion indicates some effect on metabolism, but G. sylvestre did not lower and even raised SBP.

Puig L. **Pharmacodynamic interaction with phototoxic plants during PUVA therapy [letter].** Br J Dermatol 1997;136(6):973-4.

Qi J, Toyoshima A, Honda Y, Mineshita S. **Pharmacokinetic study on acetaminophen: interaction with a Chinese medicine.** J Med Dent Sci 1997;44(1):31-5.

To know the influences of a Chinese traditional medicine (KAKKONTO) on the metabolism of acetaminophen (APAP), we have carried out pharmacokinetic studies on APAP under KAKKONTO coadministration in humans and rats. In humans, the pharmacokinetic parameters were calculated from the blood APAP concentration-time curves of each volunteer. The parameters did not show any significant differences between the KAKKONTO-coadministration group (group K) and the APAP-administration group (group A). KAKKONTO, when given at two different doses, did not show any significant effects on blood APAP level. In rats, the blood APAP level was significantly higher than that of group A ($p < 0.01$) only in the 100 mg/kg of group K at 0.25 h after APAP administration. There were no other significant differences.

Rabinkov A, Miron T, Konstantinovski L, Wilchek M, Mirelman D, Weiner L. **The mode of action of allicin: trapping of radicals and interaction with thiol containing proteins.** Biochim Biophys Acta 1998;1379(2):233-44.
BIOSIS COPYRIGHT: BIOL ABS. Allicin (thio-2-propene-1-sulfinic acid S-allyl ester) is the main biologically active component of garlic clove extracts. Its biological activity was attributed to either antioxidant activity or thiol disulfide exchange. Antioxidant properties of both allicin and its precursor, alliin (+ S-allyl-L-cysteine sulfoxide), were investigated in the Fenton oxygen-radical generating system (H2O2-Fe(II)). Using the spin trapping technique and ESR, it was found that both compounds possessed significant antioxidant activity. The reaction between allicin and L-cysteine was studied by 1H and 13C-NMR, and a S-thiolation product, S-allylmercaptocysteine, was identified. Allicin irreversibly inhibited SH-protease papain, NADP+-dependent alcohol dehydrogenase from Thermoanaerobium brockii (TBAD), and the NAD+-dependent alcohol dehydrogenase from horse liver (HLAD). All the three enzymes could be reactivated with thiol containing compounds. Papain could be reactivated with glutathione, TBAD with dithiothreitol or 2-mercaptoethanol (2-ME) but not by glutathione, while HLAD could be reactivated only with 2-ME. This study demonstrates that in addition to its antioxidant activity, the major biological effect of allicin should be attributed to its rapid reaction with thiol containing proteins.

Rohnert U, Koske D, Schneider W, Elstner EF. **Inhibition by Salix- extracts and Phytodolor of copper-catalyzed oxidative destruction.** Z Naturforsch [C] 1998;53(3-4):233-40.
Oxidation of low density lipoprotein (LDL) by copper ions is strongly inhibited by different aqueous extracts (Salix spec (SE); Fraxinus-Dolidago-Populus (Phytodolor)(PD) in a concentration range between 4 and 7 micrograms/ml. 10 to 50 microM salicylic acid (SA) stimulate LDL-oxidation whereas higher concentrations (10 to 500 micromM) showed no effect. Likewise ethene release from 2-keto-4-methylthiobutyrate (KMB) is strongly inhibited by the above extracts in a reaction driven by dihydroxyfumarate (DHF) in the presence of copper ions. This system may represent some features of the diabetic situation where DHF as an endiole may stand for certain Amadori products. In order to find out whether the inhibitory effects are due to copper chelation we tested the copper-dependent conversion of photodynamic ethane release from alpha-linolenic acid into ethene formation. Copper chelation is apparently only partially involved in inhibition of copper-dependent oxidations and only at a certain concentration of extracts from salix spec (SE) or extracts from Fraxinus-Solidago-Populus (Phytodolor)(PD).

Romano EL, Montano RF, Brito B, Apitz R, Alonso J, Romano M, Gebran S, Soyano A. **Effects of Ajoene on lymphocyte and macrophage membrane-dependent functions.** Immunopharmacol Immunotoxicol 1997;19(1):15-36.
Ajoene, (E, Z) -4, 5, 9-trithiadeca-1, 6, 11-triene 9 oxide, is a compound originally isolated from ethanolic extracts of garlic that impairs platelet aggregation by inhibiting the functional exposure of platelet integrins GPIIb/IIIa. In vitro, Ajoene is toxic for several tumoral cell lines, and exert an antiproliferative effect on T. cruzi and murine malaria parasites. Here we show that Ajoene strongly inhibited the proliferation induced in human lymphocytes by the mitogens phytohemagglutinin (PHA), phorbol myristate acetate (PMA) and anti-CD3, and the capping formation induced in B lymphocytes by anti-IgM antibodies. On macrophages, Ajoene was also found to partially inhibit the lypopolysaccharide-induced production of Tumor Necrosis Factor (TNF), and to decrease the phagocytic activity of thioglycolate-elicited mouse peritoneal macrophages for IgG-opsonized, human erythrocytes. Ajoene also partially prevented the lytic effect of human and rabbit TNF on Actinomycin D-treated WEHI 164 cells. These results strongly suggest that Ajoene is a potent modulator of membrane-dependent functions of immune cells.

Roth GN, Chandra A, Nair MG. **Novel bioactivities of Curcuma longa constituents.** J Nat Prod 1998;61(4):542-5.
Bioassay-directed fractionation of ethyl acetate extract from Curcuma longa Linn. rhizomes yielded three curcuminoids, which displayed topoisomerase I and II enzyme inhibition activity. Curcumin III (3) was the most active curcuminoid, inhibiting topoisomerase at 25 micrograms mL-1. Curcumin I (1) and curcumin II (2) inhibited the topoisomerases at 50 micrograms mL-1. Fractionation of the volatile oil from the rhizomes afforded ar-turmerone (4), which displayed mosquitocidal activity with an LD100 of 50 micrograms mL-1 on Aedes aegyptii larvae. Bioassay-directed fractionation of hexane extract from the turmeric leaves yielded labda-8(17),12-diene-15,16 dial (5) with antifungal activity against Candida albicans at 1 micrograms mL-1 and inhibited the growth of Candida kruseii and Candida parapsilosis at 25 micrograms mL-1. In addition, 5 displayed 100% mosquitocidal activity on A. aegyptii larvae at 10 micrograms mL-1.

Ryu BK, Ahn BO, Oh TY, Kim SH, Kim WB, Lee EB. **Studies on protective effect of DA-9601, Artemisia asiatica extract, on acetaminophen- and CCl4-induced liver damage in rats.** Arch Pharm Res 1998;21(5):508-13.
The hepatoprotective effect of DA-9601, a quality-controlled extract of Artemisia asiatica, on liver damage induced by acetaminophen (APAP) and carbon tetrachloride (CCl4) was investigated by means of serum-biochemical, hepatic-biochemical, and histopathological examinations. Doses of DA-9601 (10, 30, or 100 mg/kg) were administered intragastrically to each rat on three consecutive days i.e. 48 h, 24 h and 2 h before a single administration of APAP (640 mg/kg, i.p.) or CCl4 (2 ml/kg, p.o.). Four h and 24 h after hepatotoxin treatment, the animals were sacrificed for evaluation of liver damage. Pretreatment of DA-9601 reduced the elevation of serum ALT, AST, LDH and histopathological changes such as centrilobular necrosis, vacuolar degeneration and inflammatory cell infiltration dose-dependently. DA-9601 also prevented APAP- and CCl4-induced hepatic glutathione (GSH) depletion and CCl4-induced increase of hepatic malondialdehyde (MDA), a parameter of lipid peroxidation, in a dose-

dependent manner. These findings suggest that pretreatment with DA-9601 may reduce chemically induced liver injury by complex mechanisms which involve prevention of lipid peroxidation and preservation of hepatic GSH.

Ryu JH, Lee HJ, Jeong YS, Ryu SY, Han YN. **Yomogin, an inhibitor of nitric oxide production in LPS-activated macrophages.** Arch Pharm Res 1998;21(4):481-4.
In activated macrophages the inducible form of nitric oxide synthase (i-NOS) generates high amounts of toxic mediator, nitric oxide (NO) which contributes to the circulatory failure associated with septic shock. A sesquiterpene lactone compound (yomogin) isolated from medicinal plant Artemisia princeps Pampan inhibited the production of NO in LPS-activated RAW 264.7 cells by suppressing i-NOS enzyme expression. Thus, yomogin may be a useful candidate for the development of new drugs to treat endotoxemia and inflammation accompanied by the overproduction of NO.

Satoh K, Nagai F, Ushiyama K, Yasuda I, Seto T, Kano I. **Inhibition of Na+,K(+)-ATPase by 1,2,3,4,6-penta-O-galloyl-beta-D-glucose, a major constituent of both moutan cortex and Paeoniae radix.** Biochem Pharmacol 1997;53(4):611-4.
The inhibition of Na+,K(+)-ATPase activity by various constituents of Moutan Cortex and Paeoniae Radix was studied. 1,2,3,4,6-Penta-O-galloyl-beta-D-glucose (PGG), a major component of both crude drugs, strongly inhibited Na+,K(+)-ATPase activity (IC50 = 2.5 x 10(-6) M), whereas galloylpaeoniflorin, benzoic acid, and catechin were weakly inhibitory, and albiflorin, oxypaeoniflorin, paeoniflorin, paconol, and phenol were ineffective. The inhibition of Na+,K(+)-ATPase activity by PGG was decreased in the presence of BSA or phospholipids. The inhibition mode of PGG was noncompetitive with respect to ATP. The K0.5 value for Na+ was increased by the addition of PGG from 9.1 to 12.3 mM, whereas that for K+ was not altered. PGG also inhibited K(+)-dependent p-nitrophenyl phosphatase activity with an IC50 value of 5.3 x 10(-6) M, and the extent of the inhibition increased at higher concentrations of K+. The K0.5 value for K+ was decreased by the addition of PGG from 3.3 to 2.0 mM. These results suggested that the inhibition of Na+,K(+)-ATPase activity is caused by interaction of PGG with the enzyme in the E2 state. The inhibitory effect of Moutan Cortex or Paeoniae Radix is considered to be mainly attributable to PGG.

Schempp H, Denke A, Mann E, Schneider W, Elstner EF. **Biochemical activities of extracts from Hypericum perforatum L. 3rd Communication: modulation of peroxidase activity as a simple method for standardization.** Arzneimittelforschung 1999;49(2):115-9.
Alcoholic extracts from the herb "St. John's wort" (Hypericum perforatum L.) are widely used to counteract depressive situations, where the question on the mainly active principle is still under discussion. Thus, standardization of the drug on the basis of dry matter has been chosen instead of the popular leading component, hypericin. Inhibition of myeloperoxidase-catalyzed dimerization of enkephalins by Hypericum extracts has recently been reported. This method is based on the separation and quantification of enkephalin dimers by HPLC. In order to simplify this assay myeloperoxidase could be substituted by the cheaper horseradish peroxidase and the enkephalins by the amino acid tyrosine without loss of significance. In this communication we represent a more rapid photometric method based on peroxidase-catalyzed indole acetic acid oxidation suitable for quick, simple and economic drug standardization.

Schliebs R, Liebmann A, Bhattacharya SK, Kumar A, Ghosal S, Bigl V. **Systemic administration of defined extracts from Withania somnifera (Indian Ginseng) and Shilajit differentially affects cholinergic but not glutamatergic and GABAergic markers in rat brain.** Neurochem Int 1997;30(2):181-90.
Although some promising results have been achieved by acetylcholinesterase inhibitors, an effective therapeutic intervention in Alzheimer's disease still remains an important goal. Sitoindosides VII-X, and withaferin-A, isolated from aqueous methanol extract from the roots of cultivated varieties of Withania somnifera (known as Indian Ginseng), as well as Shilajit, a pale-brown to blackish brown exudation from steep rocks of the Himalaya mountain, are used in Indian medicine to attenuate cerebral functional deficits, including amnesia, in geriatric patients. The present investigation was conducted to assess whether the memory-enhancing effects of plant extracts from Withania somnifera and Shilajit are owing to neurochemical alterations of specific transmitter systems. Therefore, histochemistry to analyse acetylcholinesterase activity as well as receptor autoradiography to detect cholinergic, glutamatergic and GABAergic receptor subtypes were performed in brain slices from adult male Wistar rats, injected intraperitoneally daily with an equimolar mixture of sitoindosides VII-X and withaferin-A (prepared from Withania somnifera) or with Shilajit, at doses of 40 mg/kg of body weight for 7 days. Administration of Shilajit led to reduced acetylcholinesterase staining, restricted to the basal forebrain nuclei including medial septum and the vertical limb of the diagonal band. Systemic application of the defined extract from Withania somnifera, however, led to differential effects on AChE activity in basal forebrain nuclei: slightly enhanced AChE activity was found in the lateral septum and globus pallidus, whereas in the vertical diagonal band AChE activity was reduced following treatment with sitoindosides VII-X and withaferin-A. These changes were accompanied by enhanced M1-muscarinic cholinergic receptor binding in lateral and medial septum as well as in frontal cortices, whereas the M2-muscarinic receptor binding sites were increased in a number of cortical regions including cingulate, frontal, piriform, parietal and retrosplenial cortex. Treatment with Shilajit or the defined extract from Withania somnifera affected neither GABAA and benzodiazepine receptor binding nor NMDA and AMPA glutamate receptor subtypes in any of the cortical or subcortical regions studied. The data suggest that Shilajit and the defined extract from Withania somnifera affect preferentially events in the cortical and basal forebrain cholinergic signal transduction cascade. The drug-induced increase in cortical muscarinic acetylcholine receptor capacity might partly explain the cognition-enhancing and memory-improving effects of extracts from Withania somnifera observed in animals and humans.

Siegers CP, Robke A, Pentz R. **Effects of garlic preparations on superoxide production by phorbol ester activated granulocytes.** Phytomedicine 1999;6(1):13-6.
Sulfur containing constituents of garlic are considered responsible for conveying the antioxidative properties of garlic preparations. The radical scavenging properties of garlic preparations against oxygen radicals, specifically their ability to inhibit the formation of superoxide anions, were investigated using human granulocytes activated with 10 nM phorbol myristyl acetate (PMA). A garlic powder preparation inhibited the production of superoxide with a calculated IC50 of 390 micrograms/ml. An 8-10% alliin enriched garlic extract (alliinase inactivated) did not inhibit superoxide production even at concentrations as high as 1000 micrograms/ml. When the extract was mixed with garlic powder (90% garlic powder, 10% garlic

extract), there was a clear inhibition of superoxide production with an IC50 value of 295 micrograms/ml. An even stronger inhibitory effect could be achieved when garlic powder was added to garlic extract (10% garlic powder, 90% extract, IC50 = 160 micrograms/ml). These experimental results suggest that the alliin metabolite allicin may be responsible for the oxygen radical scavenging properties of garlic.

Siess MH, Le Bon AM, Canivenc-Lavier MC, Suschetet M. **Modification of hepatic drug-metabolizing enzymes in rats treated with alkyl sulfides.** Cancer Lett 1997;120(2):195-201.
Natural compounds which elevate detoxification enzymes and/or reduce activating enzymes could be considered as good candidates to protect against cancer. In this work, we studied the modulation of hepatic drug-metabolizing enzymes in rats treated with dimethyl sulfide (DMS), dimethyl disulfide (DMDS), methylpropyl disulfide (MPDS), dipropyl sulfide (DPS), dipropyl disulfide (DPDS) and diallyl disulfide (DADS) issued from Allium species. Compounds containing methyl groups had little or no effect. Compounds with two propyl groups or two allyl groups provoked a pleiotropic response on drug-metabolizing enzymes. DPS, DPDS and DADS induced ethoxyresorufin O-deethylase, methoxyresorufin O-demethylase and mostly pentoxyresorufin O-dependentylase and decreased nitrosodimethylamine N-demethylase and erythromycin N-demethylase. These modifications of enzyme activities were accompanied by an increase of CYP 2B1,2 and a decrease of CYP 2E1, evidenced by immunoblotting. The same treatments stimulated some phase II enzyme activities such as glutathione transferase and UDP-glucuronyl transferases. This pattern of induction and/or inhibition of drug metabolizing enzymes was qualitatively similar to that elicited by the enzyme inducer, phenobarbital. The magnitude of the effects produced by DPDS was smaller than those produced by DADS and DPS. Our results suggest a possible protective effect of alkyl sulfides as well as diallyl disulfide, on the first step of carcinogenesis via the modulation of enzymes involved in carcinogen metabolism.

Singh A, Singh SP. **Modulatory potential of smokeless tobacco on the garlic, mace or black mustard-altered hepatic detoxication system enzymes, sulfhydryl content and lipid peroxidation in murine system.** Cancer Lett 1997;118(1):109-14.
The present study evaluates the potential of smokeless tobacco to modify the chemopreventive efficacy of minor dietary constituents, including garlic, mace or black mustard, via modulating the competing pathways of hepatic detoxication system and antioxidant defense mechanism in murine system. Garlic (100 mg/kg b.w. per day) by gavage and mace (1% w/w) or black mustard (1% w/w) in diet induced a significant increase in the levels of glutathione-S-transferase (GST), acid-soluble sulfhydryl (-SH), cytochrome b5 (Cyt.b5) and cytochrome P-450 (Cyt.P-450) in murine liver. The hepatic levels of GST and -SH were significantly depressed whereas microsomal Cyt.b5, Cyt.P-450 and MDA levels were elevated in groups treated with smokeless tobacco (50 or 100 mg/kg b.w. per day). The data revealed the inhibitory potential of smokeless tobacco on garlic-induced hepatic GST/GSH system besides the significant augmentation by smokeless tobacco on garlic or mace or black mustard-induced microsomal cytochromes. The possible implications of modulation in competing bioactivation and detoxication pathways in the process of chemical carcinogenesis are discussed.

Song K, Milner JA. **Heating garlic inhibits its ability to suppress 7, 12-dimethylbenz(a)anthracene-induced DNA adduct formation in rat mammary tissue.** J Nutr 1999;129(3):657-61.
The present studies compared the impact of heating, either by microwave or convection oven, on the ability of garlic to reduce the in vivo bioactivation of 7,12-dimethylbenz(a)anthracene (DMBA) in 55-d-old female Sprague-Dawley rats. In study 1, rats were fed a semipurified casein-based diet and treated by gastric gavage thrice weekly for 2-wk with crushed garlic (0.7 g in 2 mL corn oil) or the carrier prior to DMBA treatment (50 mg/kg body weight). Providing crushed garlic reduced by 64% ($P < 0.05$) the quantity DMBA-induced DNA adducts present in mammary epithelial cells compared to controls. In study 2, microwave treatment for 60 s, but not 30 s, decreased ($P < 0.05$) the protection provided by garlic against DMBA-induced adduct formation. In study 3, allowing crushed garlic to stand for 10 min prior to microwave heating for 60 s significantly ($P < 0.05$) restored its anticarcinogenic activity. Microwave heating of garlic for 30 s resulted in a 90% loss of alliinase activity. Heating in a convection oven (study 4) also completely blocked the ability of uncrushed garlic to retard DMBA bioactivation. Study 5 revealed that providing either 0.105 micromol diallyl disulfide or S-allyl cysteine by gastric gavage thrice weekly for 2 wk was effective in retarding DMBA bioactivation but isomolar alliin was not. These studies provide evidence that alliinase may be important for the formation of allyl sulfur compounds that contribute to a depression in DMBA metabolism and bioactivation.

Sonoda Y, Kasahara T, Mukaida N, Shimizu N, Tomoda M, Takeda T. **Stimulation of interleukin-8 production by acidic polysaccharides from the root of Panax ginseng.** Immunopharmacology 1998;38(3):287-94.
The root of Panax ginseng C.A. Meyer, is a well-known important Chinese traditional medicine used as a stomachic, tonic, sedative and as an elixir called Ginseng in China and Japan. The precise mechanism of the biological actions of this plant is not fully understood. In order to elucidate the immunomodulating activities of this plant, we examined the direct effects of four of its components, acidic polysaccharides isolated in previous studies, on cytokine (interleukin-8; IL-8) production by a human monocytic cell line, THP-1, and human blood monocytes in vitro, as IL-8 is a potent inflammatory cytokine involved in neutrophil chemotaxis and activation. We found that one component, ginsenan S-IIA, is a potent inducer of IL-8 production by human monocytes and THP-1 cells, and this induction is accompanied by increased IL-8 mRNA expression.

Sovova M, Fiserova J, Sova J, Opletal L. **[Pharmaceutical significance of the species of the genus Solidago. Part 1. Glycosides of Solidago virgaurea L.].** Ceska Slov Farm 1998;47(3):103-9. (Cze)

Stanic G, Gavric D, Brkic D, Plazibat M. **[Elymus repens (L.) Gould and Cynodon dactylon (L.) Pers.--botanical and pharmacologic data].** Farm Glas 1997 Dec;53:369-77. (Scr)

Sumioka I, Matsura T, Kasuga S, Itakura Y, Yamada K. **Mechanisms of protection by S-allylmercaptocysteine against acetaminophen-induced liver injury in mice.** Jpn J Pharmacol 1998;78(2):199-207.
S-Allylmercaptocysteine (SAMC), one of the water-soluble organosulfur compounds in ethanol

extracts of garlic (Allium sativum L.), has been shown to protect mice against acetaminophen (APAP)-induced liver injury. In this study, we examined the mechanisms underlying this hepatoprotection. SAMC (100 mg/kg, p.o.) given 2 and 24 hr before APAP administration (500 mg/kg, p.o.) suppressed the plasma alanine aminotransferase activity increases 3 to 12 hr after APAP administration significantly. The hepatic reduced glutathione levels of vehicle-pretreated mice decreased 1 to 6 hr after APAP administration, but SAMC pretreatment suppressed the reductions 1 to 6 hr after APAP administration significantly. These inhibitory effects of SAMC were dose-dependent (50-200 mg/kg) 6 hr after APAP administration. As SAMC pretreatment (50-200 mg/kg) suppressed hepatic cytochrome P450 2E1-dependent N-nitrosodimethylamine demethylase activity significantly in a dose-dependent manner, we suggest that one of its protective mechanisms is inhibition of cytochrome P450 2E1 activity. SAMC pretreatment also suppressed the increase in hepatic lipid peroxidation and the decrease in hepatic reduced coenzyme Q9 (CoQ9H2) levels 6 hr after APAP administration. The hepatic CoQ9H2 content of the SAMC pretreatment group was maintained at the normal level. Therefore, we suggest that another hepatoprotective mechanism of SAMC may be attributable to its antioxidant activity.

Tao X, Schulze-Koops H, Ma L, Cai J, Mao Y, Lipsky PE. **Effects of Tripterygium wilfordii hook F extracts on induction of cyclooxygenase 2 activity and prostaglandin E2 production.** Arthritis Rheum 1998;41(1):130-8.
OBJECTIVE. Extracts of the Chinese herbal remedy Tripterygium wilfordii Hook F (TWHF) have been reported to be effective in the treatment of patients with a variety of inflammatory and autoimmune diseases, but the mechanism of this therapeutic effect has not been completely delineated. The present study was designed to assess the effects of TWHF on the in vitro synthesis of prostaglandin E2 (PGE2) and on the expression of the cyclooxygenase isoforms, COX-1 and COX-2, in various human cell types. METHODS. Monocytes from human peripheral blood (HM), fibroblasts from rheumatoid arthritis synovial tissue (RASF), human neonatal foreskin fibroblasts (HFF), and the histiocytic cell line U937 were cultured for designated time periods with or without lipopolysaccharide (LPS), and in the presence or absence of varying concentrations of the following inhibitors: the methanol/chloroform (T2) extract of TWHF, the ethyl acetate (EA) extract of TWHF, a purified diterpenoid component of TWHF (triptolide), dexamethasone, and indomethacin. Culture supernatants were harvested for PGE2 content assays. Total RNA was extracted from the cells and analyzed for COX-1 and COX-2 messenger RNA (mRNA) expression using reverse transcriptase-polymerase chain reaction or Northern blotting. RESULTS. Both the T2 and EA extracts inhibited PGE2 synthesis in the LPS-stimulated HM, RASF, and HFF cells, which was reflected by a marked suppression in the levels of mRNA for COX-2. In contrast, neither extract inhibited PGE2 production in U937 cells that did not express COX-2. Triptolide also inhibited LPS-stimulated induction of COX-2 mRNA and synthesis of PGE2, at the same inhibitory concentration as seen with the EA extract. The effects of T2, EA, and triptolide paralleled the inhibitory action of dexamethasone. CONCLUSION. The data indicate that both the T2 and EA extracts of TWHF, as well as the triptolide component, inhibit PGE2 production in a variety of human cells by blocking the up-regulation of COX-2.

Teng L, Crooks PA, Dwoskin LP. **Lobeline displaces [3H]dihydrotetrabenazine binding and releases [3H]dopamine from rat striatal synaptic vesicles: comparison with d-**

amphetamine. J Neurochem 1998;71(1):258-65.
Lobeline, an alkaloid from Indian tobacco (Lobelia inflata), is classified as a nicotinic agonist and is currently used as a smoking cessation agent. However, our previous in vitro studies demonstrate that lobeline does not act as a nicotinic agonist but alters presynaptic dopamine (DA) storage by potently inhibiting DA uptake into synaptic vesicles. Recently, d-amphetamine has been reported to act at the level of the synaptic vesicle to alter presynaptic function. The present in vitro studies further elucidate the mechanism of lobeline's action and compare its effects with those of d-amphetamine. [3H]Dihydrotetrabenazine ([3H]DTBZ), used routinely to probe a high-affinity binding site on the vesicular monoamine transporter (VMAT2), bound to vesicle membranes from rat striatum with a KD of 1.67 nM and Bmax of 8.68 pmol/mg of protein. Lobeline inhibited [3H]DTBZ binding with an IC50 of 0.90 microM, consistent with its previously reported IC50 of 0.88 microM for inhibition of [3H]DA uptake into vesicles. These results suggest that lobeline specifically interacts with DTBZ sites on VMAT2 to inhibit DA uptake into synaptic vesicles. Interestingly, d-amphetamine inhibited [3H]DTBZ binding to vesicle membranes with an IC50 of 39.4 microM, a concentration 20 times greater than reported for inhibition of VMAT2 function, suggesting that d-amphetamine interacts with a different site than lobeline on VMAT2 to inhibit monoamine uptake. Kinetic analysis of [3H]DA release from [3H]DA-preloaded synaptic vesicles in the absence of drug revealed a t1/2 of 2.12 min. Lobeline and d-amphetamine evoked [3H]DA release with EC50 values of 25.3 and 2.22 microM, respectively. At a concentration 10 times the EC50, lobeline and d-amphetamine significantly decreased the t1/2 of [3H]DA release to 1.58 and 1.48 min, respectively. Thus, in contrast to d-amphetamine, which is equipotent in inhibiting DA uptake and promoting release from the synaptic vesicles, lobeline more potently (28-fold) inhibits DA uptake (via an interaction with the DTBZ site on VMAT2) than it evokes DA release to redistribute presynaptic DA storage.

Tozawa F, Dobashi I, Horiba N, Sakai Y, Sakai K, Suda T. **Saireito (a Chinese herbal drug) decreases inhibitory effect of prednisolone and accelerates the recovery of rat hypothalamic-pituitary-adrenal axis.** Endocr J 1998;45(1):69-74.
Saireito, a saiko agent (a Chinese herbal drug), increases the synthesis and secretion of ACTH by stimulating hypothalamic CRH release. In the present study, we examined the effect of food containing saireito (1.5%) on the recovery of the hypothalamic-pituitary-adrenal axis after treating male rats with prednisolone (PSL, 200 microM) in drinking water for 14 days. Saireito was administered during and after PSL administration. The rats were decapitated at various times after PSL administration. Tail-pinch stress had been applied to some rats. The plasma ACTH response to tail-pinch stress in the PSL + saireito group recovered to the control level on day 1, but that in the group given PSL alone recovered on day 3. The ACTH level in the anterior pituitary and the CRH level in the median eminence of the PSL + saireito group returned to the control level on day 3, and that in the group given PSL alone returned to it on day 5. These results indicate that the administration of saireito reduces the negative feedback effect of PSL on the hypothalamus and pituitary and accelerates the recovery of the hypothalamic CRH and pituitary ACTH level after glucocorticoid treatment.

Turi M, Turi E, Koljalg S, Mikelsaar M. **Influence of aqueous extracts of medicinal plants on surface hydrophobicity of Escherichia coli strains of different origin.** APMIS 1997;105(12):956-62.

The adhesion of microbes on host cells is of decisive importance in the development of Gram-negative microbe-induced infections and can be influenced by the surface hydrophobicity of the microbial cell. The hydrophobicity of 155 Escherichia coli strains of different origin was determined by the salt aggregation test (SAT). Among the strains isolated from faecal samples of healthy persons only 16.7% showed aggregative properties, whereas among the strains isolated from the urine of patients with pyelonephritis and the faecal samples of calves and pigs with diarrhoea some 40.0%-60.0% were aggregative. The influence of aqueous extracts prepared from bearberry leaves, St. John's wort herbs, wild camomile and marigold flowers on hydrophobicity of 40 E. coli and 20 Acinetobacter baumannii strains was investigated. The decoctions of bearberry and St. John's wort increased remarkably the hydrophobicity of both microbial species. The infusions of wild camomile and marigold completely blocked the aggregative properties of the investigated strains. Bactericidal action was relatively low in the case of bearberry and St. John's wort and completely lacking in the case of wild camomile and marigold. Thus, one of the probable and potentially important action mechanisms of the four medicinal plants studied is their ability to influence the surface characteristics of the microbial cells and thereby their putative virulence properties.

Uebelhack R, Franke L, Schewe HJ. **Inhibition of platelet MAO-B by kava pyrone-enriched extract from Piper methysticum Forster (kava-kava).** Pharmacopsychiatry 1998;31(5):187-92.
Kava-kava, a psychoactive beverage, induces relaxation, improves social interaction, promotes sleep and plays an important role in the sociocultural life in the islands of the South Pacific. On the other hand, standardized extracts of kava-kava roots are used for the therapy of anxiety, tension and restlessness. Kava pyrones, the major constituents of kava kava, are generally considered to be responsible for the pharmacological activity in humans and animals. To obtain more information on the mechanisms by which kava-kava exerts psychotropic properties we investigated the in vitro effects of kava-kava extract and pure synthetic kava pyrones on human platelet MAO-B, in comparison to amitriptyline, imipramine and brofaromine. Kava-kava extract was found to be a reversible inhibitor of MAO-B in intact platelets (IC50 24 microM) and disrupted platelet homogenates (IC50 1.2 microM). Structural differences of kava pyrones resulted in a different potency of MAO-B inhibition. The order of potency was desmethoxyyangonin > (+/-)-methysticin > yangonin > (+/-)-dihydromethysticin > (+/-)-dihydrokavain > (+/-)-kavain. The two most potent kava pyrones, desmethoxyyangonin and (+/-)-methysticin displayed a competetive inhibition pattern with mean Ki 0.28 microM and 1.14 microM respectively. The inhibition of MAO-B by kava pyrone-enriched extracts might be an important mechanism for their psychotropic activity.

Vadiraja BB, Gaikwad NW, Madyastha KM. **Hepatoprotective effect of C-phycocyanin: protection for carbon tetrachloride and R-(+)-pulegone-mediated hepatotoxicty in rats.** Biochem Biophys Res Commun 19998;249(2):428-31.
Effect of C-phycocyanin (from Spirulina platensis) pretreatment on carbontetrachloride and R-(+)-pulegone-induced hepatotoxicity in rats was studied. Intraperitoneal (i.p.) administration (200 mg/kg) of a single dose of phycocyanin to rats, one or three hours prior to R-(+)-pulegone (250 mg/kg) or carbontetrachloride (0.6 ml/kg) challenge, significantly reduced the hepatotoxicity caused by these chemicals. For instance, serum glutamate pyruvate transaminase

(SGPT) activity was almost equal to control values. The losses of microsomal cytochrome P450, glucose-6-phosphatase and aminopyrine-N-demethylase were significantly reduced, suggesting that phycocyanin provides protection to liver enzymes. It was noticed that the level of menthofuran, the proximate toxin of R-(+)-pulegone was nearly 70% more in the urine samples collected from rats treated with R-(+)-pulegone alone than rats treated with the combination of phycocyanin and R-(+)-pulegone. The possible mechanism involved in the hepatoprotection is discussed. Copyright 1998 Academic Press.

Veronesi B, Oortgiesen M, Carter JD, Devlin RB. **Particulate matter initiates inflammatory cytokine release by activation of capsaicin and acid receptors in a human bronchial epithelial cell line.** Toxicol Appl Pharmacol 1999;154(1):106-15.
Recent experiments have shown that human bronchial epithelial cells (i.e., BEAS-2B) release pro-inflammatory cytokines (i.e., IL-6 and TNFalpha) in a receptor-mediated fashion in response to the neuropeptides, substance P (SP), calcitonin gene-related protein (CGRP), and the prototype botanical irritant capsaicin. In the present experiments, we examined the relevance of these receptors to particulate matter (PM)-associated cellular inflammation. BEAS-2B cells, exposed to residual oil fly ash particles (ROFA), responded with an immediate (

Wang F, Yang LC, Liu M, Cheng YL, Jia HM. **[Primary study on antagonizing effects of anti-snake venom Chinese herbs on endothelin-1 and sarafotoxin 6b].** Zhongguo Zhongyao Zazhi 1997;22(10):620-2. (Chi)
IPA COPYRIGHT: ASHP To investigate the pharmacologic effects of Chinese herbs used as anti-snake venom, oral extracts from 5 herbs were evaluated for effects on endothelin-1 and sarafotoxin 6b. All 5 herbs demonstrated acute death reduction caused by endothelin-1 and sarafotoxin 6b.

Wang YQ, Bai LJ, He XW. **[Study of scavenging action of Shengmaiyin decoction on hydroxyl radical].** Zhongguo Zhongyao Zazhi 1998;23(1):45-7. (Chi)
IPA COPYRIGHT: ASHP The scavenging action of Shengmaiyin decoction and its individual ingredients, Radix ginseng, R. ophiopogonis, and Fructus schisandrae was investigated. The decoction was better for antioxidation than single ingredients.

Wenisch C, Parschalk B, Zedwitz-Liebenstein K, Wernsdorfer W, Graninger W. **The effect of artemisinin on granulocyte function assessed by flow cytometry.** J Antimicrob Chemother 1997;39(1):99-101.
The effect of dihydroartemisinin, artemisinin and artesunate (0.1, 0.5, 5 and 50 mg/L) on phagocytic function and release of reactive oxygen products by neutrophils was studied by flow cytometry. Incubation with dihydroartemisinin, artemisinin and artemether resulted in a decreased capacity to phagocytose Escherichia coli (0.1-50 mg/L: 62-40%, 66-32% and 59-47% of the control values, respectively; $P < 0.001$ for all). Conversely, the derivatives enhanced the intracellular generation of reactive oxygen intermediates (0.1-50 mg/L: 146-140%, 174-197% and 188-136% of the control values, respectively; $P < 0.001$ for all). Artemisia derivatives enhance the reactive oxygen response of neutrophils but depress their phagocytic ability at therapeutic blood levels.

Xu J, Xie J, Feng P, Su Z. **Oxygen transfer characteristics in the compact callus aggregates of Rhodiola sachalinensis.** Chin J Biotechnol 1998;14(2):99-107.
The effective diffusivity of oxygen in compact callus aggregates (CCA) of Rhodiola sachalinensis was extremely small, varying from 0.34 x 10(-11) to 5.4 x 10(-9) m2/s and increasing with particle diameter. The calculated results indicated that severe oxygen limitations occurred in the CCA aggregates. However, the direct determination of the viability of the cells demonstrated that the CCA aggregates contained a high fraction of viable cells. It was suggested that the tissue differentiation or plasmodesmata within the CCA aggregates may provide capillaries for improving transport of oxygen and other nutrients.

Yin MC, Cheng WS. **Inhibition of Aspergillus niger and Aspergillus flavus by some herbs and spices.** J Food Protect 1998;61(1):123-5.
BIOSIS COPYRIGHT: BIOL ABS. The inhibitory effect of water-soluble extracts of garlic bulbs, green garlic, green onions, hot peppers, ginger, Chinese parsley, and basil on the growth of Aspergillus niger and Aspergillus flavus was examined. Garlic bulbs, green garlic, and green onions showed an inhibitory effect against these two fungi. The influence of heat, acid, and salt upon the inhibitory effect of these three herbs was further studied. Increasing the temperature from 60 to 100~C resulted in a significant ($P < 0.05$) decrease in the inhibitory effect of garlic bulbs against the fungi tested. Green garlic and green onion lost their antifungal activity against A. niger after being treated at 80 and 60~C, respectively. For A. flavus, the inhibitory effect of green garlic declined significantly ($P < 0.05$) with an increase in temperature. However, the antifungal activity of green onions against A. flavus was heat stable. For both fungi tested in this study, the antifungal activity of these spice plants was not affected by acid treatments at pH values 2, 4, or 6, or salt by treatments at concentrations of 0.1, 0.2, 0.3, and 0.4 M ($P > 0.05$).

Yokozawa T, Dong E, Oura H, Nonaka G, Nishioka I. **Magnesium lithospermate B ameliorates cisplatin-induced injury in cultured renal epithelial cells.** Exp Toxicol Pathol 1997;49(5):343-6.
A study was conducted to clarify whether magnesium lithospermate B ameliorates cisplatin-induced renal injury in terms of lactate dehydrogenase and malondialdehyde leakage from LLC-PK1 cells in culture. Magnesium lithospermate B was shown to suppress the cytotoxicity of cisplatin, the suppressive effect increasing with the dose of magnesium lithospermate B.

Yoshikawa M, Murakami T, Ueno T, Yashiro K, Hirokawa N, Murakami N, Yamahara J, Matsuda H, Saijoh R, Tanaka O. **Bioactive saponins and glycosides. VIII. Notoginseng (1): new dammarane-type triterpene oligoglycosides, notoginsenosides-A, -B, -C, and -D, from the dried root of Panax notoginseng (Burk.) F.H. Chen.** Chem Pharm Bull (Tokyo) 1997;45(6):1039-45.
The glycosidic fraction from the dried roots of Panax notoginseng (Burk.) F.H. Chen was found to show protective effect on liver injury induced by D-galactosamine and lipopolysaccharide. From the glycosidic fraction with hepatoprotective effect, nine new dammarane-type triterpene oligoglycosides, notoginsenosides-A, -B, -C, -D, -E, -G, -H, -I, and -J and an acetylenic fatty acid glycoside, notoginsenic acid beta-sophoroside, were isolated together with fourteen known dammarane-type triterpene oligoglycosides. The structures of notoginsenosides-A, -B, -C and -D were determined on the basis of chemical and physicochemical evidence, which included the

chemical correlation with ginsenoside-Rb1 using photosensitized oxygenation, as follows: notoginsenoside A; 3-O-[beta-D-glucopyranosyl (1-->2)-beta-D-glucopyranosyl]-20-O-[beta-D-glucopyranosyl (1-->6)-beta-D-glucopyranosyl] 3 beta, 12 beta,20(S),25-tetrahydroxydammar -23-ene; B; 3-O-[beta-D-glucopyranosyl (1-->2)-beta-D-glucopyranosyl]-20-O-[beta-D-glucopyranosyl (1-->6)-beta-D- glucopyranosyl] 3 beta, 12 beta,20(S)-trihydroxydammar-25-en-24-one, C; 3-O-[beta-D-glucopyranosyl (1-->2)-beta-D-glucopyranosyl]-20-O-[beta-D -glucopyranosyl (1-->6)-beta-D-glucopyranosyl] 3 beta,12 beta,20(S)- trihydroxy-24 zeta-hydroperoxydammar-25-ene, and D; 3-O-[beta-D-xylopyranosyl (1-->2)-beta-D-glucopyranosyl (1-->2)-beta-D-glucopyranosyl]-20-O-[beta-D-xylopyranosyl (1-->6)-beta-D-glucopyranosyl (1-->6)-beta-D-glucopyranosyl]20(S)-protopanaxadiol, respectively.

Yoshikawa M, Murakami T, Yashiro K, Yamahara J, Matsuda H, Saijoh R, Tanaka O. **Bioactive saponins and glycosides. XI. Structures of new dammarane-type triterpene oligoglycosides, quinquenosides I, II, III, IV, and V, from American ginseng, the roots of Panax quinquefolium L.** Chem Pharm Bull (Tokyo) 1998;46(4):647-54.
The methanolic extract and 1-butanol-soluble fraction of American ginseng, the roots of Panax quinquefolium L., were found to exhibit a protective effect on liver injury induced by D-galactosamine and lipopolysaccharide. Five new dammarane-type triterpene oligoglycosides called quinquenosides I, II, III, IV, and V were isolated together with fourteen known dammarane-type triterpene oligoglycosides such as chikusetsusaponin IVa, pseudo-ginsenoside-RC1, malonyl-ginsenoside-Rb1, and notoginsenosides-A,-C, and -K from the 1-butanol-soluble fraction. From the ethyl acetate-soluble fraction, four known acetylenic compounds and 6'-O-acetyl ginsenoside-Rg1 were isolated. The structures of quinquenosides I, II, III, IV, and V were determined on the basis of chemical and physicochemical evidence as 3-O-[6-O-(E)-2-butenoyl-beta-D-glucopyranosyl(1-->2)-beta-D- glucopyranosyl]-20-O-(beta-D-glucopyranosyl) 20(S)-protopanaxadiol (quinquenoside I), 3-O-[6-O-(E)-2-octenoyl-beta-D- glucopyranosyl(1-->2)-beta-D-glucopyranosyl]-20-O-[beta-D-glucopy- ranosyl (1-->6)-beta-D-glucopyranosyl] 20(S)-protopanaxadiol (quinquenoside II), 3-O-[beta-D-glucopyranosyl (1-->2)-6-O-acetyl-beta-D-glucopyranosyl]-20-O-(beta-D-glucopyran- osyl) 20(S)-protopanaxadiol (quinquenoside III), 3-O-[beta-D-glucopyranosyl(1-->2)-beta-D-glucopyranosyl]-20-O-bet- a-D- glucopyranosyl(1-->6)-beta-D-glucopyranosyl]-3 beta, 7 beta, 20(S)-trihydroxydammar-5,24-diene (quinquenoside IV), and 3-O-[beta-D-glucopyranosyl(1-->2)-beta-D-glucopyranosyl]-20-O-[al- pha-D-glucopyranosyl(1-->4)-beta-D-glucopyranosyl(1-->6)-beta-D-glucopy- ranosyl] 20(S)-protopanaxadiol (quinquenoside V).

Yotsumoto H, Yanagita T, Yamamoto K, Ogawa Y, Cha JY, Mori Y. **Inhibitory effects of oren-gedoku-to and its components on cholesteryl ester synthesis in cultured human hepatocyte HepG2 cells: evidence from the cultured HepG2 cells and in vitro assay of ACAT.** Planta Med 1997;63(2):141-5.
The pharmacological effects of Oren-gedoku-to (OGT), a Japanese-Chinese traditional herbal medicinal mixture on lipid biosynthesis were investigated in cultured human hepatocyte HepG2 cells. The addition of OGT (0.5 and 4.2 mg/ml), which had no effect on cell proliferation and cellular protein content, caused a marked decrease in the cellular cholesterol content, particularly cholesteryl ester content following 24 h incubation. The incorporation of 14C-oleate into cellular cholesteryl ester fraction was also reduced remarkably during incubation for 6 and 24 h. The

effects of OGT, its components and its main active chemicals on acyl-coenzyme A:cholesterol acyltransferase (ACAT) activity were studied in vitro to explore the mechanism by which OGT inhibits cholesteryl ester formation. The data confirmed that OGT, in a dose-dependent manner, and its components (Scutellaria baicalensis, Coptis japonica, Gardenia jasminoides and Phellodendron amurense) remarkably inhibit ACAT activity. Among the main active chemicals of OGT, baicalein, a kind of flavonoid, decreased ACAT activity in a dose-dependent fashion from the level of 10(-6)M. These results strongly suggest that OGT reduces the cholesteryl ester formation in human hepatocytes by inhibiting ACAT, and that baicalein may, in part, be responsible for ACAT inhibition.

Zava DT, Blen M, Duwe G. **Estrogenic activity of natural and synthetic estrogens in human breast cancer cells in culture.** Environ Health Perspect 1997;105(Suppl 3):637-45.
We investigated the estrogenic activity of various environmental pollutants (xenobiotics), in particular the xenoestrogen o,p-DDT, and compared their effects with those of endogenous estrogens, phytoestrogens, and mycoestrogens on estrogen receptor binding capacity, induction of estrogen end products, and activation of cell proliferation in estrogen-sensitive human breast cancer cells in monolayer culture. We also quantified the levels of phytoestrogens in extracts of some common foods, herbs, and spices and in human saliva following consumption of a high phytoestrogen food source (soy milk) to compare phytoestrogen abundance and bioavailability relative to the reported xenoestrogen burden in humans. Results show that natural endogenous estrogens, phytoestrogens, mycoestrogens, and xenoestrogens bind estrogen receptor (ER) in intact cells, but demonstrate marked differences in their ability to induce end products of estrogen action and to regulate cell proliferation. All of the different classes of estrogens stimulated cell proliferation at concentrations that half-saturated ER, but only some classes were able to induce estrogen-regulated end products. Genistein, a common phytoestrogen found in soy foods, differed from the xenoestrogen DDT in its effects on cell proliferation and ability to induce estrogen-regulated end products. Moreover, we found that many of the foods, herbs, and spices commonly consumed by humans contain significant amounts of phytoestrogens, and consumption of soy milk, a phytoestrogen-rich food, markedly increases the levels of phytoestrogens in saliva. In conclusion, our in vitro results predict that a diet high in phytoestrogens would significantly reduce the binding of weak xenoestrogens to ER in target tissues in vivo.

Zava DT, Dollbaum CM, Blen M. **Estrogen and progestin bioactivity of foods, herbs, and spices.** Proc Soc Exp Biol Med 1998;217(3):369-78.
In this study we report on the content and bioactivity of plant (phyto) estrogens and progestins in various foods, herbs, and spices, before and after human consumption. Over 150 herbs traditionally used by herbalists for treating a variety of health problems were extracted and tested for their relative capacity to compete with estradiol and progesterone binding to intracellular receptors for progesterone (PR) and estradiol (ER) in intact human breast cancer cells. The six highest ER-binding herbs that are commonly consumed were soy, licorice, red clover, thyme, tumeric, hops, and verbena. The six highest PR-binding herbs and spices commonly consumed were oregano, verbena, tumeric, thyme, red clover and damiana. Some of the herbs and spices found to contain high phytoestrogens and phytoprogestins were further tested for bioactivity based on their ability to regulate cell growth rate in ER (+) and ER (-) breast cancer cell lines and

to induce or inhibit the synthesis of alkaline phosphatase, an end product of progesterone action, in PR (+) cells. In general, we found that ER-binding herbal extracts were agonists, much like estradiol, whereas PR-binding extracts, were neutral or antagonists. The bioavailability of phytoestrogens and phytoprogestins in vivo were studied by quantitating the ER-binding and PR-binding capacity of saliva following consumption of soy milk, exogenous progesterone, medroxyprogesterone acetate, or wild mexican yam products containing diosgenin. Soy milk caused a dramatic increase in saliva ER-binding components without a concomitant rise in estradiol. Consumption of PR-binding herbs increased the progestin activity of saliva, but there were marked differences in bioactivity. In summary, we have demonstrated that many of the commonly consumed foods, herbs, and spices contain phytoestrogens and phytoprogestins that act as agonists and antagonists in vivo.

Zhao C, Shichi H. **Prevention of acetaminophen-induced cataract by a combination of diallyl disulfide and N-acetylcysteine.** J Ocul Pharmacol Ther 1998;14(4):345-55.
Injection of acetaminophen (APAP) (350 mg/kg body weight) into C57BL/6 mice in which cytochrome P450 (CYP) 1A1/1A2 had been induced produced acute cataract and other ocular tissue damage. Treatment of APAP-injected mice with one of the major organosulfides in garlic oil, diallyl disulfide (DADS) (200 mg/kg body weight), prevented cataract development and prolonged survival time. N-acetyl L-cysteine (NAC) (500 mg/kg body weight), a prodrug that stimulates glutathione synthesis, also prolonged survival time but was effective only weakly to prevent cataract formation. A combination of DADS and NAC completely prevented cataractogenesis, and all of the treated animals survived APAP toxicity. Neither DADS nor NAC inhibited CYP 1A1/1A2 induction as determined by their effect on the induction of hepatic microsomal ethoxyresorufin O-dealkylase (ERD) activity. However, in the in vitro enzyme assay, DADS, but not NAC, was a potent inhibitor of ERD activity (IC50 = 3.5 mM). Treatment with DADS or NAC slowed but did not stop the decrease of hepatic glutathione (GSH) content. At 4 hours after APAP injection, hepatic GSH began to increase only when DADS and NAC were administered together. These results suggest that the protective effect of DADS is due to its inhibition of biotransformation of APAP to the reactive metabolite N-acetyl-p-benzoquinone imine (NAPQI) by CYP 1A1/1A2 enzymes and that NAC provides protection by increasing cellular cysteine level and GSH synthesis, thus facilitating detoxification of NAPQI by glutathione conjugation. Assay of plasma glutamate-pyruvate transaminase activity, an indicator of liver necrosis, showed that treatment with DADS and NAC together effectively protected the liver. Therefore, the decrease of GSH as much as 30% of normal concentration, by itself, is not responsible for liver damage. The primary cause of hepatic necrosis is rapid accumulation of NAPQI.

Zhu M, Chan KW, Ng LS, Chang Q, Chang S, Li RC. **Possible influences of ginseng on the pharmacokinetics and pharmacodynamics of warfarin in rats.** J Pharm Pharmacol 1999;51(2):175-80.
We evaluated the significance of a reported clinical case of drug-drug interaction between ginseng and warfarin using a robust pharmacokinetic/pharmacodynamic approach in a rat model. The influence of ginseng on the pharmacokinetics and pharmacodynamics of oral warfarin after a single dose (2 mg kg(-1)) and at steady state (0.2 mg kg(-1) daily x 6 days) was studied in male Sprague-Dawley rats. Prothrombin time was employed as a pharmacodynamic index. Warfarin

plasma concentration and vitamin K content in the ginseng extract were assessed by validated HPLC assays. The pharmacokinetics of warfarin after a single dose were not altered in the presence of ginseng; peak plasma concentration (control 7.8+/-0.5; ginseng 7.3+/-2.5 microg mL(-1)), time to peak (control 2.6+/-1.0; ginseng 3.1+/-1.1 h), elimination half-life (control 14.3+/-5.8; ginseng 10.6+/-3.1 h), and oral clearance (control 17.5+/-3.3; ginseng 20.2+/-5.5 mL h(-1)) were not significantly different (P>0.05). Similarly, alterations in the pharmacokinetics of warfarin were not detected under the multiple dosing paradigm. Under both dosing conditions, ginseng also showed no significant impact on the pharmacodynamics of warfarin as assessed by the area under the prothrombin time vs time curve (multiple dosing; control 3776+/-619, ginseng 3830+/-362 sh) and maximum prothrombin time (control 57.2+/-11.8, ginseng 63.3+/-9.1 s). Furthermore, the content of vitamin K was undetectable in the ginseng decoction. In conclusion, current data obtained in the rat showed no significant impact of ginseng on the pharmacokinetics/pharmacodynamics of warfarin when they are concomitantly administered.

Therapeutic Use

Piper methysticum (kava kava). Altern Med Rev 1998;3(6):458-60.
Piper methysticum (kava kava) is a plant native to the Pacific Island region, and has been used ceremonial for thousands of years. The active ingredients are a group of substances know as kava lactones (AKA kava pyrones). Four lactones in kava have been found to have significant analgesic and anesthetic effects via non-opiate pathways. Kava's most popular application is as a natural anxiolytic, comparing favorably in several studies to a number prescription medications, including benzodiazepines. CNS effects seem to be mediated by several mechanisms. Studies have been conflicting regarding its GABA-receptor-binding capacity, although this has been found to occur in some studies. In vitro kava has been found to block norepinephrine uptake. It also has some anti-convulsant capabilities, which appear to be mediated by Na+ channel receptor sites. The therapeutic dosage is in the range of 50-70 mg kava lactones three times daily. The most common side effect, usually seen only with long-term, heavy usage of the herb, is a scaly skin rash called "kava dermopathy." It has also been know to potentiate other medications such as barbiturates and Xanax.

[To diagnose and treat sinusitis. 8th Congress of the Society for Phytotherapy. Symposium: "Phytotherapy in Sinusitis". Wurzburg 27 November 1997]. Dtsch Med Wochenschr 1998;123(10 Suppl):1-4. (Ger)

Abe S, Tansho S, Ishibashi H, Inagaki N, Komatsu Y, Yamaguchi H. **Protective effect of oral administration of a traditional medicine, Juzen-Taiho-To, and its components on lethal Candida albicans infection in immunosuppressed mice.** Immunopharmacol Immunotoxicol 1998;20(3):421-31.
Protective effects of a kampo medicine, Juzen-taiho-to (TJ-48) and its herbal components against experimental candidiasis in cyclophosphamide-induced immunosuppressive mice were investigated. ICR mice were immunosuppressed by intraperitoneal treatment with cyclophosphamide (day-4) and were orally given TJ-48 or one of its 10 herbal components for 4 consecutive days (day-4--1). They were then challenged intravenously with a lethal dose of Candida albicans (day 0). An oral dose of 1 g/kg/day of TJ-48 prolonged their life span. A

similar protective effect was obtained by treatment with its component drugs Ginseng radix, Glycyrrhizae radix, Atractylodis lancea rhizoma or Cnidii rhizoma. These herbal components were suggested to have a main role in the protective effect of Juzen-taiho-to against Candida infection.

Agrawal AK, Tripathi DM, Sahai R, Gupta N, Saxena KC, et al. **Management of giardiasis by the herbal drug Pippali Rasayana: clinical study.** J Ethnopharmacol 1997;56(3):233-6.
IPA COPYRIGHT: ASHP The effectiveness of Pippali Rasayana, an Indian Ayurvedic drug prepared from Palash (Butea monosperma) and Pippali (Piper longum), administered at an oral dose of 1 g 3 times daily for 15 days to 25 patients and 25 placebo controls suffering from giardiasis is reported. After 15 days of treatment there was a complete disappearance of trophozoites and cysts from stools of 23 of the patients. General signs and symptoms of ill health and abdominal discomfort, presence of mucus, pus cells, and RBCs were significantly reduced. There was a marked improvement in the clinical and hematological profile of the patients. Spontaneous recovery in 20% of cases was recorded in placebo controls.

Ahmad H, Tijerina MT, Tobola AS. **Preferential overexpression of a class MU glutathione S-transferase subunit in mouse liver by myristicin.** Biochem Biophys Res Commun 1997;236(3):825-8.
The present studies were undertaken to elucidate the mechanism of induction of glutathione S-transferase (GST) in mouse liver by myristicin, an active constituent of parsley leaf. A/J albino mice, given 5 to 50 mg doses of myristicin, showed 4- to 14-fold increase in liver GST specific activity over the control. GST purified from equal amounts of control and myristicin-treated livers indicated a marked increase in the GST activity. A relatively higher increase in GST activity towards 2,4-dichloronitrobenzene and a profound increase in the levels of GST mu on Western blot analysis of the myristicin-treated mouse liver suggest a preferential induction of GST mu. Results of the study also indicate that out of the two mu class GST subunits (Mr. 26,500 and Mr. 25,000) expressed in liver only one (Mr. 26,500) is significantly elevated. Myristicin treatment caused a slight change in the GST pi levels while the levels of GST alpha showed a modest increase. These results suggest that myristicin could be an effective chemopreventive agent, particularly for carcinogens that are detoxified by the mu class GST.

Ahn YO. **Diet and stomach cancer in Korea.** Intl J Cancer Suppl 1997;(10):7-9.
BIOSIS COPYRIGHT: BIOL ABS. Stomach cancer is the most prevalent malignant neoplasm in Korea. As of 1991-1992 in Seoul, the cumulative rates reported for the age span 0-74 were 7.6% in males and 3.1% in females. A recent case-control study reported that several food items and cooking methods are associated with increased or decreased risk of stomach cancer among Koreans. An increased risk of stomach cancer was noted among people who frequently consume broiled meats and fishes, salted side dishes (salted/fermented fish products) and salty stewed foods, such as soybean paste thick stew. Frequent consumption of mung bean pancake, tofu, cabbage, spinach and sesame oil decreased the risk. Analysis by cooking method showed that risk of stomach cancer from the same foods varied with preparation. For meat and fish, pan frying was associated with decreased risk, whereas stewing or broiling was associated with increased risk. Pickled vegetables increased the risk, whereas fresh vegetables did not. In a recent cohort study in Seoul, green vegetables and soybean foods were associated with a

decreased risk of stomach cancer. Case-control and cohort studies have reported that ginseng intake decreased the risk of gastric cancer.

Aida Y, Kasama T, Takeuchi N, Chiba M, Tobinaga S. **Pharmacological activities of khellactones, compounds isolated from Peucedanum japonicum THUNB. and Peucedanum praeruptorium DUNN.** Methods Find Exp Clin Pharmacol 1998;20(4):343-51.
The spasmolytic and antiallergic effects of AA and BB, compounds isolated from Peucedanum japonicum THUNB. (P. japonicum THUNB.) and Peucedanum praeruptorium DUNN. (P. praeruptorium DUNN.), were investigated in isolated smooth muscle and rat PCA. AA and BB showed noncompetitive antagonistic effects on Ach- and histamine-induced contraction in the isolated guinea pig ileum. Both AA and BB at 10(-6) g/ml caused a slight shift to the right of the dose-response curve for Ca2+ in isolated guinea pig ileum, and a concentration up to 3 x 10(-6) g/ml displayed noncompetitive antagonistic effects. The Ba2+ (3 x 10(-4) g/ml)-induced contraction in ileum and the histamine (10(-3) g/ml)-induced contraction in trachea were obtained to relaxation by AA and BB in a concentration-dependent fashion. AA and BB showed noncompetitive antagonist action on serotonin-induced contraction of the rat uterus excised 24-48 h after subcutaneous injection of female rats with estradiol. But, AA and BB were found to have hardly any inhibitory effect on rabbit thoracic aorta contractions induced by epinephrine (3 x 10(-6) g/ml). When the effect of oral administration of 40 mg/kg dose of BB was tested on the rat homologous PCA using anti-egg albumin mouse serum dilutions (1:100, 1:250, 1:500 and 1:750), it inhibited the 1:750 serum reaction 42.6%, but the inhibition rates for the other dilutions were 12-20%. Thus, based on the results of testing AA and BB, compounds isolated from P. japonicum THUNB. and P. praeruptorium DUNN. were confirmed to possess a spasmolytic effect on different types of smooth muscle and a mild antiallergic effect. These findings are of interest in regard to the medical uses of P. japonicum THUNB. and P. praeruptorium DUNN. as a herbal drug for bronchial asthma, spasmolytic effect, etc.

Akah PA, Gamaniel KS, Samson A, Wambebe CO. **Evaluation of Nigerian traditional medicine: effects of Gakani, a herbal anti-asthmatic drug.** J Ethnopharmacol 1997;55(2):87-92.
The anti-asthmatic potential of Gakani, a popular herbal drug in Nigeria was investigated. The LD50 values of the freeze-dried aqueous extract in mice and rats were 20.9 +/- 2.4 mg/kg and 18.6 +/- 4 mg/kg, respectively. The extract unsurmountably blocked the effects of histamine and isoprenaline on the guinea pig tracheaL chain. It produced initial dose-related contractions of the isolated guinea pig ileum and rat stomach strip, which was followed by persistent autoinhibition and inhibition of histamine- and 5-hydroxytryptamine (5-HT)-induced responses of the two preparations, respectively. The extract had good anti-inflammatory effect in rats, causing a dose-related inhibition of the increase in the paw circumference (acute inflammation) induced by subplantar injection of fresh egg albumin. These results highlight the anti-asthmatic and toxic potential of this preparation and the need for a systemic approach in the study of traditional medicines.

Akah PA, Nwambie AI, Gamaniel KS, Wambebe C. **Experimental study of the anticonvulsant plants used for treatment of infantile convulsion in Nigeria.** Brain Res Bull 1997;44(5):611-3.
In Nigeria, convulsion, especially in children, is managed by traditional healers employing plant

decoctions. A number of herbs are used for this purpose. We have carried out some preliminary studies on some of these traditional anticonvulsant plants. The experimental models were pentylenetetrazole- and electroshock-induced convulsions in mice. The acute toxicity (LD50) and the median effective (ED50) doses of the extracts of these plants were determined. Most of these plants exhibited potent anticonvulsant activity. The average onset of convulsion was delayed, while the average duration of convulsion was significantly reduced. Most of the animals showed signs of central nervous system depression. The results indicate that these plants possess anticonvulsant property, and this activity may be linked to their ability to depress the central nervous system.

Al-Khalil S, Alkofahi A, El-Eisawi D, Al-Shibib A. **Transtorine, a new quinoline alkaloid from Ephedra transitoria.** J Nat Prod 1998;61(2):262-3.
Transtorine (1), a new quinoline alkaloid, isolated from the aerial part of Ephedra transitoria by column chromatography, was identified as 4-quinolone-2-carboxylic acid. The structure was determined by spectroscopic methods. Transtorine exhibited growth inhibitory activity against the common bacteria, Enterobacter cloacae, Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus aureus.

Alali FQ, Zhang Y, Rogers L, Mclaughlin JL. **(2,4-cis and trans)-gigantecinone and 4-deoxygigantecin, bioactive nonadjacent bis-tetrahydrofuran annonaceous acetogenins, from Goniothalamus giganteus.** J Nat Prod 1997;60(9):929-33.
Two new acetogenins, (2,4-cis and trans)-gigantecinone (1), isolated as a mixture, and 4-deoxygigantecin (2), a known acetogenin whose absolute stereochemistry has not been determined previously, were isolated using activity-directed fractionation, from the bark of Goniothalamus giganteus. A key step in solving their absolute stereochemistries was the preparation of 1,4-diol formaldehyde acetal derivatives (1b and 2a). Using the advanced Mosher ester method and circular dichroism, the absolute stereochemistries of 1 and 2 were revealed and were found to be the same as that of gigantecin (3), which supports a common biogenetic origin. Both 1 and 1b showed potent and selective cytotoxicities against the PC-3 human prostate adenocarcinoma cell line. Against yellow fever mosquito larvae, 1 and 2 were more potent than rotenone in pesticidal activity. Longimicin C and a mixture of (2,4-cis and trans)-isoannonacin were also isolated for the first time from this species.

Alam MI, Gomes A. **Adjuvant effects and antiserum action potentiation by a (herbal) compound 2-hydroxy-4-methoxy benzoic acid isolated from the root extract of the Indian medicinal plant 'sarsaparilla' (Hemidesmus indicus R. Br.).** Toxicon 1998;36(10):1423-31.
The adjuvant effect and antiserum potentiation of a compound 2-hydroxy-4-methoxy benzoic acid were explored in the present investigation. This compound, isolated and purified from the Indian medicinal plant Hemidesmus indicus R. Br, possessed antisnake venom activity. Rabbits immunized with Vipera russellii venom in the presence and absence of the compound along with Freund's complete adjuvant, produced a precipitating band in immunogel diffusion and immunogel electrophoresis. The venom neutralizing capacity of this antiserum showed positive adjuvant effects as evident by the higher neutralization capacity (lethal and hemorrhage) when compared with the antiserum raised with venom alone. The pure compound potentiated the lethal action neutralization of venom by commercial equine polyvalent snake venom antiserum in

experimental models. These observations raised the possibility of the use of chemical antagonists (from herbs) against snake bite, which may provide a better protection in presence of antiserum, especially in the rural parts of India.

Alvarez L, Rios MY, Esquivel C, Chavez MI, Delgado G, Aguilar MI, Villarreal ML, Navarro V. **Cytotoxic isoflavans from Eysenhardtia polystachya.** J Nat Prod 1998;61(6):767-70.
Two new cytotoxic isoflavans, (3S)-7-hydroxy-2',3',4',5', 8-pentamethoxyisoflavan (1) and (3S)-3',7-dihydroxy-2',4',5', 8-tetramethoxyisoflavan (2), were isolated from the bark and trunks of Eysenhardtia polystachya (Leguminosae), together with the known constituents stigmasterol, isoduartin, cuneatin, 7-hydroxy-2',4', 5'-trimethoxyisoflavone, and 3,4-dimethoxy-8, 9-(methylenedioxy)pterocarpan. The structures of 1 and 2 were elucidated on the basis of spectroscopic methods. The antimicrobial, cytotoxic, and insecticidal potential of some of these compounds were evaluated. The isoflavans 1, 2, and isoduartin (2', 7-dihydroxy-3',4',8-trimethoxyisoflavan) displayed moderate cytotoxic activity against KB cell lines.

Ameri A. **Effects of the alkaloids 6-benzoylheteratisine and heteratisine on neuronal activity in rat hippocampal slices.** Neuropharmacology 1997;36(8):1039-46.
Alkaloids of different Aconitum species are employed as analgesics in traditional Chinese folk medicine. The present study was designed in order to investigate the effects of the structurally related alkaloids 6-benzoylheteratisine and heteratisine on neuronal activity in rat hippocampus. Experiments were performed as extracellular recordings of stimulus evoked population spikes in rat hippocampal slices. 6-Benzoylheteratisine (0.01-10 microM) inhibited the ortho- and antidromic population spike as well as the field EPSP in a concentration- and frequency-dependent manner. Heteratisine (1-100 microM) was a less potent inhibitor. It exerted a depression of the orthodromic spike, but failed to affect the antidromic population spike. 6-Benzoylheteratisine (10 microM) diminished epileptiform activity induced by bicuculline. In hippocampal neurons, this compound reduced the peak amplitude of the sodium current. There was no effect of heteratisine on the sodium current in concentrations up to 100 microM. It is concluded that the frequency-dependent action of 6-benzoylheteratisine suggests an inhibition of neuronal activity which underlies epileptiform burst discharges. The predominant effect is a suppression of neuronal activity due to a blockade of sodium channels.

Annuk H, Hirmo S, Turi E, Mikelsaar M, Arak E, Wadstrom T. **Effect on cell surface hydrophobicity and susceptibility of Helicobacter pylori to medicinal plant extracts.** FEMS Microbiol Lett 1999;172(1):41-5.
Effects on aqueous extracts of medicinal plants on ten Helicobacter pylori strains were studied by the salt aggregation test to determine the possibility to modulate their cell surface hydrophobicity and by an agar diffusion assay for detection of antimicrobial activity. It was established that aqueous extracts of bearberry and cowberry leaves enhance cell aggregation of all H. pylori strains tested by the salt aggregation test, and the extract of bearberry possessed a remarkable bacteriostatic activity. Pure tannic acid showed a result similar to that of bearberry and cowberry extracts which contained a large amount of tannins. In contrast, extracts of wild camomile and pineapple-weed, which blocked aggregation of H. pylori, contained small amounts of tannins and did not reveal any antimicrobial activity. Tannic acid seems to be the component

of bearberry and cowberry aqueous extracts with the highest activity to decrease cell surface hydrophobicity as well as in antibacterial activity against H. pylori.

Ansar S, Iqbal M, Athar M. **Nordihydroguairetic acid is a potent inhibitor of ferric-nitrilotriacetate-mediated hepatic and renal toxicity, and renal tumour promotion, in mice.** Carcinogenesis 1999;20(4):599-606.
Ferric-nitrilotriacetate (Fe-NTA) is a known renal carcinogen. In the present study, we report the effect of a potent lignin-derived herbal antioxidant, nordihydroguairetic acid (NDGA), against Fe-NTA-mediated tissue toxicity. Fe-NTA (alone) treatment of mice enhances ornithine decarboxylase activity to 259% in liver and 341% in kidney and increases [3H]thymidine incorporation in DNA to 250% in liver and 324% in kidney compared with the corresponding saline-treated controls. The enhanced ornithine decarboxylase activity and DNA synthesis showed a reduction to 138 and 123%, respectively, in liver at a higher dose of 2 mg NDGA/day/animal whereas in kidney the reduction was to 118 and 102%, respectively, compared with the corresponding saline-treated controls. In the Fe-NTA (alone)-treated group, a 12% renal tumour incidence was recorded whereas, in N-diethylnitrosamine (DEN)-initiated and Fe-NTA-promoted animals, the percentage tumour incidence was increased to 68% as compared with untreated controls. No tumour incidence was recorded in the DEN-initiated, non-promoted group. The administration of NDGA, afforded >80% protection against DEN- and Fe-NTA-mediated renal tissue injury in vivo. Fe-NTA treatment also enhanced hepatic and renal microsomal lipid peroxidation to 170 and 205% of saline-treated controls, respectively, and hydrogen peroxide generation by >2.5-fold in both tissues accompanied by a 51 and 21% decrease in the level of glutathione and 35-48 and 35-50% decrease in the activities of glutathione-metabolizing and antioxidant enzymes in liver and kidney, respectively. These changes were reversed significantly in animals receiving a pre-treatment of NDGA. Our data show that NDGA can abrogate the toxic and tumour-promoting effects of Fe-NTA in liver and kidney of mice and can serve as a potent chemopreventive agent to suppress oxidant-induced tissue injury and tumorigenesis.

Arisawa M, Hayashi K, Nikaido T, Koike K, Sasaki T, et al . **Screening of some marine organism extracts for cAMP phosphodiesterase inhibition, cytotoxicity, and antiviral activity against HSV-1.** Int J Pharmacogn 1997;35(1):6-11.
IPA COPYRIGHT: ASHP Extracts of 71 samples of 56 kinds of marine products were subjected to an inhibitory test for cyclic AMP (cAMP) phosphodiesterase, and to cytotoxic and antiviral screening tests. Seven extracts of marine products showed significant abilities to inhibit cAMP phosphodiesterase and 5 extracts showed significant cytotoxicity against KB cells at concentrations under 20 mcg/ml. Eight extracts of marine products showed higher therapeutic indexes against herpes simplex virus type 1 (HSV-1).

Awang DV. **Parthenocide: demise of a facile theory of feverfew activity.** J Herbs Spices Med Plants 1998;5(4):95-8.
IPA COPYRIGHT: ASHP Since the publication of 2 migraine clinical studies in which a dried alcoholic extract of Tanacetum parthenium (L.) (feverfew) containing 0.35% parthenolide demonstrated no activity and dried powdered leaves containing 0.2% parthenolide demonstrated

a significant reduction in pain intensity and severity of symptoms, the theory that parthenolide is the active ingredient in T. parthenium is discussed.

Awang DV. **Saw palmetto, African prune and stinging nettle for benign prostatic hyperplasia (BPH).** Can Pharm J 1997 Nov;130:37-40, 43-44, 62.
IPA COPYRIGHT: ASHP The beneficial effects of saw palmetto (Serenoa repens), African prune (Prunus africana), and stinging nettle (Urtica dioica) for the treatment of benign prostatic hyperplasia (BPH) are discussed.

Batey RG, Bensoussan A, Fan YY, Bollipo S, Hossain MA. **Preliminary report of a randomized, double-blind placebo-controlled trial of a Chinese herbal medicine preparation CH-100 in the treatment of chronic hepatitis C.** J Gastroenterol Hepatol 1998;13(3):244-7.
The treatment of chronic hepatitis C is relatively unsatisfactory and many patients have turned to unproven alternative medicines to modify the course of their illness. We report a study of a Chinese herbal medicine preparation CH-100 in the management of chronic hepatitis C. Patients with documented chronic hepatitis C were randomly allocated to receive active herbal or placebo tablets (five tablets thrice daily). Patients were followed monthly and evaluated by a Western and a traditional Chinese medical practitioner. Therapy was monitored by measurement of liver function tests, creatinine and full blood count on a monthly basis. Twenty patients in each group were well matched for age, sex, duration of illness, previous interferon therapy and alcohol intake. Active Chinese herbal medication was associated with a significant reduction in alanine aminotransferase (ALT) levels over the 6 month study period ($P < 0.03$). No patient cleared the virus but four normalized their ALT on treatment. Appropriately prescribed Chinese herbal medicine may have a role in the management of chronic hepatitis C and further controlled studies are indicated.

Batz F. **Integrating herbal therapy into practice.** Am Drug 1998 May;215:58-65.
IPA COPYRIGHT: ASHP The integration of herbal therapy into pharmacy practice is discussed, including the uses and precautions of commonly used herbs, quality and regulatory issues associated with herbal medicine, examples of herbal adverse reactions, herb-drug interactions, toxic herbs, information sources for herbal medicine, and the pharmacist's role in assisting patients in the safe use of herbs. This article qualifies for 2 hours U.S. CE credit by the ACPE.

Baxter A. **Treating depression with St. John's wort.** N Z Pharm1998 Jan;18:35.
IPA COPYRIGHT: ASHP The effectiveness and possible mechanism of action of Hypericum perforatum (St. John's wort) for the treatment of depression are discussed.

Beal FC. **Herbals and homeopathic remedies as formulary items?** Am J Health Syst Pharm 1998;55(12):1266-7.

Benoit-Vical F, Valentin A, Cournac V, Pelissier Y, Mallie M, Bastide JM. **In vitro antiplasmodial activity of stem and root extracts of Nauclea latifolia S.M. (Rubiaceae).** J Ethnopharmacol 1998;61(3):173-8.

Aqueous extracts from Nauclea latifolia S.M. (Rubiaceae), a plant commonly used in Ivory Coast by traditional healers for the treatment of malaria, were tested on two strains of Plasmodium faliparum: FcB1-Colombia (chloroquine-resistant) and a Nigerian strain (chloroquine-sensitive). The extracts were obtained from stems and roots of the plant in two forms, infusion and decoction, both methods used by most traditional healers. The in vitro activity of N. latifolia extracts on P. falciparum was assessed both visually and by a radioactive method. The visual analysis allowed determination of the time of extract action on the erythrocytic cycle, as well as the parasitic stage of most inhibitory effect. Similar results were obtained applying fresh, frozen or lyophilized extracts. The IC50 values determined were within the range already reported for other antimalarial plants such as Azadirachta indica A. Juss (Meliaceae) or Artemisia annua L. (Asteraceae). Aqueous extracts of N. latifolia inhibited P. falciparum (FcB1 strain) mainly at the end of the erythrocytic cycle (32nd to 48th hour).

Berthold HK, Sudhop T, Von Bergmann K. **Effect of a garlic oil preparation on serum lipoproteins and cholesterol metabolism: randomized controlled trial.** JAMA 1998 Jun 17;279:1900-2.
IPA COPYRIGHT: ASHP A randomized, double blind, placebo controlled, crossover study evaluating the antilipemic effects and mechanism of an enteric-coated garlic oil (Tegra) preparation was conducted in 25 hypercholesterolemia patients, mean age 58 yr, who received 5 mg of the garlic oil preparation twice daily and a matching placebo each for 12 wk in a crossover fashion with a 4 wk placebo washout between treatment periods. Lipoprotein levels were virtually unchanged at the end of both treatment periods. Cholesterol absorption, cholesterol synthesis, mevalonic acid excretion, and changes in the ratio of lathosterol to cholesterol in the serum were not different during garlic and placebo treatment. It was concluded that garlic therapy for the treatment of hypercholesterolemia cannot be recommended on the basis of this study.

Bhandari U, Sharma JN, Zafar R. **The protective action of ethanolic ginger (Zingiber officinale) extract in cholesterol fed rabbits.** J Ethnopharmacol 1998;61(2):167-71.
The effects of ethanolic extract of ginger (200 mg/kg, p.o.) were studied in cholesterol fed rabbits. The marked rise in serum and tissue cholesterol, serum triglycerides, serum lipoproteins and phospholipids that followed 10 weeks of cholesterol feeding, was significantly reduced by the ethanolic ginger extract and results were compared with gemfibrozil, a standard orally effective hypolipidaemic drug. The severity of aortic atherosclerosis as judged by gross grading was more marked in pathogenic, i.e. the hypercholesterolemic group, while animals receiving ginger extract along with cholesterol showed a lower degree of atherosclerosis. The results indicate that ginger is definitely an antihyperlipidaemic agent.

Bhattacharya SK, Kumar A. **Effect of Trasina, an ayurvedic herbal formulation, on experimental models of Alzheimer's disease and central cholinergic markers in rats.** J Altern Complement Med 1997;3(4):327-36.
Trasina is a herbal formulation of some Indian medicinal plants classified in Ayurveda, the classic Indian system of medicine, as Medhyarasayanas or drugs reputed to improve memory and intellect. Earlier experimental and clinical investigations have indicated that the formulation has a memory-facilitating action. In this investigation, the effect of Trasina, after subchronic

administration for 21 days, was assessed on two rodent models simulating some biochemical features known to be associated with Alzheimer's disease (AD). The models, in rats, included intracerebroventricularly (i.c.v.) administered colchicine (15 micrograms/rat) and lesioning of nucleus basalis magnocellularis (nbm) by ibotenic acid (10 micrograms/rat). Retention of an active avoidance response was used as the memory parameter. In addition, the effect of Trasina was evaluated on i.c.v. colchicine-induced depletion of acetylcholine (ACh) concentrations, reduction in choline acetyltransferase (ChAT) activity, and decrease in muscarinic cholinergic receptor (MCR) binding in rat brain frontal cortex and hippocampus. The behavioral and biochemical investigations were done 7, 14, and 21 days after colchicine or ibotenic acid lesioning. Trasina (200 and 500 mg/kg) was administered orally (p.o.) once daily for 21 days, the first drug administration being given just prior to lesioning. Colchicine and ibotenic acid induced marked retention deficit of active avoidance learning that was attenuated in a dose-dependent manner by Trasina after 14 and 21 days of treatment. Frontal cortical and hippocampal ACh concentrations, ChAT activity and MCR binding was significantly reduced after colchicine treatment. Trasina (200 and 500 mg/kg) reversed these deficits after 14 and 21 days of treatment. The findings indicate that the herbal formulation exerts a significant nootropic effect after subchronic treatment that may be due to reversal of perturbed cholinergic function.

Bhattarai NK. **Traditional herbal medicines used to treat wounds and injuries in Nepal.** Trop Doct 1997;27(Suppl 1):43-7.
In rural Nepalese societies, due to the lack of modern health services and facilities, folk herbal preparations are still the dominant method of therapy for common ailments. These remedies are fairly well accepted, easily available, bear a minimal cost and are generally the only available resource. Information on the curative properties of 42 plant species from 40 genera and 23 families that are used to treat wounds and injuries, has been documented. These herbal remedies are based on ancestral knowledge and personal experience. Their successful use indicates that they are alive and functioning in the rural localities. Although the techniques of preparation of drugs or dosage forms employed by traditional healers have generally been observed to be poor and in most cases do not comply with the requirements of modern pharmaceutical practices, there are trends towards the development and modernization of practice including the standardization of specific dosage, storage of drugs, use of specific types of containers and their labelling. A critical evaluation of the phytochemistry and pharmacology of the alleged curative plants and the traditional pharmaceutical practices employed has been strongly recommended. In rural Nepalese societies, the number and distribution of traditional herbal practitioners and faith healers greatly exceed all other health workers. Their influence should be applied to the task of motivating the rural populace to adopt authentic herbal remedies and other health-related hygienic behaviour.

Birt DF, Mitchell D, Gold B, Pour P, Pinch HC. **Inhibition of ultraviolet light induced skin carcinogenesis in SKH-1 mice by apigenin, a plant flavonoid.** Anticancer Res 1997;17(1a):85-91.
Apigenin, a widely distributed plant flavonoid, was previously found to inhibit chemically induced ornithine decarboxylase (ODC) activity and skin tumor promotion. The purpose of the present research was to determine if apigenin is effective in the prevention of ultraviolet-B light (UVB) induced skin carcinogenesis. Further studies ascertained if apigenin would be expected to

absorb UVB light in a manner to prevent DNA damage in a cell free system. ODC activity was induced with 0.45 J/cm2 ultraviolet A and B (UVA/B) light. Apigenin (5 mumoles/200 microliters DMSO:acetone, 1:9) treatment from 12 hours before until 1 hour following UVA/B exposure was effective in inhibition (25-45% inhibition) of ODC activity measured at 28 hours following UVA/B exposure. Mouse skin carcinogenesis was induced by exposure to a total dose of 40 J/cm2 UVB over 11 weeks. Treatment with 10 mumoles apigenin in 200 microliters DMSO:acetone (1:9) prior to each UVB exposure resulted in reduction in cancer incidence (52% inhibition) and an increase in tumor free survival in comparison with control mice ($P < 0.01$). Apigenin (0-100 microM) did not prevent the in vitro production of photoproducts in salmon sperm DNA suggesting that apigenin did not inhibit UVA/B induced ODC activity or UVB induced skin carcinogenesis by simply absorbing ultraviolet light or decreasing DNA damage.

Bordia A, Verma SK, Srivastava KC. **Effect of ginger (Zingiber officinale Rosc.) and fenugreek (Trigonella foenumgraecum L.) on blood lipids, blood sugar and platelet aggregation in patients with coronary artery disease.** Prostaglandins Leukot Essent Fatty Acids 1997;56(5):379-84.
In a placebo-controlled study the effect of ginger and fenugreek was examined on blood lipids, blood sugar, platelet aggregation, fibrinogen and fibrinolytic activity. The subjects included in this study were healthy individuals, patients with coronary artery disease (CAD), and patients with non-insulin-dependent diabetes mellitus (NIDDM) who either had CAD or were without CAD. In patients with CAD powdered ginger administered in a dose of 4 g daily for 3 months did not affect ADP- and epinephrine-induced platelet aggregation. Also, no change in the fibrinolytic activity and fibrinogen level was observed. However, a single dose of 10 g powdered ginger administered to CAD patients produced a significant reduction in platelet aggregation induced by the two agonists. Ginger did not affect the blood lipids and blood sugar. Fenugreek given in a dose of 2.5 g twice daily for 3 months to healthy individuals did not affect the blood lipids and blood sugar (fasting and post prandial). However, administered in the same daily dose for the same duration to CAD patients also with NIDDM, fenugreek decreased significantly the blood lipids (total cholesterol and triglycerides) without affecting the HDL-c. When administered in the same daily dose to NIDDM (non-CAD) patients (mild cases), fenugreek reduced significantly the blood sugar (fasting and post prandial). In severe NIDDM cases, blood sugar (both fasting and post prandial) was only slightly reduced. The changes were not significant. Fenugreek administration did not affect platelet aggregation, fibrinolytic activity and fibrinogen.

Bowers LD. **Oral dehydroepiandrosterone supplementation can increase the testosterone/epitestosterone ratio.** Clin Chem 1999;45(2):295-7.
BIOSIS COPYRIGHT: BIOL ABS. RRM RESEARCH ARTICLE PFAFFIA PANICULATA PANAX GINSENG PTYCHOPETALUM OLACOIDES LENTINUS EDODES CAMELLIA SINESIS SUMA GINSENG MUIRA PAAN SHITAKE MUSHROOM HUMAN CAMELIA SINESIS MEDICINAL PLANT ATHLETES PHARMACOGNOSY DEHYDROEPIANDROSTERONE SAFETY DIETARY SUPPLEMENT ORAL ADMINISTRATION TESTOSTERONE-EPITESTOSTERONE RATIO SHITAKE MUSHROOM EXTRACT GREEN TEA EXTRACT ENDOCRINE SYSTEM ATHLETIC PERFORMANCE TOXICOLOGY.

Brinkeborn RM, Shah DV, Degenring FH. **Echinaforce and other Echinacea fresh plant preparations in the treatment of the common cold. A randomized, placebo controlled, double-blind clinical trial.** Phytomedicine 1999;6(1):1-6.
The aim of this randomized, double-blind, placebo controlled study was to investigate the efficacy and safety of different doses and preparations of Echinacea purpurea in the treatment of common cold. 246 of 559 recruited healthy, adult volunteers caught a common cold and took 3 times daily 2 tablets of either Echinaforce (Echinacea purpurea-preparation from 95% herba and 5% radix), Echinacea purpurea concentrate (same preparation at 7 times higher concentration), special Echinacea purpurea radix preparation (totally different from that of Echinaforce) or placebo until they felt healthy again but not longer than 7 days. The primary endpoint was the relative reduction of the complaint index defined by 12 symptoms during common cold according to the doctor's record. Echinaforce and its concentrated preparation were significantly more effective than the special Echinacea extract or placebo. All treatments were well tolerated. Among the Echinacea groups the frequency of adverse events was not significantly higher than in the placebo group. Therefore, Echinacea concentrate as well as Echinaforce represent a low-risk and effective alternative to the standard symptomatic medicines in the acute treatment of common cold.

Brown CS, Freeman EW, Ling FW. **Update on the treatment of premenstrual syndrome.** Am J Manage Care 1998 Feb;4:266-74, 277-8.
IPA COPYRIGHT: ASHP An overview of nonpharmacological and pharmacological treatments for premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) is presented, including a discussion of how to diagnosis PMS and PMDD and how to differentiate between the 2 syndromes, proposed etiologies of PMS, and the role of nonpharmacologic treatments in PMS, including diet, sodium and caffeine restriction, exercise, behavioral modification, and stress reduction. The role of nonprescription treatments in PMS, including OTC menstrual products, vitamins and minerals, prostaglandin inhibitors, and herbal treatments, is described as well as the role of prescription treatments, including psychotropic agents, hormonal agents, and diuretics, and surgical intervention in PMS. This article qualifies for 2 hours U.S. CE credit by the ACPE.

Brown DJ, Dattner AM. **Phytotherapeutic approaches to common dermatologic conditions.** Arch Dermatol 1998;134(11):1401-4.
In this review, we discuss some common herbal preparations historically used for dermatologic conditions and recent studies that support their use. The traditional practice of topically treating dermatologic conditions with plant-derived medicines predates the cultures of ancient Egypt and remains vital today in the industrialized cultures of both the United States and Europe. Recent scientific studies lend support to some of the claims of herbal practitioners for the safety and efficacy of many herbs. The studies also elucidate, in some cases, the mechanisms by which these herbs act. With the growing interest in alternative and complementary therapies, practitioners need more information. Clinical studies and collected observations will help define specific indications for choice of herbal treatment based on both the skin disorder and the unique characteristics of the patient involved.

Brown DJ, Foster S. **Phytotherapy: herbal medicine meets clinical science. Part 2.** America's Pharm 1997 Jun;119:31-48.

IPA COPYRIGHT: ASHP A review is presented of the development of phytotherapy, key points of the Dietary Supplement Health and Education Act of 1994, commonly prescribed and top selling phytomedicine products, and the indications, active constituents, mechanism of action, dosage, and side effects of Vaccinium myrtillus (bilberry), Tanacetum parthenium (feverfew), Allium sativum (garlic), ginseng, Crateagus oxyacantha (hawthorn), Hypericum perforatum (St. John's Wort), and Vitex agnus-castus. This article qualifies for 2 hours U.S. CE credit by the ACPE.

Bruno Blanch L, Bros M, Baldini O, Spegazzini E. **Diuretic activity of Artemisia annua L. extracts.** Acta Farm Bonaerense 1998 Apr-Jun;17:131-4.

Buchness MR. **Alternative medicine and dermatology.** Semin Cutan Med Surg 1998;17(4):284-90.
Because of increasing interest in the treatment and prevention of disease using nonconventional modalities, particularly in Western countries, it is important for practitioners of traditional Western medicine to remain open-minded about the use of alternative treatments. If the patient perceives the physician to be disapproving of the use of alternative treatments, she may not divulge the use of such treatments to the physician, even though alternative treatments can lead to adverse effects and to drug-herb interactions. The demographics and the reasons why patients seek alternative treatment are discussed. The scientific literature on the use of herbal and physical modalities is reviewed. Because of the large body of literature on the use of herbal remedies, the emphasis is on the current, most popular herbs in use by the general population, as well as on herbs used specifically for dermatologic disease.

Carruthers-Czyzewski P, Dewar J. **Diabetes.** Can Pharm J 1997 Sep;130:32-4, 37, 52.
IPA COPYRIGHT: ASHP The treatment of diabetes with conventional drug therapies supplemented with complementary therapies, such as herbal remedies and traditional Chinese medicine, are described.

Carruthers-Czyzewski P, Dewar J. **Hypertension.** Can Pharm J 1997 Apr;130:35-9.
IPA COPYRIGHT: ASHP An overview of effective complementary therapies for hypertension in the elderly is presented, including mind-body intervention, diet and nutrition, manual healing, and herbal medicines.

Castro VR. **Chromium in a series of Portuguese plants used in the herbal treatment of diabetes.** Biol Trace Elem Res 1998;62(1-2):101-6.
Chromium (Cr3+) is an essential micronutrient for humans. Its main action is thought to be the regulation of blood sugar, because chromium deficiency is associated with diabetic-like symptoms, and chromium supplementation is correlated with increased glucose tolerance and insulin sensitivity. Some Portuguese aromatic plants are utilized as tisanes by diabetic people as medicinal plants. Their active principle is not yet known, and the importance of their chromium content in the claimed therapeutic properties should not be discarded. Therefore, determination of chromium in some Portuguese medicinal plants was performed by flameless atomic absorption. All the analyzed plants contain chromium at the normal level for this element, but the

plants used to prepare tisanes to help diabetic conditions contain higher levels (2.2 microg/g dry wt+/-0.88; n=11) than the others (0.88 microg/g dry wt+/-0.18; n=17).

Cerrato PL. **Herbal therapy: more than just folklore.** RN 1997;60(8):51-3.

Chavez ML, Chavez PI. **Echinacea.** Hosp Pharm 1998 Feb;33:180-8.
IPA COPYRIGHT: ASHP A review of the therapeutic use of Echinacea species is presented, and proprietary product names, plant name synonyms, taxonomy, history of therapeutic use, chemical constituents, physiological effects, dosage and administration, adverse effects, contraindications, and clinical trials of the therapeutic effectiveness of Echinacea species preparations are considered.

Chen GW, Chung JG, Ho HC, Lin JG. **Effects of the garlic compounds diallyl sulphide and diallyl disulphide on arylamine N-acetyltransferase activity in Klebsiella pneumoniae.** J Appl Toxicol 1999;19(2):75-81.
Arylamine N-acetyltransferase (NAT) activities with 2-aminofluorene (2-AF) were determined in the bacterium Klebsiella pneumoniae. Cytosols or suspensions of K. pneumoniae with or without specific concentrations of diallyl sulphide (DAS) or diallyl disulphide (DADS) as co-treatment showed different percentages of 2-AF acetylation. The data indicated that there was decreased NAT activity associated with increased levels of DAS or DADS in K. pneumoniae. In growth studies on K. pneumoniae it was demonstrated that DAS or DADS elicited a dose-dependent bacteriocide effect on K. pneumoniae. For the cytosol examinations, the apparent values of Km and Vmax were 0.96+/-0.09 mM and 7.87+/-0.79 nmol min(-1) mg(-1) protein, respectively, for 2-AF. However, when DAS or DADS was added to the reaction mixtures, the apparent values of Km and Vmax were 0.16+/-0.04 mM and 0.99+/-0.16 nmol min(-1) mg(-1) protein with DAS, respectively, and 0.14+/-0.18 mM and 0.85+/-0.10 nmol min(-1) mg(-1) protein with DADS, respectively, for 2-AF. For the intact bacteria examination, the apparent values of Km and Vmax were 0.57+/-0.06 mM and 2.00+/-0.14 nmol min(-1) per 10x10(10) CFU, respectively, for 2-AF. However, when DAS or DADS was added to the reaction mixtures, the apparent of values of Km and Vmax were 0.41+/-0.04 mM and 1.30+/-0.10 nmol min(-1) per 10x10(10) CFU with DAS, respectively, and 0.34+/-0.04 mM and 1.08+/-0.08 nmol min(-1) per 10x10(10) CFU with DADS, respectively, for 2-AF. This report is the first demonstration to show that the garlic components DAS and DADS would affect K. pneumoniae growth and NAT activity.

Chen GW, Chung JG, Hsieh CL, Lin JG. **Effects of the garlic components diallyl sulfide and diallyl disulfide on arylamine N-acetyltransferase activity in human colon tumour cells.** Food Chem Toxicol 1998;36(9-10):761-70.
Diallyl sulfide (DAS) and diallyl disulfide (DADS), major components of garlic, were used to determine inhibition of arylamine N-acetyltransferase (NAT) activity in a human colon tumour (adenocarcinoma) cell line. Two assay systems were performed, one with cellular cytosols (9000g supernatant), the other with intact bacterial cell suspensions. The NAT activity in a human colon tumour cell line was inhibited by DAS and DADS in a dose-dependent manner in both system: that is, the greater the concentration of DAS and DADS in the reaction, the greater the inhibition of NAT activities in both systems. The data also indicated that DAS and DADS

decrease the apparent values of Km and Vmax of NAT enzymes from human colon tumour cells in both systems examined. This is the first report to demonstrate that garlic components do affect human colon tumour cell NAT activity.

Chiou LC, Ling JY, Chang CC. **Chinese herb constituent beta-eudesmol alleviated the electroshock seizures in mice and electrographic seizures in rat hippocampal slices.** Neurosci Lett 1997;231(3):171-4.
We have found that beta-eudesmol, a sesquiterpenol constituent of Chinese herb antagonized organophosphate-induced lethal toxicity by reversing the neuromuscular failure and reducing the occurrence of convulsions. Its possible antiepileptic action was further explored in electroshock seizure mice in vivo and in high potassium treated rat hippocampal slices in vitro. At a dose with little effect on the motor activity, beta-eudesmol prevented the convulsions and lethality induced by maximal electroshock but not those by pentylenetetrazol or picrotoxin. At subeffective doses, beta-eudesmol and phenytoin showed additive effect in preventing electroshock seizures. Extracellular recording of field potentials in CA1 pyramidal layer of hippocampal slices showed that beta-eudesmol reduced the high potassium (8.5 microM)-induced electrographic seizure activity. The potential of beta-eudesmol to serve as an antiepileptic or a conjuvant in phenytoin therapy is suggested.

Chithra P, Sajithlal GB, Chandrakasan G. **Influence of Aloe vera on the glycosaminoglycans in the matrix of healing dermal wounds in rats.** J Ethnopharmacol 1998;59(3):179-86.
IPA COPYRIGHT: ASHP The effects of Aloe vera gel on glycosaminoglycan components in the granulation tissue of healing dermal wounds were studied in rats following oral or topical administration of the gel. The amount of ground substance synthesized was higher in treated wounds; in particular, hyaluronic acid and dermatan sulfate levels were increased. The levels of the reported glycohydrolases were elevated upon treatment with the gel, indicating increased turnover of the matrix. Both topical and oral doses of the gel had a positive effect on the synthesis of glycosaminoglycans, thereby beneficially modulating wound healing.

Chithra P, Sajithlal GB, Chandrakasan G. **Influence of Aloe vera on the healing of dermal wounds in diabetic rats.** J Ethnopharmacol 1998;59(3):195-201.
IPA COPYRIGHT: ASHP The effects of Aloe vera gel on the healing of full thickness dermal wounds were studied in diabetic rats following oral or topical administration of the gel. Treatment of wounds with the gel enhanced the process of wound healing, possibly by influencing phases such as inflammation, fibroplasia, collagen synthesis and maturation, and wound contraction. The effects may have been due to the reported hypoglycemic effects of the gel.

Coombs MD, Dunachie SJ, Brooker S, Haynes J, Church J, Warrell DA. **Snake bites in Kenya: a preliminary survey of four areas.** Trans R Soc Trop Med Hyg 1997;91(3):319-21.
Primary data were collected on the incidence, severity and species responsible for snake bites in 4 areas of Kenya: (i) Kakamega and western Kenya, (ii) Lake Baringo and Laikipia, (iii) Kilifi and Malindi, and (iv) northern Kenya. The overall average frequency of snake bite was 13.8 per 100,000 population per year (range 1.9-67.9). The minimum rate of snake bite mortality was 0.45/100,000/year. Thirty-four of the 50 units visited reported no knowledge of death from snake

bite in the last 5 years. Possible reasons for the low estimates are discussed. Traditional treatments were common, especially the use of herbal remedies and incisions at the wound site.

Cott JM, Fugh-Berman A. **Is St. John's wort (Hypericum perforatum) an effective antidepressant?** J Nerv Ment Dis 1998;186(8):500-1.
SJW is a remarkably safe antidepressant with an apparently unique mode of action. Although it has demonstrated efficacy in mild and moderate depression when compared with placebo or tricyclic antidepressants, several research areas beg to be explored. Its effects should be compared with serotonin reuptake inhibitors. Studies in severely depressed patients are lacking, as are studies on its utility as a therapeutic adjunct to standard antidepressants.

Dai Y, Kou JP, Liu LH. **Anti-allergic effect of an aqueous extract of wu-hu-tang.** J Ethnopharmacol 1997;55(2):127-32.
Wu-Hu-Tang (WHT), a Chinese formulation which consists of seven crude drugs, has been used for the treatment of asthma for hundreds of years. In this paper, an investigation on the anti-allergic activity of an aqueous extract of WHT was undertaken to find the pharmacological basis for the ethnomedical use of the formulation. WHT produced a significant inhibition on the homologous passive cutaneous anaphylaxis (PCA) in rats and the heterologous PCA in mice, decreased the degranulation of mast cells of calvarial periosteum in rats, inhibited the release of anaphylactic mediators from sensitized lung tissues of guinea pigs and the contraction of isolated guinea pigs ileum induced by histamine. These results indicated that the therapeutic activity of WHT for asthma may be related to its inhibitory effects on immediate hypersensitivity.

De La Motte S, Bose-O'reilly S, Heinisch M, Harrison F. **[Double blind comparison of a preparation of pectin/chamomile extract and placebo in children with diarrhea].** Arzneim Forsch 1997;47(11):1247-9. (Ger)
IPA COPYRIGHT: ASHP To examine the efficacy of a preparation of pectin/chamomile extract compared with placebo in children with diarrhea, a prospective, double blind, randomized, parallel group study was conducted in 79 children (ages 6 months-5.5 yr) with uncomplicated diarrhea who received either a preparation containing apple pectin and Matricaria chamomilla (chamomile) extract (Diarrhoesan) or placebo in addition to the usual rehydration and realimentation diet. At the end of 3 days of treatment, the diarrhea had ended significantly more frequently in the pectin/chamomile (33/39) than in the placebo group (23/40). Pectin/chamomile reduced the duration of diarrhea significantly by at least 5.2 h. The parents documented their well-being in a diary twice daily; in contrast to placebo, a trend of continuous improvement was observed in the pectin/chamomile group. The parents expressed their contentment more frequently (82%) with pectin/chamomile than with placebo. There were no further differences between the treatment groups.

Delfosse M. **[Artemisia annua for the treatment of malaria].** J Pharm Belg 1998;53(4):276-7. (Fre)

Dhuley JN, Naik SR. **Effect of Rhinax on bacterial lipopolysaccharide induced endotoxemia in rats.** Indian J Exp Biol 1998;36(3):315-7.
Administration of lipopolysaccharide (LPS) at 3 mg/kg, i.p. in rats resulted in reduced food

intake, febrile hyperthermia, decreased body weight and reduced muscle performance in treadmill tests. It also induced some biochemical changes like increased serum levels of transaminases, acid phosphatase, pseudocholinesterase, free fatty acids and decreased blood glucose and liver glycogen levels. Rhinax (RHX), a herbal formulation, at 160 mg/kg, p.o. improved muscle performance but had no effect on the elevated temperature or the reduced body weight of rats weakened by LPS. It also normalised various biochemical alterations induced by LPS. The results of these studies indicate efficacy of RHX as an antifatigue agent to improve muscular performance.

Dhuley JN, Naik SR. **Protective effect of Rhinax, a herbal formulation, against CCl4-induced liver injury and survival in rats.** J Ethnopharmacol 1997;56(2):159-64.
Rhinax, a herbal formulation, was investigated for its protective activity against CCl4-induced liver injury and survival in rats. Oral administration of Rhinax at a dose of 80 mg/kg significantly reduces the hepatotoxic effects of CCl4. It also significantly improves the survival of rats at a dose of 160 mg/kg. On the basis of these observations, we conclude that Rhinax possesses anti-hepatotoxic activity and that the observed activity may be due to the increased activity of cytochrome P450, thereby exerting an inhibitory effect on reductive pathways of CCl4.

Dion ME, Agler M, Milner JA. **S-allyl cysteine inhibits nitrosomorpholine formation and bioactivation.** Nutr Cancer 1997;28(1):1-6.
Water extracts of garlic, deodorized garlic powder, and onions, but not leeks, were found to significantly ($p < 0.05$) reduce the in vitro formation of N-nitrosomorpholine (NMOR), a known liver carcinogen. Addition of increasing quantities (20, 40, and 80 mM) of S-allyl cysteine (SAC), a water-soluble compound in processed garlic, depressed NMOR formation by 16%, 27%, and 43%, respectively ($p < 0.05$). The ability of SAC to block NMOR formation decreased as the NaNO7 and morpholine concentrations increased. SAC and its non-allyl analog S-propyl cysteine effectively blocked NMOR formation. SAC and S-propyl cysteine were less effective than isomolar cysteine in reducing NMOR formation ($p < 0.05$). The oil-soluble sulfur compounds diallyl disulfide (DADS), dipropyl disulfide, and diallyl sulfide were ineffective inhibitors of NMOR generation ($p > 0.05$). SAC and DADS reduced the mutagenicity of NMOR in Salmonella typhimurium TA100 ($p < 0.05$). SAC at 70 mumol/plate reduced the number of histidine revertants per plate by 51% ($p < 0.05$), whereas DADS at 0.12 mumol/plate reduced mutant colony number by 76% ($p < 0.05$). SAC and DADS were more effective than isomolar cysteine in reducing NMOR mutagenicity ($p < 0.05$). The ability of sulfur compounds in garlic and onions to depress nitrosamine formation and bioactivation in these studies is consistent with epidemiologic evidence that higher intake of allium plants is associated with a reduction in the risks of some cancers.

Dirsch VM, Gerbes AL, Vollmar AM. **Ajoene, a compound of garlic, induces apoptosis in human promyeloleukemic cells, accompanied by generation of reactive oxygen species and activation of nuclear factor kappaB.** Mol Pharmacol 1998;53(3):402-7.
The pharmacological role of garlic in prevention and treatment of cancer has received increasing attention, but thorough investigations into the molecular mechanisms of action of garlic compounds are rare. The present study demonstrates that ajoene, a major compound of garlic

induces apoptosis in human leukemic cells, but not in peripheral mononuclear blood cells of healthy donors. The effect was dose and time dependent. Apoptosis was judged by three criteria, morphology of cells, quantification of subdiploid DNA content by flow cytometry, and detection of DNA fragmentation by gel electrophoresis. Ajoene increased the production of intracellular peroxide in a dose- and time-dependent fashion, which could be partially blocked by preincubation of the human leukemic cells with the antioxidant N-acetylcysteine. Interestingly, N-acetylcysteine-treated cells showed a 50% loss of ajoene-induced apoptosis. Moreover, ajoene was demonstrated to activate nuclear translocation of the transcription factor nuclear factor kappaB, an effect that was abrogated in N-acetylcysteine-loaded cells. These results suggested that ajoene might induce apoptosis in human leukemic cells via stimulation of peroxide production and activation of nuclear factor kappaB. This is a novel aspect in the biological profile of this garlic compound and an important step in elucidating the underlying molecular mechanisms of its antitumor action.

Dirsch VM, Kiemer AK, Wagner H, Vollmar AM. **Effect of allicin and ajoene, two compounds of garlic, on inducible nitric oxide synthase.** Atherosclerosis 1998;139(2):333-9. Inducible nitric oxide synthase (iNOS) has recently been shown to be present in human atherosclerotic lesions and to promote the formation of deleterious peroxynitrite. Allicin and ajoene are discussed as active compounds with regard to the beneficial effects of garlic in atherosclerosis. The aim of this study was to investigate the effect of allicin and ajoene on the iNOS system in lipopolysaccharide (LPS)-stimulated RAW 264.7 macrophages. Ajoene (IC50 2.5-5 microM) and allicin (IC50 15-20 microM) dose dependently reduced nitrite accumulation, a parameter for NO synthesis, in supernatants of LPS-stimulated (1 microg/ml, 20 h) macrophages. Accordingly, reduced iNOS enzyme activities were measured by conversion of L-[3H]arginine to L-[3H]citrulline in homogenates of LPS-activated cells treated with ajoene or allicin. None of these compounds, however, showed a direct effect on the catalytic-activity of iNOS. Consequently, iNOS protein and mRNA expression in ajoene (10 microM) or allicin (50 microM) treated cells were evaluated by Western blot and Northern blot analysis, respectively. Markedly reduced iNOS protein as well as mRNA levels were demonstrated. These observations indicate that allicin and ajoene inhibit the expression of iNOS in activated macrophages. The possible link of this effect to the beneficial features attributed to garlic is discussed.

Downs A. **Comparing antiscabies treatments [letter; comment] [see comments].** Arch Dermatol 1997;133(4):526.

Draelos ZD. **Skin lightening agents provide dermatologists with various treatment options.** Cosmet Derm 1997 Jan;10:13-5.
IPA COPYRIGHT: ASHP A brief overview of different topical skin lightening agents that have cosmetic and therapeutic applications, including sunscreens, hydroquinone alone (Melanex; Eldoquin; Eldopaque) or in combination with other agents, tretinoin, azelaic acid (Azelex), botanical extracts, vitamins, and currently prohibited materials such as mercurials, and their mechanisms of action, is presented.

Dragsted LO, Strube M, Leth T. **Dietary levels of plant phenols and other non-nutritive components: could they prevent cancer?** Eur J Cancer Prev 1997;6(6):522-8.

Several non-nutritive components in fruits, vegetables, herbs and spices have been found to inhibit tumour formation in experimental animals exposed to carcinogens. The active non-nutritive components vary with respect to their chemical structures, and may be classed as phenols, terpenes, indoles, isothiocyanates, allyl sulphides or others. They also seem to work by different mechanisms, being inducers or inhibitors of various enzymes, antioxidants, scavengers of reactive metabolites, or inducers of apoptosis. The dietary levels are generally in the order of 1-100 mg/day for most classes of compounds in the Danish population, and similar levels are expected in most northern European countries. These levels are very low compared with the levels used in most animal experiments, where non-nutritive factors have individually been shown to have inhibitory actions on tumorigenesis. Human long-term intervention trials with antioxidants have generally been discouraging. In human short-term intervention studies, where increased dietary levels of specific vegetables or fruits are studied, doses are also comparatively low. Effects on important enzymes have been reported in several such studies, indicating that low levels of non-nutritive factors could influence carcinogenesis by specific mechanisms. Meta-analyses of cohort studies on specific food items rich in specific non-nutritive components, indicate that carotenoid- or glucosinolate-rich foods protect against some cancers, while flavonoid rich food items do not uniformly show protective effects.

Dweck AC. **Skin treatment with plants of the Americas.** Cosmet Toiletries 1997 Oct;112:47-8, 50, 52-6, 59-60, 63-4, 66.
IPA COPYRIGHT: ASHP North and South American plants used to treat skin conditions, including Thuja occidentalis, Smilax species (sarsparilla), Stellaria media (chickweed), Echinacea species, and Anaphalis margaritacea (pearly everlasting; cottonweed) for psoriasis, Polemonium caeruleum (Jacob's ladder), Sanguinaria canadensis L. (bloodroot), Centaurium erythraea (centaury), Trifolium pratense (clover), Ephedra distachya, Hydrastis canadensis (golden seal), Hamamelis virginiana (witch hazel), Simmondsia chinensis (jojoba), Carica papaya (papaya), and Achillea millefolium (milfoil) for eczema, Artemisia tridentata (big sagebrush), Trillium species (birthroot), Grindelia robusta (gum plant), Clematis virginiana, and Eupatorium perfoliatum (boneset) for wounds, cuts and other skin problems, and others for miscellaneous uses, are presented.

Efendy JL, Simmons DL, Campbell GR, Campbell JH. **The effect of the aged garlic extract, 'Kyolic', on the development of experimental atherosclerosis.** Atherosclerosis 1997;132(1):37-42.
The aged garlic extract 'Kyolic' lowers serum cholesterol levels in humans and experimental animals and thus is presumed to have a protective effect against atherosclerosis. However, to date no studies have examined the effect of this substance on the actual development of the disease. In the present study, the right carotid artery of 24 rabbits was de-endothelialized by balloon catheterisation in order to produce a myointimal thickening. After 2 weeks the rabbits were randomly assigned to four groups: Group I received a standard diet; Group II received the standard diet supplemented with 800 microl/kg body weight/day 'Kyolic'; Group III received a 1% cholesterol supplemented standard diet; and Group IV received a 1% cholesterol supplemented standard diet plus 'Kyolic'. After 6 weeks, the cholesterol diet caused a 6-fold increase in serum cholesterol level (Group III; 6.4 +/- 0.6 mmol/l) compared to normal diet (Group I; 1.2 +/- 0.4 mmol/l) ($P < 0.05$) with only a minor, non-significant reduction seen by the

addition of 'Kyolic' (Group IV; 6.2 +/- 0.7 mmol/l). Group III rabbits developed fatty streak lesions covering approximately 70 +/- 8% of the surface area of the thoracic aorta, which was significantly reduced to 25 +/- 3% in the 'Kyolic'-treated Group IV. No lesions were present in Groups I and II. The hypercholesterolaemic diet caused an increase in aortic arch cholesterol (2.1 +/- 0.1 mg cholesterol/g tissue) which was significantly reduced by 'Kyolic' supplementation (1.7 +/- 0.2 mg cholesterol/g tissue) ($P < 0.05$). 'Kyolic' significantly inhibited the development of thickened, lipid-filled lesions in the pre-formed neointimas produced by balloon-catheter injury of the right carotid artery in cholesterol-fed rabbits (intima as percent of artery wall, Group III 42.6 +/- 6.5% versus Group IV 23.8 +/- 2.3%, $P < 0.01$), but had little effect in rabbits on a standard diet (Group II 18.4 +/- 5.0% versus Group I 16.7 +/- 2.0%). In vitro studies showed that 'Kyolic' has a direct effect on inhibition of smooth muscle proliferation. In conclusion, 'Kyolic' treatment reduces fatty streak development, vessel wall cholesterol accumulation and the development of fibro fatty plaques in neointimas of cholesterol-fed rabbits, thus providing protection against the onset of atherosclerosis.

El-Sabban F, Radwan GM. **Influence of garlic compared to aspirin on induced photothrombosis in mouse pial microvessels, in vivo.** Thromb Res 1997;88(2):193-203. Effect of garlic on photochemically-induced platelet aggregation in pial microvessels of the mouse, in vivo, was compared to that of acetyl salicylic acid (ASA). Three trials were carried out, in which garlic at doses of 12.5, 25, 50 and 100 mg/kg and ASA doses of 25, 50 and 100 mg/kg were used. Each trial included treatment groups of male mice, approximately 30 g, and a control group. Animals were anesthetized (urethane, 1-2 mg/g, i.p.), the trachea was intubated and a craniotomy was performed. Induction of platelet aggregation was made by activation of circulating sodium fluorescein (0.1 ml of 5% solution/25 g, i.v.) with an intense mercury light. Garlic, ASA and vehicle solutions were injected, i.p., 60 min prior to the photochemical insult. The time for the first platelet aggregate to appear in pial arterioles was significantly delayed ($P < 0.001$) only by the 100 mg/kg garlic dose and by all ASA doses. The effect of this garlic dose on first aggregate was comparable to that of the 25 and 50 mg/kg ASA doses. Only the ASA doses delayed ($P < 0.05$) the appearance of first aggregate in venules. Arteriolar and venular diameter changes were not different among groups of all trials. Data of this study documented that garlic was capable of delaying platelet aggregation in mouse pial arterioles, in vivo.

Etienne JJ, Pham Duc TL. **Putting oils to the test.** Soap Perfum Cosmet 1997 May;70:45-6. IPA COPYRIGHT: ASHP The antioxidant and anti-elastase effects of some essential oils were studied in vitro, the anti-erythematous effects of an emulsion cream of rose oil, chamomile oil, marjoram oil, and hay absolute were examined in 6 healthy subjects (ages 20-50 yr) who applied the cream to the forearm before or after irradiation, and the anti-erythematous effects of a cream containing the essential oils/absolute mixture in liposomes were studied in 10 subjects who applied the cream to the forearm and 15 erythrositic subjects who applied the cream or placebo to the face. The cream had no effect when applied after irradiation. However, pretreatment with the cream protected the skin from a provoked erythema. After application of the liposome formulation to the forearm, a mean decrease of 9% of the erythema stress was found on the treated site. After application of the liposome formulation to the face, the decrease of skin redness on the treated zone at 8 days was -8% and at 28 days was -21%.

Fanelli SL, Castro GD, De Toranzo EG, Castro JA. **Mechanisms of the preventive properties of some garlic components in the carbon tetrachloride-promoted oxidative stress. Diallyl sulfide; diallyl disulfide; allyl mercaptan and allyl methyl sulfide.** Res Commun Mol Pathol Pharmacol 1998;102(2):163-74.
Previous studies evidenced that garlic extracts and/or garlic components were able to prevent against chemically induced tumors or acute toxic effects of chemicals (e.g. CCl4 induced liver injury). The chemopreventive potential of garlic has been attributed to the presence in it of several bioactive organosulfur compounds. Those components might act as antioxidants able to scavenge free radicals. In the present work we describe initial studies on the antioxidative-stress properties of some garlic components such as: diallyl disulfide (DDS), diallyl sulfide (DAS), allyl mercaptan (AMT) and allyl methyl sulfide (AMS). We found that DAS, DDS and AMT but not AMS were able to trap trichloromethyl and trichloromethylperoxyl free radicals. Further, DDS but not DAS or AMT also inhibited CCl4 promoted liver microsomal lipid peroxidation. DAS, but not DDS, AMT or AMS was able to react with free radicals arised during UVC activation of hydrogen peroxide or terbutyl hydroperoxide but not with those produced during UVC activation of terbutyl peroxide. However, all garlic components tested absorbed energy from UVC and became partially destroyed in the process. AMT, but not DDS, AMS or DAS was able to destroy 4-hydroxynonenal, a key reactive aldehyde produced during lipid peroxidation. AMT and DDS were also able to prevent UVC plus CCl4 promoted oxidation of albumin in vitro, but DAS and AMS failed to do so. Results suggest that the antioxidative stress properties of garlic might result from the contributions of its sulfur component in different steps and not necessarily from the contribution of only one of them.

Fleischhacker R. **[Echinacea as an immune stimulant: stand of scientific progress].** Dtsch Apoth Ztg 1998 May 14;138:54-7. (Ger)
IPA COPYRIGHT: ASHP A critical examination of the pharmacological test methods and results of clinical trials evaluating the use of Echinacea preparations, such as Echinacea purpurea (Asteraceae), is presented. It was concluded that recent studies show no conclusive scientific evidence of clinical relevance of the preparations.

Foote J, Cohen B. **Medicinal herb use and the renal patient.** J Ren Nutr 1998;8(1):40-2.
Medicinal herb use, although a popular branch of alternative medicine, may be inappropriate for the renal patient. The pharmacological activity, chemical components, and microbial content of herbs, as well as their ability to interfere with prescription medications, make medicinal herbs potentially dangerous for the renal patient. The purpose of this report is to inform the medical professional of the implications of renal patients using medicinal herbs.

Fujimiya Y, Suzuki Y, Katakura R, Ebina T. **Tumor-specific cytocidal and immunopotentiating effects of relatively low molecular weight products derived from the basidiomycete, Agaricus blazei Murill.** Anticancer Res 1999;19(1a):113-8.
Currently, some natural herbal extracts are believed to have a marked tumoricidal effect and low toxicity for normal tissues. We investigated the effect of relatively low molecular weight products extracted from the basidiomycete, Agaricus blazei Murill, on MethA tumor cell growth with the aim of producing synthetic derivatives based on these products. Inoculation of the low molecule fraction (LM) into the primary tumor of a two-tumor model resulted in the marked

inhibition of the tumor, not only in the right flank, but also in the non-injected left flank. Chromatographic purification and physicochemical characterization showed the main tumoricidal activity to be located in a low molecule fraction-3 (LM-3), containing alpha-1,4-glucan-beta-1,6-glucan complex with an average molecular weight of 20 kDa. A11 LM fractions and crude ATF showed in vitro selective cytotoxicity for MethA tumor cells, having no effect on normal cells. Serum levels of immunosuppressive acidic protein (IAP) in mice receiving LM fractions, particularly LM-3, significantly increased, indicating the possible activation of granulocytes. We speculate that the inhibition of the distant tumor might be due to the increased migration of granulocytes, enhanced by the effect of extract injections at the primary tumor site.

Fukushima S, Takada N, Hori T, Wanibuchi H. **Cancer prevention by organosulfur compounds from garlic and onion.** J Cell Biochem Suppl 1997;27:100-5.
Environmental compounds are known to be involved in both the generation and prevention of many human cancers. It is important to discover naturally occurring or synthetic compounds which can block the process of carcinogenesis. We have focused attention on several organosulfur compounds (OSCs) in garlic and onion, and analyzed their potential for chemoprevention in the post-initiation stage in a liver medium-term bioassay (Ito test) and a multi-organ carcinogenesis bioassay. In the ITO test, rats were given diethylnitrosamine (DEN), 200 mg/kg b.w., i.p.; starting 2 weeks later they were treated with test chemicals for 6 weeks and then killed. All rats were subjected to 2/3 hepatectomy 1 week after the start of test chemical treatment. Inhibitory effects of a number of compounds could be identified in terms of reduced numbers and areas of liver glutathione S-transferase placental (GST-P) positive foci. In the multi-organ carcinogenesis bioassay, rats were given DEN, N-methyl-N-nitrosourea, N-butyl-N-(4-hydroxybutyl)nitrosamine, N,N'-dimethylhydrazine, and dihydroxy-dipropylnitrosamine during the first 4 weeks, followed by test chemicals for 24 weeks. Various organs were examined. As a result, oil-soluble OSCs such as methyl propyl disulfide and propylene sulfide demonstrated inhibitory effects on the development of GST-P positive foci. Moreover, water-soluble OSCs such as S-methylcysteine and cysteine similarly decreased GST-P focus formation. In contrast, OSCs such as diallyl sulfide, diallyl trisulfide, and allyl methyl trisulfide enhanced formation of such altered hepatocellular foci. Inhibitory potential for colon and renal carcinogenesis was observed in rats treated with diallyl disulfide. Thus, the results indicate that some OSCs exert chemopreventive effects on chemical carcinogenesis. It must, however, be borne in mind that they may also demonstrate promotion potential, depending on the organ examined.

Fukutake M, Yokota S, Kawamura H, Iizuka A, Amagaya S, Fukuda K, Komatsu Y. **Inhibitory effect of Coptidis Rhizoma and Scutellariae Radix on azoxymethane-induced aberrant crypt foci formation in rat colon.** Biol Pharm Bull 1998;21(8):814-7.
This study was conducted to obtain effective cancer chemopreventive agents with low toxicity from medicinal herbs. The effect of aqueous extracts from 9 medicinal herbs with antiinflammatory effect were examined on the formation of azoxymethane (AOM)-induced aberrant crypt foci (ACF), putative preneoplastic lesions of the colon. Male F344 rats were treated with 15 mg/kg body weight of AOM once a week for two weeks. Herbal extract consisting of 2% of the diet was administered from 1 d prior to the first carcinogen treatment. The number of AOM-induced ACF per colon was counted at 4 week. Extracts of Coptidis

Rhizoma and Scutellariae Radix significantly inhibited AOM-induced ACF formation. The number of ACF was decreased to 54% and 78% of that of the control by 2% Coptidis Rhizoma and Scutellariae Radix extract in the diet, respectively. Berberine and Baicalin, major ingredients of Coptidis Rhizoma and Scutellariae Radix, inhibited ACF formation at a dose equivalent to the amount in each herbal extract. Therefore, to investigate the mechanisms of action of berberine and baicalein which is the active substances of orally administered baicalin, their effects on cyclooxygenase 1 and 2 activities were studied. Berberine was found to inhibit cyclooxygenase 2 activity without inhibition of cyclooxygenase 1 activity, and baicalein inhibited cyclooxygenase 1 activity. Thus, Coptidis Rhizoma and Scutellariae Radix suppressed experimental colon carcinogenesis, and their chemopreventive effects were explained from the inhibition of berberine on cyclooxygenase 2 activity and baicalein on cyclooxygenase 1 activity.

Fyfe L, Armstrong F, Stewart J. **Inhibition of Listeria monocytogenes and Salmonella enteriditis by combinations of plant oils and derivatives of benzoic acid: the development of synergistic antimicrobial combinations.** Int J Antimicrob Agents 1997;9(3):195-9.
This study describes inhibitory properties of combinations of oil of fennel, oil of anise or oil of basil with either benzoic acid or methyl-paraben against Listeria monocytogenes and Salmonella enteriditis. Micro-organisms were cultured at 37 degrees C in broth and viable counts measured over a 48-h period. S. enteriditis was particularly sensitive to inhibition by a combination of oil of anise, fennel or basil with methyl-paraben where there was < 10 CFU/ml after 1 h. L. monocytogenes was less sensitive to inhibition by each combination however there was a significant reduction in growth of 4-8 log by combinations of all oils and methyl-paraben at 8, 24 and 48 h. Synergistic inhibition by one or more combinations was evident against each micro-organism.

Gehlot D, Bohra A. **Antimicrobial activity of various plant part extracts of Aerva persica.** Adv Plant Sci 1998;11(1):109-11.
BIOSIS COPYRIGHT: BIOL ABS. Extracts of various plant parts of Aerva persica has been tested for their antimicrobial activity against human pathogenic bacterial strains of Staphylococcus aureus and Salmonella typhi and plant pathogenic fungal species Macrophomina phaseolina. Aqueous and alcoholic extracts were tested against all the micro organisms. All the plant parts showed antibacterial and/or antifungal activity.

Geliebter J, Tiwari R, Wu JM. **PC-SPES in prostate cancer [letter].** N Engl J Med 1999;340(7):567-8.

Gharzouli K, Khennouf S, Amira S, Gharzouli A. **Effects of aqueous extracts from Quercus ilex L. root bark, Punica granatum L. fruit peel and Artemisia herba-alba Asso leaves on ethanol-induced gastric damage in rats.** Phytother Res 1999;13(1):42-5.
The gastroprotective effect of tannic acid and the aqueous extract of Quercus ilex L. root bark, Punica granatum L. fruit peel and Artemisia herba-alba Asso leaves was investigated in the rat against ethanol-induced damage. Tannic acid, Q. ilex and P. granatum extracts gave 100% precipitation of ovine haemoglobin in vitro, whereas A. herba-alba extract was devoid of any protein-binding property. Oral administration of these plant extracts or tannic acid induced a significant decrease in gastric lesions (47.7%-76%). The observed protection was more

pronounced when the test solution was given at the same time with ethanol, except for Q. ilex extract. The acid content of the stomach was significantly increased by P. granatum (368%) and A. herba-alba (251%) extracts prepared in ethanol. It is suggested that monomeric and polymeric polyphenols can strengthen the gastric mucosal barrier.

Goepel M, Hecker U, Krege S, Rubben H, Michel MC. **Saw palmetto extracts potently and noncompetitively inhibit human alpha1-adrenoceptors in vitro.** Prostate 1999;38(3):208-15.
BACKGROUND: We wanted to test whether phytotherapeutic agents used in the treatment of lower urinary tract symptoms have alpha1-adrenoceptor antagonistic properties in vitro. METHODS: Preparations of beta-sitosterol and extracts of stinging nettle, medicinal pumpkin, and saw palmetto were obtained from several pharmaceutical companies. They were tested for their ability to inhibit [3H]tamsulosin binding to human prostatic alpha1-adrenoceptors and [3H]prazosin binding to cloned human alpha1A- and alpha1B-adrenoceptors. Inhibition of phenylephrine-stimulated [3H]inositol phosphate formation by cloned receptors was also investigated. RESULTS: Up to the highest concentration which could be tested, preparations of beta-sitosterol, stinging nettle, and medicinal pumpkin were without consistent inhibitory effect in all assays. In contrast, all tested saw palmetto extracts inhibited radioligand binding to human alpha1-adrenoceptors and agonist-induced [3H]inositol phosphate formation. Saturation binding experiments in the presence of a single saw palmetto extract concentration indicated a noncompetitive antagonism. The relationship between active concentrations in vitro and recommended therapeutic doses for the saw palmetto extracts was slightly lower than that for several chemically defined alpha1-adrenoceptor antagonists. CONCLUSIONS: Saw palmetto extracts have alpha1-adrenoceptor-inhibitory properties. If bioavailability and other pharmacokinetic properties of these ingredients are similar to those of the chemically defined alpha1-adrenoceptor antagonists, alpha1-adrenoceptor antagonism might be involved in the therapeutic effects of these extracts in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction.

Gossel TA, Wuest JR. **Patient counseling: benign prostatic hyperplasia.** Part 2. Medical management. Ohio Pharm 1998 Apr;47:7-10, 23.
IPA COPYRIGHT: ASHP The causes and etiology of benign prostatic hyperplasia are identified, and patient information on treatment with terazosin hydrochloride (Hytrin), doxazosin mesylate (Cardura), tamsulosin hydrochloride (Flomax), prazosin hydrochloride (Minipress), hormones, anti-androgens, flutamide (Eulexin), finasteride (Proscar), and Serenoa repens (saw palmetto) is presented. This article qualifies for 1.5 hours U.S. CE credit by the ACPE.

Gould MN. **Cancer chemoprevention and therapy by monoterpenes.** Environ Health Perspect 1997;105(Suppl 4):977-9.
Monoterpenes are found in the essential oils of many plants including fruits, vegetables, and herbs. They prevent the carcinogenesis process at both the initiation and promotion/progression stages. In addition, monoterpenes are effective in treating early and advanced cancers. Monoterpenes such as limonene and perillyl alcohol have been shown to prevent mammary, liver, lung, and'other cancers. These compounds have also been used to treat a variety of rodent cancers, including breast and pancreatic carcinomas. In addition, in vitro data suggest that they may be effective in treating neuroblastomas and leukemias. Both limonene and perillyl alcohol

are currently being evaluated in phase I clinical trials in advanced cancer patients. The monoterpenes have several cellular and molecular activities that could potentially underlie their positive therapeutic index. The monoterpenes inhibit the isoprenylation of small G proteins. Such inhibitions could alter signal transduction and result in altered gene expression. The results of a new gene expression screen-subtractive display-have identified or confirmed several up- or downregulated genes in regressing mammary carcinomas. For example, these regressing tumors overexpress the mannose 6-phosphate/IGF II receptor. The product of the gene both degrades the mammary tumor mitogen IGF II and activates the cytostatic factor TGF-beta. These and other alterations in the gene expression of mammary carcinomas lead to a G1 cell cycle block, followed by apoptosis, redifferentiation, and finally complete tumor regression in which tumor parenchyma is replaced by stromal elements. It is likely that monoterpenes prevent mammary cancer during their progression stage by mechanisms similar to those that occur during therapy. In contrast, prevention of mammary cancer by polycyclic hydrocarbons such as 7,12-dimethylbenz[a]anthracene occur by the induction of detoxifying phase II hepatic enzymes.

Grauds C. **St. John's Wort for depression.** Pharm Times 1997 Oct;63:40.
IPA COPYRIGHT: ASHP The history of the use of St. John's Wort (Hypericum perforatum) for depression and wound healing is briefly presented.

Grimm W, Muller HH. **A randomized controlled trial of the effect of fluid extract of Echinacea purpurea on the incidence and severity of colds and respiratory infections [see comments].** Am J Med 1999;106(2):138-43.
PURPOSE: Fluid extracts of Echinacea purpurea are widely used for the prevention and treatment of colds and respiratory infections, although the clinical efficacy of this agent has not been proven. PATIENTS AND METHODS: A total of 109 patients with a history of more than 3 colds or respiratory infections in the preceding year were randomly assigned to receive 4 mL fluid extract of Echinacea purpurea or 4 mL placebo-juice twice a day in a double-blind manner. (One patient withdrew his consent before taking the first dose of the allocated medication; thus, only 108 patients were included for analysis.) The incidence and severity of colds and respiratory infections were determined during 8 weeks of follow-up, based on patient reported symptoms together with findings on physical exam. The severity of each infection was graded by the investigators. Relative risks (RR) and 95% confidence intervals (CI) were estimated. RESULTS: During the 8-week treatment period, 35 (65%) of 54 patients in the Echinacea group and 40 (74%) of 54 patients in the placebo group had at least one cold or respiratory infection [RR = 0.88; 95% CI (0.60, 1.22)]. The average number of colds and respiratory infections per patient was 0.78 in the Echinacea group, and 0.93 in the placebo group [difference = 0.15; 95% CI (-0.12, 0.41), P = 0.33]. Median duration of colds and respiratory infections was 4.5 days in the Echinacea group and 6.5 days in the placebo group (95% CI: -1, +3 days; P = 0.45). There were no significant differences between treatment groups in the number of infections in each category of severity. Side effects were observed in 11 patients (20%) of the Echinacea group and in seven patients (13%) of the placebo group (P = 0.44). CONCLUSION: Treatment with fluid extract of Echinacea purpurea did not significantly decrease the incidence, duration or severity of colds and respiratory infections compared to placebo.

Guerra M, Rodriguez M, Ramos I, Galvez MA, Garcia MI, et al . **[Antimicrobial activity of creams elaborated from Cuban medicinal plants].** Rev Mex Cien Farm 1997 Jul-Aug;28:28-31. (Spa)
IPA COPYRIGHT: ASHP The in vitro antimicrobial activity of 5 cream formulations elaborated from medicinal plants grown in Cuba and of 3 active ingredients employed for the formulation of these creams is reported. Aloe vera and Matricaria recutita showed a low antimicrobial activity, while Senna alata and Cymbopogom citratus showed remarkable antifungal activity. It was concluded that these results corroborated the pharmacological effects proposed for these creams and justified the traditional use of these medicinal plants in Cuba.

Guirguis WR. **Oral treatment of erectile dysfunction: from herbal remedies to designer drugs.** J Sex Marital Ther 1998;24(2):69-73.
The erect penis has always been a symbol of power, virility, and fertility. Inability to obtain or maintain an erection, known clinically as erectile dysfunction, is a major health problem. It can cause considerable distress, unhappiness, and relationship problems. The search has therefore continued from time immemorial to find an effective safe, and easy to administer treatment for erectile problems. Although a number of these treatments became available in the last two decades, they all had problems with efficacy, safety, or ease of administration. Clinicians in this field often are told at the end of an assessment interview, "I wish you have a magic pill". An effective and safe oral treatment is, no doubt, the most acceptable and easy to use option. Finding such a treatment has always been the dream of many scientists, and many attempts have been made over the years. These ranged from herbal remedies used by native healers, mostly in Eastern countries, to the more sophisticated designer drugs, which are based on a better understanding of the physiological mechanism of erection. This article describes some of these attempts.

Gunning K, Steele P. **Echinacea for the prevention of upper respiratory tract infections.** J Fam Pract 1999;48(2):93.

Habtemariam S. **Cistifolin, an integrin-dependent cell adhesion blocker from the anti-rheumatic herbal drug, gravel root (rhizome of Eupatorium purpureum).** Planta Med 1998;64(8):683-5.
During routine screening of medicinal plants for small molecular weight inhibitors of cell adhesion, the crude ethanolic extract of the anti-rheumatic herbal drug gravel root (rhizome of Eupatorium purpureum), was identified as a potent inhibitor of some beta 1 and beta 2 integrin-mediated cell adhesions. The active principle of gravel root has now been isolated and identified as 5-acetyl-6-hydroxy-2,3-dihydro-cis-2-isopropenyl-3- tiglinoyloxybenzofuran (1). Compound 1 inhibited integrin-dependent cell-cell and cell-protein interactions in vitro with EC50 values between 7-20 micrograms/ml. As with indomethacin, 1 administered orally two hours before induction of inflammation (in rat paw) by carrageenan inhibited oedema formation in a dose (10 and 50 mg/kg)-dependent manner. It appears that 1 has therapeutic potential for diseases where integrin adhesion molecules play a significant role.

Habtemariam S. **Extract of corn silk (stigma of Zea mays) inhibits the tumour necrosis factor-alpha- and bacterial lipopolysaccharide-induced cell adhesion and ICAM-1**

expression. Planta Med 1998;64(4):314-8.
Treatment of human endothelial cells with cytokines such as tumour necrosis factor-alpha (TNF) or E. coli lipopolysaccharide (LPS) induces the expression of several adhesion molecules and enhances leukocyte adhesion to endothelial cell surface. Interfering with this leukocyte adhesion or adhesion molecules upregulation is an important therapeutic target for the treatment of bacterial sepsis and various inflammatory diseases. In the course of screening marketed European anti-inflammatory herbal drugs for TNF antagonistic activity, a crude ethanolic extract of corn silk (stigma of Zea mays) exhibited significant activity. The extract at concentrations of 9-250 micrograms/ml effectively inhibited the TNF- and LPS-induced adhesiveness of EAhy 926 endothelial cells to monocytic U937 cells. Similar concentration ranges of corn silk extract did also block the TNF and LPS but not the phorbol 12-myristate 13-acetate-induced ICAM-1 expression on EAhy 926 endothelial cell surface. The extract did not alter the production of TNF by LPS-activated macrophages and failed to inhibit the cytotoxic activity of TNF. It is concluded that corn silk possesses important therapeutic potential for TNF- and LPS-mediated leukocyte adhesion and trafficking.

Hachida M, Zhang XL, Lu H, Hoshi H, Koyanagi H. **Inhibitory effect of Multiglycosidorum tripterygii on coronary arteriosclerosis after heart transplantation.** Transplantation 1998;65(11):1446-50.
BACKGROUND: Graft coronary arteriosclerosis (GCA) is the major limiting factor for long-term survival after heart transplantation. In this study, we investigated the effect of Multiglycosidorum tripterygii (MT) on GCA and platelet-derived growth factor A (PDGF-A) mRNA expression of transplanted hearts. METHODS: Two groups of Lewis rats (n=7/group) underwent heterotopic heart transplantation from Wistar-King donors and were treated with either cyclosporine (CsA;10 mg/kg/day) or MT (30 mg/kg/ day). Histological evaluations of rejection and coronary arteriosclerosis, as well as Northern blot analysis on graft PDGF-A mRNA expression were made 60 days after transplantation. RESULTS: Morphometric results indicated no significant difference in rejection between the CsA- and MT-treated groups. However, the extent of GCA in the MT-treated group was significantly less than that seen in the CsA-treated group (P

Hageman GJ, Van Herwijnen MH, Schilderman PA, Rhijnsburger EH, Moonen EJ, Kleinjans JC. **Reducing effects of garlic constituents on DNA adduct formation in human lymphocytes in vitro.** Nutr Cancer 19997;27(2):177-85.
A water extract of raw garlic (RGE) and two organosulfur compounds, diallyl sulfide and S-allylcysteine (SAC), were evaluated for their relative effectiveness in reducing benzo[a]pyrene (BaP)-DNA adduct formation in stimulated human peripheral blood lymphocytes in vitro. In replicate experiments, RGE significantly inhibited BaP-DNA adduct formation at concentrations of 0.001, 0.01, and 0.1 mg/ml. SAC also significantly decreased BaP-DNA adduct formation at concentrations of 0.01 and 0.1 mg/ml. For diallyl sulfide, no significant reduction in BaP-DNA adduct formation was found. BaP-DNA adduct formation was not associated with cell viability or proliferation of peripheral blood lymphocytes after the various treatments. No clear scavenging activity was detected for the garlic constituents. Aryl hydrocarbon hydroxylase activity was not decreased, nor was formation of sulfate and glucuronide conjugates of 3-hydroxy-BaP increased in the presence of RGE and SAC, indicating that increased glutathione S-

transferase activity or a more efficient repair of BaP-DNA adducts may explain the observed effects. In addition, reactive oxygen species-induced 8-oxodeoxyguanosine in DNA was reduced in the presence of SAC. It is concluded that raw garlic and SAC may be useful in the prevention of BaP-associated tumorigenesis and that further evaluation of their preventive potential in humans at risk appears feasible.

Hageman G, Krul C, Van Herwijnen M, Schilderman P, Kleinjans J. **Assessment of the anticarcinogenic potential of raw garlic in humans.** Cancer Lett 1997;114(1-2):161-2.

Hahm KB, Kim JH, You BM, Kim YS, Cho SW, Yim H, Ahn BO, Kim WB. **Induction of apoptosis with an extract of Artemisia asiatica attenuates the severity of cerulein-induced pancreatitis in rats.** Pancreas 1998;17(2):153-7.
The aim of this study was to test the hypothesis that apoptosis can protect against experimental pancreatitis and induction of apoptosis by an extract of Artemisia asiatica (DA-9601) is beneficial in cerulein-induced pancreatis in rats. Pancreatitis was induced in 6-week-old male SPF Sprague-Dawley rats by two intravenous (i.v.) administrations of 40 microg/kg cerulein. To investigate the effects of DA-9601 on the severity of pancreatitis and extent of apoptosis, rats were treated with intragastric DA-9601, 30 mg/kg (D30), 100 mg/kg (D100), or 300 mg/kg (D300), intraperitoneal superoxide dismutase, 10,000 U/kg (SOD), and i.v. gabexate mesilate, 40 mg/kg (Foy), three times (30 min before cerulein injection, 30 and 90 min after cerulein injection). The control group was administered vehicle alone. Ten rats were included in each treatment group and control group. Rats were sacrificed 5 h after cerulein treatment. Serum amylase, histological activity index (HAI), pancreatic lipid peroxide levels, and apoptotic index [in situ hybridization by terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end-labeling (TUNEL)] were determined. Gel electrophoresis was performed for the presence of DNA fragmentations. The results were as follows. Serum amylase was significantly increased in all cerulein-treated groups compared to normal controls ($p < 0.001$). The HAI was significantly decreased in only the D300 group compared to the controls ($p < 0.05$). The apoptotic index of the cerulein-alone group was 3.8 +/- 2.7, but the mean apoptotic indexes of the SOD and Foy groups were 16.4 +/- 4.6 and 13.3 +/- 1.8, respectively, a significant increase ($p < 0.01$). The apoptotic index was more significantly increased in the DA-9601-treated groups, dose dependently (8.4 +/- 3.4 in D30, 14.8 +/- 4.3 in D100, 24.2 +/- 4.7 in D300). A smearing pattern of DNA electrophoresis was noted in the DA-9601-treated groups. In conclusion, DA-9601, an extract of Artemisia, induced apoptosis of pancreatic acinar cells dose dependently and concomitantly attenuated the severity of pancreatitis.

Hammerschmidt DE. **Xanthium strumarium.** J Lab Clin Med 1998;132(1):86.

Hase K, Kasimu R, Basnet P, Kadota S, Namba T. **Preventive effect of lithospermate B from Salvia miltiorhiza on experimental hepatitis induced by carbon tetrachloride or D-galactosamine/lipopolysaccharide.** Planta Med 1998;63(1):22-6.
The water extract from the root of Salvia miltiorhiza Bunge showed a protective effect on cultured rat hepatocytes against carbon tetrachloride (CCl4)-induced necrosis. A further study was carried out to isolate the active constituent. Activity guided fractionation of the extract and chemical analysis gave us lithospermate B (a salt of lithospermic acid B), a tetramer of caffeic

acid. Lithospermate B was also found to have a potent hepatoprotective activity in not only in vitro but also in vivo experimental liver injuries induced by CCl4 or D-galactosamine (D-GalN)/lipopolysaccharide (LPS).

Hase K, Ohsugi M, Xiong Q, Basnet P, Kadota S, Namba T. **Hepatoprotective effect of Hovenia dulcis THUNB. on experimental liver injuries induced by carbon tetrachloride or D-galactosamine/lipopolysaccharide.** Biol Pharm Bull 1997;20(4):381-5.
The hepatoprotective effects of the fruits of Hovenia dulcis THUNB. on chemically or immunologically induced experimental liver injury models were examined. The methanol extract showed significant hepatoprotective activity against CCl4-toxicity in rats and D-galactosamine (D-GalN)/lipopolysaccharide-induced liver injury in mice. The methanol extract also significantly protected against CCl4-toxicity in primary cultured rat hepatocytes. Hepatoprotective activity-guided fractionation and chemical analysis led to the isolation of an active constituent, (+)-ampelopsin (1) from the methanol extract.

Hasegawa H, Sunge JH, Huh JD. **Ginseng intestinal bacterial metabolite IH901 as a new anti-metastatic agent.** Arch Pharmacal Res 1997;20(6):539-44.

Hattaway V. **Overeating.** N Z Pharm 1997 Dec;17:13-4, 16, 18.
IPA COPYRIGHT: ASHP The acute and chronic effects of eating more than necessary, including indigestion and obesity, are presented and treatment using antacids, appetite suppressants, herbal teas, and surgery are discussed.

He LZ, Huang ZH, Wang HR, Tu DY, Mao ZF. **Shenjincao (Palhinhaea cernua) injection for treatment of experimental silicosis of rats.** J Pharm Pharmacol 1998;50(3):351-4.
Shenjincao injection is a traditional Chinese medicine prepared from Palhinhaea cernua (L.) A. Franco et Vasc. by ultrafiltration. Its anti-silicosis action has been investigated both as a prophylactic and for treatment of the disease. Wistar rats were injected intra-tracheally with quartz dust and then divided randomly into groups-treatment and control prophylactic groups and treatment and control disease groups. After five days or eight weeks, respectively, the silica-exposed rats of the two treatment groups were injected intraperitoneally three times a week with shenjincao injection, dose 2.0 mL, for five weeks or 11 weeks, respectively. The rats were then dissected, and the ceruloplasmin content of the serum and the fresh weight, dry weight, collagen content and pathological grade of the lungs were measured. Compared with the corresponding exposed control groups for the same treatment periods the values of these parameters were reduced by 62.8% to 30.7% for rats in the prophylactic treatment group ($P < 0.01$ for all) and by 50.8% to 30.2% for the diseased group ($P < 0.01$ for all). The values for the disease-treatment group were also reduced by 37.9% to 25.9% compared with values for the exposed control group before treatment ($P < 0.01$ or $P < 0.05$). The effective coefficients for prophylactic treatment were 82.6% to 56.0%; for disease treatment they were 68.8% to 39.8%. These results show that shenjincao injection is efficacious against experimental silicosis not only when used prophylactically but also when used to treat the disease.

Higuchi Y, Ono K, Sekita S, Onodera H, Mitsumori K, Nara Y, Satake M. **Preventive effects of Shichimotsu-koka-to on renal lesions in stroke-prone spontaneously hypertensive rats.** Biol

Pharm Bull 1998;21(9):914-8.
Shichimotsu-koka-to (SKT) has been prescribed to treat patients with essential and renal hypertension. We investigated the effects of SKT on renal lesions in stroke-prone spontaneously hypertensive rats (SHRSPs). SHRSPs were given an extract of SKT by mixing it with drinking water, from 8 through 29 weeks of age, so that the average intake of SKT extract was about 1.5 g/kg/d. At 29 weeks of age, the kidneys of SHRSPs exhibited proliferative arteritis characterized by the proliferation of smooth muscle cells in the interlobular arteries, dilation and degeneration of renal tubules, infiltration of inflammatory cells and hemorrhage, with partial swelling or necrotizing of glomeruli. In particular, arteritis and periarteritis were noted. The treatment of SHRSPs with SKT ameliorated this morphological damage in the kidney and significantly decreased urea nitrogen in the serum. Treatment with SKT also strongly decreased the xanthine oxidase (XOD) activity and significantly increased the superoxide dismutase (SOD) activity in the kidney of SHRSPs; consequently, these values became close to those in normotensive Wistar Kyoto rats (WKYs). These results indicate that treatment with SKT ameliorated the histopathological damage and change in activity of enzymes related to free radicals in the kidney of SHRSPs, which may be important mechanisms for SKT for protecting SHRSPs from renal dysfunction.

Ho LJ, Chang DM, Chang ML, Kuo SY, Lai JH. **Mechanism of immunosuppression of the antirheumatic herb TWHf in human T cells.** J Rheumatol 1999;26(1):14-24.
OBJECTIVE: To investigate the immunosuppressive mechanism of Tripterygium wilfordii Hook-F (TWHf) in human T cells. TWHf, a traditional Chinese medicinal herb for rheumatoid arthritis, has been shown to inhibit the function of immune effector cells such as neutrophils, macrophages, and B lymphocytes. METHODS: T cell survival was evaluated with trypan blue exclusion assay, morphologic changes with Wright's stain, the induction of endonuclease activity with DNA fragmentation assay, and the subdiploid DNA content with flow cytometry. T cell activation was measured with interleukin 2 (IL-2) ELISA and the expression of several surface molecules with flow cytometry. RESULTS: At high dosages, TWHf caused inhibition of T cell proliferation and this mechanism was mediated through the induction of apoptosis. TWHf, in noncytotoxic dosages, was as potent as cyclosporin A and more potent than prednisolone and cyclophosphamide in inhibiting IL-2 production from activated T cells. TWHf also inhibited both phorbol 12-myristate 13-acetate induced IL-2Ralpha expression and ionomycin induced CD40 ligand expression. TWHf did not reverse downregulated expression of CD3 and CD4 by phorbol ester stimulation. CONCLUSION: This is the first evidence that the immunosuppressive mechanism of TWHf in T cells was mediated through both downregulation of T cell receptor signaling pathway and induction of cellular apoptosis, which is defective in autoimmune diseases.

Hu G, Wang X. **Research on a natural sunscreen from Chinese herbs.** Int J Cosmet Sci 1998;20(3):175-81.
IPA COPYRIGHT: ASHP The sun protection factor (SPF) values of a synthetic sunscreen agent, sulisobenzone (2-hydroxy-4-methoxybenzophenone-5-sulfonic acid; MS-40), and a Chinese herbal sunscreen preparation, which is a mixture of alcoholic extracts of Chrysanthemum ramat and Crocus sativus, were compared by conducting UV absorption measurements and optical SPF tests in vitro and by determining the SPF values of cream formulations containing 5%

sulisobenzone or 20% of the mixture of C. ramat and C. sativus. The mixture of C. ramat and C. sativus showed lower UV absorption than sulisobenzone in vitro, but both preparations exhibited the same SPF value in human volunteers.

Huang RL, Chen CC, Huang YL, Ou JC, Hu CP, Chen CF, Chang C. **Anti-tumor effects of d-dicentrine from the root of Lindera megaphylla.** Planta Med 1998;64(3):212-5.
d-Dicentrine, a naturally occurring aporphine type isoquinoline alkaloid, isolated from the root of Lindera megaphylla Hemsl. (Lauraceae), was evaluated for its potential anti-cancer activity. We found d-dicentrine significantly inhibited the growth of human hepatoma cell line HuH-7 by delaying its doubling time in tissue culture. An in vitro colony forming assay showed that d-dicentrine decreased the colony formation efficiency in both hepatoma cell lines, HuH-7 and MS-G2, used in our study. Biosyntheses of the macromolecules DNA and RNA were also strongly inhibited. An MTT assay in 21 tumor cell lines also revealed that d-dicentrine was most cytotoxic to esophageal carcinoma HCE-6, lymphoma cell lines Molt-4 and CESS, leukemia cell lines HL60 and K562, and hepatoma cell line MS-G2. An in vitro tumor growing assay in the Severe Combined immunodeficiency (SCID) mice showed that intraperitoneal injection of d-dicentrine at the dose of 100 micrograms twice a week for 4 weeks significantly inhibited the tumor incidence of leukemia cell line K562 in SCID mice. All these data indicated that d-dicentrine has potential anti-tumor applications.

Huang SP, Shieh GJ, Lee L, Teng HJ, Kao ST, Lin JG. **Inhibition effect of shengma-gegen-tang on measles virus in Vero cells and human peripheral blood mononuclear cells.** Am J Chin Med 19997;25(1):89-96.
Shengma-Gegen-Tang has long been used against measles virus in human peripheral blood mononuclear cells (PBMC) as well as in Vero cells. One hundred micrograms/ml Shengma-Gegen-Tang in PBMC displays significant anti-measles activity, whereas the same concentration in Vero cells does not. After eight days of infection, the release of virus is significantly suppressed by Shengma-Gegen-Tang in the case of PBMC. In addition, Shengma-Gegen-Tang has a selective stimulation to the secretion of cytokine TNF-alpha in PBMC. Time kinetic analysis indicated that the stimulation of secretion was rapid and could be detected only 2 hrs following the treatment of the PBMC. It rose to an optimal level in 8-12 hrs. These findings suggest that the magnification of anti-measles virus activity of this agent is lymphocyte dependent and may well be mediated by TNF-alpha.

Huang Y, Marumo K, Murai M. **Antitumor effects and pharmacological interaction of xiao-chai-hu-tang (sho-saiko-to) and interleukin 2 in murine renal cell carcinoma.** Keio J Med 1997;46(3):132-7.
Conventional therapy for renal cell carcinoma using interleukin 2 (IL-2) has shown limited antitumor action. The purpose of our study was to investigate synergistic antitumor effects of IL-2 and Xiao-Chai-Hu-Tang (XCHT), and to elucidate the mechanisms of interaction between the two drugs against the murine renal cell carcinoma cell line, Renca, in vivo. The treatment was started 5 days after subcutaneous transplantation of Renca tumor. XCHT was given at a dose of 2.5 g/kg daily for 30 days orally. IL-2 was given at a dose of 10(4) U/mouse by subcutaneous injection every other day 8 times. Combination of XCHT and IL-2 inhibited growth of the tumor and prolonged survival significantly as compared with the untreated mice. Increased cellular

infiltration was observed in tumor tissue and the lungs of mice treated with XCHT alone and by combination of XCHT and IL-2, but there were no histological changes in the liver and kidney. Elevation of serum IL-6 was observed in tumor-bearing mice, but IL-6 was significantly suppressed by administration of XCHT. The results obtained suggest that combination of XCHT and IL-2 induces enhanced immunological reaction in specific organs and tissues, and IL-6 may have a role in the synergistic effect of these two agents. It was concluded that combination of XCHT and IL-2 is useful in the treatment of patients with renal cell carcinoma.

Ikken Y, Cambero I, Marin ML, Martinez A, Haza AI, Morales P. **Antimutagenic effect of fruit and vegetable aqueous extracts against N-nitrosamines evaluated by the Ames test.** J Agric Food Chem 1998;46(12):5194-200.
BIOSIS COPYRIGHT: BIOL ABS. The inhibitory effect of nine fruit and vegetable aqueous extracts against the mutagenicity of N-nitrosodimethylamine (NDMA), N-nitrosopyrrolidine (NPYR), N-nitrosodibutylamine (NDBA), and N-nitrosopiperidine (NPIP) was evaluated by means of the Ames test. Onion extract (500 mug/plate) showed the greatest inhibitory effect (60%) against NDMA, and the mutagenicity of NPYR was inhibited markedly (54%) by apple extract (50 mug/plate). The antimutagenic effect of carrot extract (250 mug/plate) was remarkable (49%) against NDBA, and the mutagenicity of NPIP was also strongly inhibited (65 and 50%) by garlic and kiwi extracts (2000 mug/plate), respectively. Vegetable and fruit extracts that exhibited an antimutagenic effect in decreasing order against NDMA and NPYR were as follows: onion > licorice > kiwi = apple > carrot > garlic > -pineapple > broccoli; and apple > broccoli > kiwi > onion = pineapple, respectively. Decreasing orders against NDBA and NPIP were, respectively, carrot > garlic > broccoli > onion > kiwi and garlic > kiwi > broccoli > green pepper > pineapple > carrot > onion = apple.

Israel D, Youngkin EQ. **Herbal therapies for perimenopausal and menopausal complaints.** Pharmacotherapy 1997;17(5):970-84.
IPA COPYRIGHT: ASHP Selected herbal therapies touted in the lay press for common perimenopausal and menopausal complaints are examined, with advice on their use and safety based on scientific sources; general concepts related to herbal therapies, common perimenopausal and menopausal complaints, and various herbal therapies that include Agrimonia eupatoria, Angelica archangelica, Melissa officinalis, Cimicifuga racemosa, Nepeta cataria, Matricaria recutita, Chamaemelum nobile, Vitex agnus-castus, Turnera aphrodisiaca, Taraxacum officinale, A. sinensis, Trigonella foenum-graecum, Ginkgo biloba, Panax ginseng, P. quinquefolius, Centella asiatica, Humulus lupulus, Glycyrrhiza glabra, Senecio aureus, Passiflora incarnata, Salvia officinalis, Smilax species, Scutellaria lateriflora, Hypericum perforatum, valerian, and Hamamelis virginiana are discussed.

Jagetia GC, Aruna R. **The herbal preparation abana protects against radiation-induced micronuclei in mouse bone marrow.** Mutat Res 1997;393(1-2):157-63.
The induction of micronuclei was studied in mouse bone marrow treated or not with 5, 10 and 20 mg/kg b.wt. of abana (a herbal preparation) before exposure to 0-3 Gy of gamma-radiation. Whole-body irradiation of mice resulted in a dose-dependent increase in the frequency of micronuclei. Treatment of mice with various doses of abana before exposure to different doses of gamma-rays resulted in a significant reduction of the micronucleus frequency at all exposure

doses. The highest decline in the frequencies of micronuclei was observed after administration of 20 mg/kg abana, where the frequency of micronuclei was approximately 4-fold less than that of the concurrent control. The PCE/NCE ratio was significantly higher in the drug-treated group compared to DDW + irradiated control and it was almost restored to normal level after administration of 20 mg/kg abana. Our results demonstrate that abana protects mice against radiation-induced micronucleus formation and radiation-induced decline in cell proliferation.

Jeong HG, Park HY. **The prevention of carbon tetrachloride-induced hepatotoxicity in mice by alpha-hederin: inhibiton of cytochrome P450 2E1 expression.** Biochem Mol Biol Int 1998;45(1):163-70.
The protective effects of alpha-Hederin on carbon tetrachloride-induced hepatotoxicities were investigated in mice. Pretreatment with alpha-Hederin prior to the administration of carbon tetrachloride significantly prevented the increase in serum alanine aminotransferase (ALT) and lactate dehydrogenase (LDH) activity and lipid peroxidation in a dose dependent manner. Hepatic glutathione levels and glutathione-S-transferase activities were not affected by pretreatment with alpha-Hederin alone but pretreatment with alpha-Hederin protects carbon tetrachloride-induced depletion of hepatic glutathione levels. The effects of alpha-Hederin on the cytochrome P450 (P450) 2E1, the major isozyme involved in carbon tetrachloride bioactivation were investigated. alpha-Hederin markedly decreased the P450 2E1-specific activities of p-nitrophenol and aniline hydroxylation in a dose-dependent manner. Consistent with these observations, the P450 2E1 expressions were also decreased, as determined by immunoblot analysis. These results demonstrate that treatment of mice with alpha-Hederin decreases the expression and activities of P450 2E1 enzyme, and reduces biotransformation of carbon tetrachloride, and diminished carbon tetrachloride-induced liver injury.

Jeong TC, Kim HJ, Park JI, Ha CS, Park JD, Kim SI, Roh JK. **Protective effects of red ginseng saponins against carbon tetrachloride-induced hepatotoxicity in Sprague Dawley rats.** Planta Med 1997;63(2):136-40.
The protective effects of red ginseng saponins against carbon tetrachloride-induced hepatotoxicity were investigated in male Sprague Dawley rats. The total saponins of red ginseng standardized on ginsenosides-Rb1, -Rb2, -Rc, -Rd, -Re, and -Rg1 were used in the present study. The rats were administered the standardized saponins of red ginseng orally at 50, 100, and 200 mg/kg for 7 consecutive days, followed by an administration of carbon tetrachloride at 0.4 ml/kg in corn oil intraperitoneally for 24 h. The administration of saponin changed neither body and organ weights nor hematological and serum clinical parameters. The elevation of SGPT and SGOT activities induced by carbon tetrachloride was partially recovered by the administration of the saponin. The liver vacuolization and lymphoid cell aggregation by carbon tetrachloride were clearly recovered by the red ginseng saponins as examined histologically. The present results indicated that the standardized saponins of red ginseng used in these studies may partially recover the hepatotoxicity induced by carbon tetrachloride in male Sprague Dawley rats.

Jones SM, Zhong Z, Enomoto N, Schemmer P, Thurman RG. **Dietary juniper berry oil minimizes hepatic reperfusion injury in the rat.** Hepatology 1998;28(4):1042-50.
Juniper berry oil is rich in 5,11,14-eicosatrienoic acid, a polyunsaturated fatty acid similar to one found in fish oil, yet less prone to peroxidation. Dietary fish oil treatment has been shown to

effectively reduce reperfusion injury; therefore, the effects of a diet containing juniper berry oil on hepatic reperfusion injury in a low-flow, reflow reperfusion model were investigated in the rat. Rats were fed semisynthetic diets containing either juniper berry oil, fish oil, or corn oil for 14 to 16 days. Daily food consumption averaged around 20 g/d in both the control and treatment groups; average daily weight gain was around 4 g per 100 g rat weight in all three groups studied, and there were no significant differences in these parameters. Livers were initially perfused at low-flow rates to induce pericentral hypoxia followed by a 40-minute reperfusion period. Peak lactate dehydrogenase (LDH) release during reflow averaged 44 U/g/h in the corn oil group and 32 U/g/h in the fish oil group, but was only 21 U/g/h as a result of juniper berry oil treatment. Malondialdehyde (MDA), an end-product of lipid peroxidation, reached a maximum value of 62 nmol/g/h in the corn oil group, but only reached 43 nmol/g/h and 34 nmol/g/h in the fish oil and juniper berry oil groups, respectively. Both juniper berry oil and fish oil treatment improved rates of bile flow from 25 microL/g/h (corn oil) to 36 and 38 microL/g/h, respectively. Importantly, juniper berry oil reduced cell death in pericentral regions of the liver lobule by 75%. Trypan blue distribution time, an indicator of the hepatic microcirculation, was reduced by approximately 25% with fish oil and over 50% by juniper berry oil diets compared with corn oil controls. The rates of entry of fluorescein-dextran, a dye confined to the vascular space, were increased 1.8- and 2.6-fold, and rates of outflow were increased 4.4- and 4.3-fold by fish oil and juniper berry oil, respectively, also reflecting improved microcirculation. Juniper berry oil also blunted increases in intracellular calcium and release of prostaglandin E2 (PGE2) by cultured Kupffer cells stimulated by endotoxin. These results are consistent with the hypothesis that feeding a diet containing juniper berry oil reduces reperfusion injury by inhibiting activation of Kupffer cells, thus reducing vasoactive eicosanoid release and improving the hepatic microcirculation in livers undergoing oxidant stress.

Josey ES, Tackett RL. **St. John's wort: a new alternative for depression?** Int J Clin Pharmacol Ther 1999;37(3):111-9.
OBJECTIVE: The primary purpose of this article is to review the existing literature concerning the therapeutic uses, adverse effects, and possible drug interactions of St. John's wort (Hypericum perforatum) as compared to other antidepressant medications. METHODS: Reference material was obtained through database searches with time restrictions of 1985 to the present. Studies selected were those written in the English language which compared the role of St. John's wort, tricyclic antidepressants, monoamine oxidase inhibitors, and serotonin-selective reuptake inhibitors in the treatment of depression. Other studies were selected based on their evaluation of the safety and efficacy of St. John's wort as an antidepressant for a minimum of four weeks. RESULTS: A review of existing literature recognized nine clinical trials that reported the efficacy of St. John's wort as compared to placebo and to other antidepressant medications. Of these nine, four controlled studies were chosen based upon their large patient populations and their consistency in brand and dosage of St. John's wort used. These four studies demonstrated that St. John's wort was as effective as other antidepressant medications and more effective than placebo, as the clinical symptoms of depression greatly decreased upon administration of H. perforatum. The side-effect profile of H. perforatum at this time appears to be superior to any current U.S.-approved antidepressant medication. CONCLUSIONS: From the existing literature, St. John's wort appears to be a safe and effective alternative in the treatment of depression. Tricylic antidepressants and monoamine oxidase inhibitors can produce serious

cardiac side-effects, such as tachycardia and postural hypotension, and many unwanted anticholinergic side-effects, including dry mouth and constipation. St. John's wort has proven to be free of any cardiac, as well as anticholinergic, side-effects normally seen with antidepressant medications. Based upon limited studies, St. John's wort appears to be an acceptable alternative to traditional antidepressant therapy, although trials on a larger scale are warranted in this area. Hypericum is available to the lay public as an over-the-counter preparation and may be misused if not fully understood.

Jutte SB, Kier K. **Feverfew in migraine prevention.** Ohio Pharm 1998 Apr;47:16-7.
IPA COPYRIGHT: ASHP A brief overview of the use of Tanacetum parthenium (feverfew) for migraines is presented including mechanism of action and clinical studies.

Kaido TL, Veale DJ, Havlik I, Rama DB. **Preliminary screening of plants used in South Africa as traditional herbal remedies during pregnancy and labor.** J Ethnopharmacol 1997;55(3):185-91.
IPA COPYRIGHT: ASHP Crude decoctions of 3 plants indigenous to South Africa, Agapanthus africanus (leaves), Pentanisia prunelloides (roots), and Gunnera perpensa (roots), which are used as traditional herbal remedies during pregnancy and labor, were prepared, and the pharmacologic activity of each decoction in the isolated uterus and ileum of Sprague-Dawley rats and effect of pretreatment with each decoction on the response of the uterus to oxytocin (Syntocinon) and the ileum to acetylcholine hydrochloride were studied. A. africanus and P. prunelloides exhibited direct smooth muscle activity in the uterus and ileum, while G. perpensa exhibited such activity only in the uterus. All plant extracts potentiated the initial response of the uterus to oxytocin, but P. prunelloides reduced the maximum response of the uterus to oxytocin. A. africanus and P. prunelloides potentiated the initial response of the ileum to acetylcholine, but all plant decoctions inhibited the maximum response of the ileum to acetylcholine.

Kamei T, Kumano H, Beppu K, Iwata K, Masumura S. **Response of healthy individuals to ninjin-yoei-to extract--enhancement of natural killer cell activity.** Am J Chin Med 1998;26(1):91-5.
After administering 15 g/day of Ninjin-Yoei-To (NYT) for one week to healthy people whose NK activity had already been increased by physiological response, a further increase in NK activity was observed after two days. This increased level of NK activity continued during the administration of NYT for a one-week period. The maintaining and reinforcing effect on the immune surveillance system by NYT may be useful for prevention of carcinogenesis.

Kanai S, Okano H, Abe H. **Efficacy of toki-shigyakuka-gosyuyu-syokyo-to (danggui-sini-jia-wuzhuyu-shengjiang-tang) on peripheral circulation in autonomic disorders.** Am J Chin Med 1997;25(1):69-78.
To investigate the improvement in peripheral circulation in autonomic disorders, we monitored skin temperature in the tails of rats by thermography before and after the oral administration of boiled water extract of Toki-shigyakuka-gosyuyu-syokyo-to (TSGS-to). Oral administration of this extract elevated the temperature, calculated as the calories of radiant heat in the rat tail 5-10 min after uptake. The temperature elevation remained stable for more than 20 min. Calories were significantly reduced 60 min after uptake and almost returned to initial values 90 min later. Some

of the constituent herbs, especially Angelicae radix, Cinnamomi cortex, Evodiae fructus, and Zingiberis rhizoma, appeared to be active in relieving hypothermia.

Kanba S, Yamada K, Mizushima H, Asai M. **Use of herbal medicine for treating psychiatric disorders in Japan.** Psychiatry Clin Neurosci 1998;52(Suppl):331-3.
Alongside the Western pharmacotherapy that is now the major medical modality in Japan, we continue to offer a number of traditional remedies. We prefer to allow patients to choose between these two approaches, after explaining the advantages and potential adverse effects of each. Research into the traditional treatments continues, and we now have a number of studies available concerning the efficacy of oriental herbal medicine (Kampo medicine) in Japan. There are about 120 different prescriptions available for treatment. Herbs are believed to affect both the psyche and soma, and Kampo medicine does not differentiate between them. Improvement brought about by herbal medicine is usually mild and slow, but sometimes very drastic. Side effects are rare. Those that do occur are mostly allergic reactions to natural substances. Therefore, herbal medicine is especially useful for elderly patients and patients with physical complications. Prescription is traditionally selected by judging Sho of a patient. Sho is equivalent to a syndrome, but comprises psycho and somatic symptoms and signs obtained by traditional physical examination that focuses constitution, general physical condition, pulse, abdominal signs, and examination of the tang. However, currently modern diagnoses are also applied to deciding upon the prescription. Western physicians can select the appropriate preparation without having a special knowledge of Oriental medicine.

Karunakar N, Pillai KK, Husain SZ, Rao M. **Investigations of anti-inflammatory activity of Jigrine.** Indian J Physiol Pharmacol 1997;41(2):134-8.
Jigrine, a polypharmaceutical herbal formulation containing 14 medicinal plants is used in the Unani system of medicine for the treatment of liver ailments. The antiinflammatory activity of Jigrine (0.5 ml and 1.0 ml/kg, po), was evaluated against acute inflammation caused by carrageenin (injecting 0.1 ml of 1% carrageenin in 0.9% NaCl solution into plantar surface of the hind paw of the rat) and the effect of Jigrine (1 ml/kg/day, po for 7 days) was also studied on the sub-acute inflammation induced by cotton pellet granuloma. The paw volume, biochemical parameters like tissue AST, ALT, gamma-GTP and lipid peroxides and dry wt. of granuloma were measured to assess the anti-inflammatory activity. It showed a significant anti-inflammatory activity as evidenced by lowering the elevated levels of paw volume and biochemical parameters. But it could not reduce the sub-acute inflammation caused by cotton pellet granuloma. The study suggests that Jigrine has significant effect only on acute phase of inflammation caused by carrageenin. Antioxidant and membrane stabilizing action of Jigrine might be responsible for its anti-inflammatory effect.

Kase Y, Hayakawa T, Aburada M, Komatsu Y, Kamataki T. **Preventive effects of Hange-shashin-to on irinotecan hydrochloride-caused diarrhea and its relevance to the colonic prostaglandin E2 and water absorption in the rat.** Jpn J Pharmacol 1997;75(4):407-13.
The possible preventive effect of Kampo medicine Hange-shashin-to (TJ-14) on chronic diarrheal symptoms induced by the administration of the anticancer agent irinotecan hydrochloride (CPT-11) was investigated in the rat. Repeated oral administrations of TJ-14 at 125 and 500 mg/kg significantly prevented the reduction in body weight and the onset of chronic

diarrheal symptoms due to CPT-11 in a dose-dependent manner, even though it failed to show a definite effect on acute diarrheal symptoms. In addition, treatment with TJ-14 accelerated the healing of the intestinal tract injured by repeated dosing of CPT-11 and inhibited significantly the increase of colonic prostaglandin E2 (PGE2) which is closely related to the onset of diarrhea. TJ-14 also improved colonic water absorption impaired by repeated dosing of CPT-11 in rats. These results demonstrate that TJ-14 is an effective medicine for the prevention and/or treatment of CPT-11-induced chronic diarrheal symptoms.

Kase Y, Yuzurihara M, Iizuka S, Ishige A, Komatsu Y. **The effects of hange-shashin-to on gastric function in comparison with sho-saiko-to.** Biol Pharm Bull 1997;20(11):1155-9.
The effects of "Hange-shashin-to (TJ-14)" on gastric function were examined in comparison with "Sho-saiko-to (TJ-9)". Oral treatment with TJ-14 (125-500 mg/kg) caused dose-dependent suppression of ethanol-induced gastric injury, while it did not suppress gastric lesions induced by water-immersion stress. TJ-9 (125-500 mg/kg, p.o.) suppressed both water-immersion stress-induced gastric lesions and ethanol-induced gastric injury in a dose-dependent manner. Intraduodenal administration of TJ-14 even at 500 mg/kg did not affect gastric juice secretion, while TJ-9 at 125 to 500 mg/kg dose-dependently suppressed gastric juice secretion. TJ-14 (125-500 mg/kg, p.o.) accelerated gastric emptying in normal rats and improved the delayed gastric emptying induced by BaCl2 in a dose-dependent manner, whereas such effect was not noted with TJ-9. Oral treatment with TJ-14 at 500 mg/kg significantly suppressed apomorphine-induced vomiting, but it did not affect copper sulfate-induced vomiting. These results suggest that TJ-14 exhibits an anti-ulcer action (probably based on its ability to protect the gastric mucosa), improvement of gastric emptying and an anti-emetic action. TJ-9 also showed anti-ulcer effects, probably based on its ability to suppress gastric secretion and to protect the gastric mucosa. Thus, the present study demonstrated the effectiveness of TJ-14 and TJ-9 against gastric disease, and provided basic data which explain the differences in clinical application between these two kampo medicines.

Kavalali G, Tuncel H. **Anti-inflammatory activities of Urtica pilulifera.** Int J Pharmacogn 1997;35(2):138-40.
IPA COPYRIGHT: ASHP The effect of a mineral spirits (petroleum ether) extract of the seeds of Urtica pilulifera on carrageenan-induced hind paw edema in Wistar rats was studied. The extract of U. pilulifera showed anti-inflammatory activity in rats with induced hind paw edema.

Keane FM, Munn SE, Du Vivier AW, Taylor NF, Higgins EM. **Analysis of Chinese herbal creams prescribed for dermatological conditions.** Br Med J 1999 Feb 27;318:563-4.
IPA COPYRIGHT: ASHP A study evaluating the corticosteroid content of 11 topical Chinese herbal creams that had been received by 10 patients, ages 4 months to 36 yr, for eczema, eczema herpeticum, or scaly scalp is reported; the single patient with eczema herpeticum experienced an exacerbation while using the creams, while other patients had achieved some improvement. Eight creams, including those implicated in the exacerbations of eczema herpeticum, contained dexamethasone at concentrations ranging from 64-1500 mug/g. All were applied to areas of sensitive skin such as the face and flexures.

Khanum F, Anilakumar KR, Sudarshanakrishna KR, Viswanathan KR. **Effects of feeding fresh garlic and garlic oil on detoxifying enzymes and micronuclei formation in rats treated with azoxymethane.** Int J Vitam Nutr Res 1998;68(3):208-13.
The effect of feeding a fresh garlic or garlic oil-supplemented diet was studied in rats for a period of 23 weeks with or without the treatment of a carcinogen azoxymethane (AOM), on the modulation of detoxification enzymes and micronuclei formation. The results showed that feeding fresh garlic or garlic oil-supplemented diets tended to reduce hepatic lipid peroxidation, though not to significant levels. Glutathione content was also not altered. The catalase activity in liver of rats fed a fresh garlic-supplemented diet was reduced compared to that of the control diet; however, the activity was not affected by AOM treatment. Ingestion of garlic caused a 40 percent increase in the hepatic glutathione peroxidase activity, whereas carcinogen treatment reduced it. The activity of hepatic glutathione-S-transferase was unaffected by the feeding regimen, while it was lowered in the garlic oil diet group treated with AOM. The gamma glutamyl transpeptidase activity was elevated more than sevenfold, in the kidney of rats treated with AOM, while it was reduced almost to half when the AOM-treated rats were fed fresh garlic or garlic oil. Micronuclei formation was increased fourfold, in rats exposed to AOM whereas the increase was reduced to half when AOM-injected groups had either fresh garlic or garlic oil in their diet. From these studies, it is concluded that long-term feeding of garlic, fresh or oil, reduced the toxic effect of AOM in rats.

Khizhazi AA. **[The therapeutic and prophylactic anti-ulcerogenic action of marigold (Tagetes patula L.) and sea buckthorn (Hippophae) oils in neurogenic ulcerative lesions caused by immobilization, noise and vibration].** Lik Sprava 1998;:1:172-6. (Rus)

Kim HJ, Chun YJ, Park JD, Kim SI, Roh JK, Jeong TC. **Protection of rat liver microsomes against carbon tetrachloride-induced lipid peroxidation by red ginseng saponin through cytochrome P450 inhibition.** Planta Med 1997;63(5):415-8.
A possible role of cytochrome P450 (P450) inhibition by red ginseng saponins in carbon tetrachloride (CCl4)-induced lipid peroxidation was investigated in liver microsomes prepared from male Sprague Dawley rats. The total saponin of red ginseng standardized on ginsenosides-Rb1, -Rb2, -Rc, -Rd, -Re, and -Rg1 whose composition was studied in our previous report was used in the present study. The standardized saponin of red ginseng showed inhibitory effects on P450-associated monooxygenase activities in a dose-dependent manner, particularly p-nitrophenol hydroxylase activity which has been known to represent CCl4-activating P450 2E1 enzyme. Meanwhile, silymarin enhanced the activity of P450 2E1 enzyme in liver microsomes. When the lipid peroxidation was induced by incubating rat liver microsomes with CCl4 in the presence of NADPH, the standardized saponin significantly blocked the formation of thiobarbituric acid-reactive substances at the same concentrations showing P450 inhibition in liver microsomes. Silymarin revealed more potent protection against CCl4-induced lipid peroxidation. When the lipid peroxidation was induced by FeCl3, in which metabolic activation may not be required, only silymarin could protect the lipid peroxidation in liver microsomes. Taken together, our present results indicated that the inhibitory effects of red ginseng saponin on P450 enzymes may have a critical role in CCl4-induced lipid peroxidation in rat liver microsomes and that the mechanism of hepatoprotection by red ginseng saponin may be distinct from that of silymarin.

Kim HM, Hong DR, Lee EH. **Inhibition of mast cell-dependent anaphylactic reactions by the pigment of Polygonum tinctorium (Chung-Dae) in rats.** Gen Pharmacol 1998;31(3):361-5.
1. The effect of the pigment obtained from the stem and leaf of Polygonum tinctorium Loar (PtP) on anaphylactic reactions was studied in rats. 2. PtP totally inhibited compound 48/80-induced anaphylactic shock with doses of 10(2) and 10(3) mg/ kg. When PtP was pretreated at concentrations ranging from 10(-2) to 10(3) mg/kg, the serum histamine levels induced by compound 48/80 were reduced in a dose-dependent manner. 3. We also investigated the effect of PtP on mast cell-dependent passive cutaneous anaphylaxis (PCA) activated by anti-dinitrophenyl (DNP) IgE antibody. PtP potently inhibited PCA when administered orally, topically, intraperitoneally and intradermally. However, it did not show inhibitory activity when administered intravenously. 4. PtP inhibited dose dependently histamine release from rat peritoneal mast cells (RPMCs) induced by compound 48/80 and anti-DNP IgE. Moreover, the level of cAMP in RPMC, when PtP was added, significantly increased about 12-fold at 4 min compared with that of basal cells. 5. These results indicate that PtP may possess strong antianaphylactic activity and suggest that differences in bioavailability may cause differential activity following different administration routes.

Kim HM, Kim YY, Moon HS, Lee EH, Moon SJ, An NH. **Inhibitory effect of anaphylactic reaction of Sosiho-Tang.** Immunopharmacol Immunotoxicol 1998;20(4):567-78.
Mast cells synthesize and secrete chemical mediators which play an central role in anaphylactic reactions. Compound 48/80 is a condensation product of formaldehyde with paramethoxyphenylethylamine that reliably induces the release of chemical mediators in the mast cell granules. Aggregation of the high-affinity Fc receptor also stimulates the mast cells. The objective of the current study was to determine the effect of Sosiho-Tang (SS-Tang) on mast cell-mediated anaphylactic reaction. SS-Tang completely inhibited systemic anaphylaxis induced by compound 48/80 in mice. SS-Tang inhibited local anaphylaxis induced by anti-dinitrophenyl (DNP) IgE. In addition SS-Tang concentration-dependently inhibited histamine release in mast cells induced by compound 48/80 or anti-DNP IgE. These results indicate that SS-Tang may contain compounds with actions that inhibit mast cell degranulation.

Kim HM, Park Y, Lee EH. **Suppression of immunoglobulin E-mediated anaphylactic reaction by Hwanglyun-Haedok-Tang water extract.** J Ethnopharmacol 1998;61(2):127-34.
IPA COPYRIGHT: ASHP The results of a study on the effects of Hwanglyun-Haedok-Tang (H.H.-Tang) water extract (a decoction of 4 Korean herbs) on immunoglobulin E (IgE)-mediated anaphylaxis activated by anti-dinitrophenyl (DNP) IgE antibody in rats who were administered a total of 200 mul of H.H.-Tang water extract solution by various routes are presented. H.H.-Tang water extract potently suppressed passive cutaneous anaphylaxis when administered via intradermal, intraperitoneal, or oral routes. It showed weak suppressive activity upon intravenous administration. H.H.-Tang water extract dose-dependently suppressed anaphylactic histamine release from rat peritoneal mast cells activated by anti-DNP IgE antibody. It was concluded that H.H.-Tang water extract may possess strong anaphylactic action and that differential activity following various administration routes may be caused by differences in bioavailability.

Kim HS, Jang CG, Oh KW, Oh S, Park WK, et al . **Effects of ginseng total saponin on morphine-induced hyperactivity and conditioned place preference in mice.** J

Ethnopharmacol 1998;60(1):33-42.
IPA COPYRIGHT: ASHP To investigate the effects of ginseng on hyperactivity, conditioned place preference, and postsynaptic dopamine receptor sensitivity, mice received intraperitoneal ginseng prior to and during morphine treatment that induced hyperactivity and conditioned place preference. Ginseng inhibited hyperactivity, conditional place preference, and development of postsynaptic dopamine receptor supersensitivity.

Kim SG, Surh YJ, Sohn Y, Yoo JK, Lee JW, Liem A, Miller JA. **Inhibition of vinyl carbamate-induced hepatotoxicity, mutagenicity, and tumorigenicity by isopropyl-2-(1,3-dithietane-2-ylidene)-2-[N-(4-methylthiazol-2- yl)carbamoyl]acetate (YH439).** Carcinogenesis 1998;19(4):687-90.
Isopropyl-2-(1,3-dithietane-2-ylidene)-2-[N-(4-methylthiazol -2-yl)carbamoyl]acetate (YH439) is a novel dithioylidene malonate derivative developed for the treatment of hepatic injury. The compound has been found to down-regulate the expression of hepatic cytochrome P-450 2E1 (CYP2E1) at the transcriptional level (8). Certain organosulfur compounds present in garlic elicit protective effects on chemically induced carcinogenesis and mutagenesis and their chemopreventive activities are associated in part with inhibition of CYP2E1. As part of a program to determine the likely chemopreventive potential of YH439, we initially examined its effects on hepatotoxicity induced by vinyl carbamate (VC), a proximate carcinogen that is preferentially bioactivated by CYP2E1. A single i.p. injection of VC (125 mg/kg body wt) to male Sprague-Dawley rats resulted in severe hepatic lesions as demonstrated by elevated levels of serum enzymes such as alanine aminotransferase and aspartate aminotransferase. Histopathological evaluation of liver sections from VC-treated animals revealed that the hepatic damage mainly consisted of centrilobular necrosis with sinusoidal congestion. Oral administration of YH439 (200 mg/kg body wt) to male Sprague-Dawley rats 2 days, 1 day and 4 h prior to VC completely prevented the hepatic damage caused by this carcinogen. In another experiment, rat hepatic microsome-mediated bacterial mutagenicity of VC was suppressed by YH439 in a dose-related manner. Furthermore, pretreatment of female CD-1 mice with YH439 by gastric intubation resulted in diminution of VC-induced skin carcinogenesis.

Kim SN, Kim SY, Yim HK, Lee WY, Ham KS, Kim SK, Yoon MY, Kim YC. **Effect of dimethyl-4,4'-dimethoxy-5,6,5',6'-dimethylenedioxybiphenyl-2,2'- dicarboxylate (DDB) on chemical-induced liver injury.** Biol Pharm Bull 1999;22(1):93-5.
The effects of orally administered dimethyl-4,4'-dimethoxy-5,6,5',6'-dimethylene-dioxybiphenyl-2,2'-- d icarboxylate (DDB) on the hepatotoxicity induced by carbon tetrachloride, acetaminophen or ethanol were investigated in rats and mice. Either single or repeated DDB pretreatment (50 or 200 mg/kg) did not alter the hepatotoxicity induced by carbon tetrachloride (0.2 or 1.0 ml/kg, i.p.) in female rats as indicated by increases in the activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and sorbitol dehydrogenase (SDH) in serum. The hepatotoxicity of acetaminophen (350 mg/kg, i.p.) was also unaffected in male mice pretreated with DDB (50 mg/kg/d) for a week. However, DDB administration (50 mg/kg/d for 7 d) decreased the hepatic fatty degeneration induced by repeated ethanol treatment (0.75 g/kg, i.p., x2 times a day for a week) in rats as shown by the accumulation of triglycerides and cholesterol in the liver. Malondialdehyde (MDA) formation in liver homogenates was inhibited

by DDB treatment. The significance of the action of DDB on alcoholic fatty liver generation in clinical settings is discussed.

Kim YS, Kim DH, Kim DO, Lee BK, Kim KW, Park JN, Lee JC, Choi YS, Rim H. **The effect of diphenyl-dimethyl-dicarboxylate on cyclosporine-A blood level in kidney transplants with chronic hepatitis.** Korean J Intern Med 1997;12(1):67-9.
An adequate blood level of cyclosporine-A (CsA) is essential to keep graft function in kidney transplants. Due to a narrow therapeutic index and highly variable pharmacokinetic properties associated with CsA, drug interactions may have a significant impact on the immunosuppressive efficacy or toxicity of CsA. Numerous drug interactions of potential clinical significance involving CsA have been reported. Dephenyl-dimethyl-dicarboxylate (PMC), a hepatotonic drug, is a substance derived from the synthesis of Schizandrae fructus elements. We have experienced two cases of drug interaction between CsA and PMC in kidney transplants with chronic hepatitis. In both cases, CsA troughs decreased markedly to a subtherapeutic level following administration of PMC. We, therefore, suggest that PMC could decrease the CsA trough level and thus a close monitoring of the CsA trough level is necessary during a PMC therapy.

Kimbi HK, Fagbenro-Beyioku AF, Oyibo WA. **Antimalarial herbs against chloroquine-resistant P. yoelii nigeriensis in mice.** Indian J Malariol 1998;35(1):35-8.

Kirby AJ, Schmidt RJ. **Antioxidant activity of Chinese herbs for eczema and of placebo herbs. Part 1.** J Ethnopharmacol 1997;56(2):103-8.
IPA COPYRIGHT: ASHP Aqueous decoctions of PSE-222, a standardized mixture of Chinese herbs, were examined to determine whether their antioxidant activity could account for their anti-eczema activity using the diphenylpicrylhydrazyl (DPPH) assay for non-specific hydrogen atom donating activity and a superoxide scavenging assay. Antioxidant activity was detected in some components of both the active and placebo mixtures, but the formulated active mixture was significantly more effected than the placebo.

Kofinas C, Chinou I, Loukis A, Harvala C, Roussakis C, Maillard M, Hostettmann K. **Cytotoxic coumarins from the aerial parts of Tordylium apulum and their effects on a non-small-cell bronchial carcinoma line [letter].** Planta Med 1998;64(2):174-6.
Seven coumarins were isolated from the aerial parts of Tordylium apulum; their structures were established by spectroscopic means. All compounds were tested in vitro for their cytotoxicity against two cell line systems. The antiproliferative effects for three of them were studied at the level of the cell cycle in asynchronous cells of the NSCLC-N6 line with a flow cytometry apparatus.

Konoshima T, Takasaki M, Tokuda H, Nishino H, Duc NM, Kasai R, Yamasaki K. **Anti-tumor-promoting activity of majonoside-R2 from Vietnamese ginseng, Panax vietnamensis Ha et Grushv. (I).** Biol Pharm Bull 1998;21(8):834-8.
Seven saponins (1-7) isolated from the rhizomes and roots of Panax vietnamensis were tested for their inhibitory effects on Epstein-Barr virus early antigen (EBV-EA) induced by the tumor promoter, 12-O-tetradecanoylphorbol-13-acetate (TPA), in Raji cells as a primary screening test for anti-tumor-promoters (cancer chemopreventive agents). The ocotillol-type saponin,

majonoside-R2 (2), which is the major and characteristic constituent of this plant, exhibited a significant inhibitory effect on EBV-EA activation. Furthermore, the cell cycle analysis of 2 on Raji cells was also examined and strong inhibition was observed on the effect of the cell cycle induced by TPA. Compound 2 showed potent anti-tumor-promoting activity in two-stage carcinogenesis tests of mouse skin using 7,12-dimethylbenz[a]anthracene (DMBA) as an initiator and TPA or fumonisin B1 as a promoter. Consequently, these results suggest that majonoside-R2 (2) could be a valuable chemopreventive agent against chemical carcinogenesis.

Koo J, Arain S. **Traditional Chinese medicine in dermatology.** Clin Dermatol 1999;17(1):21-7.

Kulkarni SK, Ninan I. **Inhibition of morphine tolerance and dependence by Withania somnifera in mice.** J Ethnopharmacol 1997;57(3):213-7.
IPA COPYRIGHT: ASHP A study evaluating the protective effects of an oral, commercial root extract of Withania somnifera on the development of tolerance and dependence to morphine in mice was conducted by treating the mice with 100 mg/kg of the extract followed by a subcutaneous injection of sodium chloride (saline) or morphine (10 mg/kg) twice daily on days 1-9; the antinociceptive response to morphine was assessed by the tailflick test 30 min after the second injection and the withdrawal effects of morphine were assessed by intraperitoneal injections of naloxone (2 mg/kg) immediately after the tailflick test on day 10. Results showed that W. somnifera inhibited the development of tolerance to the analgesic response of morphine and its physical dependence. The extract per se did not produce analgesia and acute treatment did not block morphine-induced analgesia as well. However, after chronic treatment for 10 days, the extract blocked morphine-induced analgesia and inhibited development of withdrawal jumps as assessed by the naloxone test. It was concluded that W. somnifera root extract is a safe non-analgesic herbal preparation which can be used in the treatment of opiate addiction.

Kupecz D. **St. John's wort: an alternative therapy in treating depression [news].** Nurse Pract 1998;23(7):110-2.

Kurashige S, Jin R, Akuzawa Y, Endo F. **Anticarcinogenic effects of shikaron, a preparation of eight Chinese herbs in mice treated with a carcinogen, N-butyl-N'-butanolnitrosoamine.** Cancer Invest 1998;16(3):166-9.
We studied the effects of Shikaron, which is composed of 8 Chinese herb extracts, on carcinogenesis and the cytotoxic activity and cytokine production of lymphocytes in mice treated with a carcinogen, N-butyl-N'-butanolnitrosoamine (BBN). We found a significantly lower incidence of urinary bladder carcinoma in mice treated with BBN plus Shikaron 200 mg/kg/day (5 of 20 mice, 25%), than in mice treated with BBN alone (16 of 20 mice, 80%). Shikaron protected the cytotoxic activity of lymphocytes against YAC-1 cells from suppression by BBN. Cytotoxic activity against P-815 cells significantly increased in mice treated with BBN plus Shikaron, as compared with normal mice and BBN-treated mice. Shikaron also protected production of interleukin-2 and interferon-gamma by lymphocytes from suppression by BBN. These findings strongly suggest that Shikaron exerted an anticarcinogenic effect in carcinogen-treated mice through activation of NK and LAK cells and cytokine production by T lymphocytes.

Kurokawa M, Basnet P, Ohsugi M, Hozumi T, Kadota S, Namba T, Kawana T, Shiraki K. **Anti-herpes simplex virus activity of moronic acid purified from Rhus javanica in vitro and in vivo.** J Pharmacol Exp Ther 1999;289(1):72-8.
Rhus javanica, a medicinal herb, has been shown to exhibit oral therapeutic anti-herpes simplex virus (HSV) activity in mice. We purified two major anti-HSV compounds, moronic acid and betulonic acid, from the herbal extract by extraction with ethyl acetate at pH 10 followed by chromatographic separations and examined their anti-HSV activity in vitro and in vivo. Moronic acid was quantitatively a major anti-HSV compound in the ethyl acetate-soluble fraction. The effective concentrations for 50% plaque reduction of moronic acid and betulonic acid for wild-type HSV type 1 (HSV-1) were 3.9 and 2.6 microgram/ml, respectively. The therapeutic index of moronic acid (10.3-16.3) was larger than that of betulonic acid (6.2). Susceptibility of acyclovir-phosphonoacetic acid-resistant HSV-1, thymidine kinase-deficient HSV-1, and wild-type HSV type 2 to moronic acid was similar to that of the wild-type HSV-1. When this compound was administered orally to mice infected cutaneously with HSV-1 three times daily, it significantly retarded the development of skin lesions and/or prolonged the mean survival times of infected mice without toxicity compared with the control. Moronic acid suppressed virus yields in the brain more efficiently than those in the skin. This was consistent with the prolongation of mean survival times. Thus, moronic acid was purified as a major anti-HSV compound from the herbal extract of Rhus javanica. Mode of the anti-HSV activity was different from that of ACV. Moronic acid showed oral therapeutic efficacy in HSV-infected mice and possessed novel anti-HSV activity that was consistent with that of the extract.

Kurokawa M, Hozumi T, Basnet P, Nakano M, Kadota S, Namba T, Kawana T, Shiraki K. **Purification and characterization of eugeniin as an anti-herpesvirus compound from Geum japonicum and Syzygium aromaticum.** J Pharmacol Exp Ther 1998;284(2):728-35.
The hot-water extract of Geum japonicum has been shown to exhibit prophylactic and therapeutic anti-herpes simplex virus (HSV) activity in murine infection models. Eugeniin was purified as an anti-HSV compound from the extract and also was isolated from another herbal extract (Syzygium aromaticum) that had exhibited anti-HSV activity in mice. Thus the anti-HSV action of eugeniin was characterized. The effective concentration (5.0 &mgr;g/ml) for 50% plaque reduction of eugeniin for wild HSV type 1 (HSV-1) on Vero cells was 13.9-fold lower than its 50% cytotoxic concentration determined by a yield-reduction assay. Eugeniin also inhibited the growth of acyclovir-phosphonoacetic acid-resistant HSV-1, thymidine kinase-deficient HSV-1 and wild HSV type 2. Eugeniin as well as phosphonoacetic acid inhibited viral DNA and late viral protein syntheses in their infected Vero cells, but not cellular protein synthesis at its inhibitory concentrations. Purified HSV-1 DNA polymerase activity was inhibited by eugeniin noncompetitively with respect to dTTP. Its apparent Ki value for euginiin was 8.2- and 5. 8-fold lower than the Ki values of purified human DNA polymerases alpha and beta, respectively. Thus one of the major target sites of inhibitory action of eugeniin is viral DNA synthesis; the inhibitory action for viral DNA polymerase activity was novel compared with anti-HSV nucleoside analogs.

Kurokawa M, Kumeda CA, Yamamura J, Kamiyama T, Shiraki K. **Antipyretic activity of cinnamyl derivatives and related compounds in influenza virus-infected mice.** Eur J Pharmacol 1998;348(1):45-51.

Kakkon-to is composed of seven medicinal herbs and exhibited novel antipyretic activity by suppressing interleukin-1alpha production responsive to interferon in a murine intranasal influenza virus infection model. Using this model, antipyretic compounds with such novel biological activities were characterized from the herbs. The organic solvent-extractable fractions of Cinnamomum cassia among the herbs showed antipyretic activity. We selected six antipyretic compounds from 48 cinnamyl derivatives and related compounds that may be mainly involved in the fractions. Their antipyretic activity was significantly correlated with interleukin-1alpha regulatory activity. Four of them suppressed interleukin-1alpha production to a basal level and showed different mode of antipyretic action from that of aspirin in interleukin-1alpha-injected mice. Structure-bioactivity relationship of the four suggested that an ester bond played an important role for both antipyretic and interleukin-1alpha regulatory activities. These compounds may be useful in analyzing interleukin-1alpha-producing cells in fever production and the mechanism of defervescence by suppressing interferon-induced interleukin-1alpha production.

Kurokawa M, Nakano M, Ohyama H, Hozumi T, Kageyama S, Namba T, Shiraki K. **Prophylactic efficacy of traditional herbal medicines against recurrent herpes simplex virus type 1 infection from latently infected ganglia in mice.** J Dermatol Sci 1997;14(1):76-84.
Traditional herbal medicines with anti-herpes simplex virus type 1 (HSV-1) activity in vivo were examined for their prophylactic effects on recurrent HSV-1 infection in mice. Mice were intradermally infected with HSV-1 in the pinna and recurrent HSV-1 disease was induced by ultraviolet irradiation. Herbal extracts arrested the progression of recurrent HSV-1 disease, reduced the incidence of severe erythema and/or vesicles in the pinna, and/or shortened the period of severe recurrent lesions compared with water-administered mice ($P < 0.01$ or 0.05). Similarly, the prophylactic treatment of herbal extracts limited the development of recurrent skin lesions induced by stripping with cellophane tape physically. The prophylactic efficacy on recurrence was confirmed by the absence of HSV DNA in the skin lesions. HSV-1 genome was revealed to exist in the trigeminal ganglia but not in the pinna of latently infected mice before stimuli by a nested-polymerase chain reaction assay. After stimuli, HSV-1 genome was detected in both pinna and trigeminal ganglia of latently infected mice administered with water. However, prophylactic treatment decreased the rate of detection of HSV-1 genome in the stimulated pinna. Thus, the herbal extracts exhibited prophylactic efficacy against recurrent HSV-1 disease in mice and modulated the recurrent HSV-1 infection.

Kurokawa M, Yamamura J, Li Z, Sato H, Hitomi N, Tatsumi Y, Shiraki K. **Antipyretic activity of gingyo-san, a traditional medicine, in influenza virus-infected mice.** Chem Pharm Bull (Tokyo) 1998;46(9):1444-7.
Gingyo-san is composed of 10 crude drugs and used as a traditional antipyretic medicine for the treatment of the common cold and influenza virus infection. In a murine intranasal influenza infection model, fever produced by the infection has been demonstrated to be reduced by suppressing interferon-induced interleukin (IL)-1 alpha production. Thus, we focused on the serum level of IL-1 alpha which produces such novel antipyretic activity, and evaluated the relationship between defervescence and the suppression of IL-1 alpha production by Gingyo-san in influenza virus-infected mice. Fever was produced in the infected mice 33-44 h after infection. Oral administration of a hot water-extract of Gingyo-san (8.9-12.5 mg/0.25 ml/mouse x 3 per

day) significantly reduced fever production and suppressed the rise in IL-1 alpha production to the level in uninfected mice. No apparent toxicity by Gingyo-san was observed in infected mice. When the hot water-extract of each 10 of the crude components of Gingyo-san (an unknown amount extracted from 6.25 mg/0.25 ml/mouse x 3 per day for Saigae Tataricae Cornu and 3.5 mg/0.25 ml/mouse x 3 per day for the other 9) was orally administered to infected mice, 6 showed significant antipyretic activity. Of these 6, Saigae Tatricae Cornu significantly suppressed the rise in IL-1 alpha production to the basal level while the other 5 did not affect serum IL-1 alpha. Thus, of the 10 crude components of Gingyo-san, Saigae Tataricae Cornu simultaneously exhibited antipyretic and IL-1 alpha-regulatory activities. The novel antipyretic action of Gingyo-san may be mainly mediated by Saigae Tataricae Cornu which regulates the elevated serum IL-1 alpha level produced by influenza infection.

Kwon SY, An CS, Liu JR, Paek KH. **A ribosome-inactivating protein from Amaranthus viridis.** Biosci Biotechnol Biochem 1997;61(9):1613-4.
BIOSIS COPYRIGHT: BIOL ABS. An antiviral protein purified from the leaves of Amaranthus viridis was named amaranthin. The in vivo antiviral activity of amaranthin was confirmed in tobacco mosaic virus (TMV) infection test on Nicotiana glutinosa leaves. The molecular mass of the amaranthin was estimated about 30 kDa by SDS-PAGE and the pI was measured as 9.8 by isoelectric focusing (IEF) analysis. Cytotoxicity of the amaranthin using in vitro translation inhibition assay was similar to that of pokeweed antiviral protein (PAP) with IC50 of 25 pM. Depurination activity (N-glycosidase activity) against animal rRNA was also confirmed.

La Valle JB. **Treating women's health the natural way.** Drug Store News Chain Pharm 1998 Mar;8:31.
IPA COPYRIGHT: ASHP A natural approach to the management of premenstrual syndrome (PMS) is discussed, including the value of diet modification, benefits and food sources of phytoestrogens, nutritional supplements, and herbal supplements.

Laakmann G, Schule C, Baghai T, Kieser M. **St. John's wort in mild to moderate depression: the relevance of hyperforin for the clinical efficacy.** Pharmacopsychiatry 1998;31(Suppl 1):54-9.
In a randomized, double-blind, placebo-controlled, multicenter study, the clinical efficacy and safety of two different extracts of St. John's wort were investigated in 147 male and female outpatients suffering from mild or moderate depression according to DSM-IV criteria. Following a placebo run-in period of three to seven days, the patients were randomized to one of three treatment groups: During the 42-day treatment period, they received 3 x 1 tablets of either placebo, Hypericum extract WS 5573 (300 mg, with a content of 0.5% hyperforin), or Hypericum extract WS 5572 (300 mg, with a content of 5% hyperforin). The manufacturing process for the two Hypericum preparations was identical, so that they differed only in their hyperforin content. Efficacy regarding depressive symptoms was assessed on days 0, 7, 14, 28, and 42, using the Hamilton Rating Scale for Depression (HAMD, 17-item version) and the Depression Self-Rating Scale (D-S) according to von Zerssen. In addition, the severity of illness was also rated by the investigators on days 0 and 42 using the Clinical Global Impression (CGI) scale. The last observation of patients withdrawn from the trial prematurely was carried forward. At the end of the treatment period (day 42), the patients receiving WS 5572 (5% hyperforin)

exhibited the largest HAMD reduction versus day 0 (10.3 +/- 4.6 points; mean +/- SD), followed by the WS 5573 group (0.5% hyperforin; HAMD reduction 8.5 +/- 6.1 points) and the placebo group (7.9 +/- 5.2 points). As regards the change in the HAMD total score between day 0 and treatment end and its relationship to the hyperforin dose, a significant monotonic trend was demonstrated in the Jonckheere-Terpstra test (p = 0.017). In pairwise comparisons, WS 5572 (5% hyperforin) was superior to placebo in alleviating depressive symptoms according to HAMD reduction (Mann-Whitney U-test: p = 0.004), whereas the clinical effects of WS 5573 (0.5% hyperforin) and placebo were descriptively comparable. These results show that the therapeutic effect of St. John's Wort in mild to moderate depression depends on its hyperforin content.

Lahiri-Chatterjee M, Katiyar SK, Mohan RR, Agarwal R. **A flavonoid antioxidant, silymarin, affords exceptionally high protection against tumor promotion in the SENCAR mouse skin tumorigenesis model.** Cancer Res 1999;59(3):622-32.
In cancer chemoprevention studies, the identification of better antitumor-promoting agents is highly desired because they may have a wider applicability against the development of clinical cancers. Both epidemiological and animal studies have suggested that microchemicals present in the diet and several herbs and plants with diversified pharmacological properties are useful agents for the prevention of a wide variety of human cancers. Silymarin, a flavonoid isolated from milk thistle, is used clinically in Europe and Asia as an antihepatotoxic agent, largely due to its strong antioxidant activity. Because most antioxidants afford protection against tumor promotion, in this study, we assessed the protective effect of silymarin on tumor promotion in the SENCAR mouse skin tumorigenesis model. Application of silymarin prior to each 12-O-tetradecanoylphorbol 13-acetate (TPA) application resulted in a highly significant protection against tumor promotion in 7,12-dimethylbenz(a)anthracene-initiated mouse skin. The protective effect of silymarin was evident in terms of reduction in tumor incidence (25, 40, and 75% protection, P < 0.001, X2 test), tumor multiplicity (76, 84, and 97% protection, P < 0.001, Wilcoxon rank sum test), and tumor volume (76, 94, and 96% protection, P < 0.001, Student's t test) at the doses of 3, 6, and 12 mg per application, respectively. To dissect out the stage specificity of silymarin against tumor promotion, we next assessed its effect against both stage I and stage II of tumor promotion. Application of silymarin prior to that of TPA in stage I or mezerein in stage II tumor promotion in dimethylbenz(a)anthracene-initiated SENCAR mouse skin resulted in an exceptionally high protective effect during stage I tumor promotion, showing 74% protection against tumor incidence (P < 0.001, X2 test), 92% protection against tumor multiplicity (P < 0.001, Wilcoxon rank sum test), and 96% protection against tumor volume (P < 0.001, Student's t test). With regard to stage II tumor promotion, silymarin showed 26, 63, and 54% protection in tumor incidence, multiplicity, and volume, respectively. Similar effect of silymarin to that in anti-stage I studies, were also observed when applied during both stage I and stage II protocols. In other studies, silymarin significantly inhibited: (a) TPA-induced skin edema, epidermal hyperplasia, and proliferating cell nuclear antigen-positive cells; (b) DNA synthesis; and (c) epidermal lipid peroxidation, the early markers of TPA-caused changes that are associated with tumor promotion. Taken together, these results suggest that silymarin possesses exceptionally high protective effects against tumor promotion, primarily targeted against stage I tumors, and that the mechanism of such effects may involve inhibition of promoter-induced edema, hyperplasia, proliferation index, and oxidant state.

Lee BM, Lee SK, Kim HS. **Inhibition of oxidative DNA damage, 8-OHdG, and carbonyl contents in smokers treated with antioxidants (vitamin E, vitamin C, beta-carotene and red ginseng).** Cancer Lett 1998;132(1-2):219-27.
BIOSIS COPYRIGHT: BIOL ABS. The chemopreventive effects of antioxidants (vitamin E, beta-carotene, vitamin C and red ginseng) on oxidative DNA and protein (globin) damages were comparatively investigated in the peripheral blood of smokers (: 20 cigarettes/day). Smokers showed a lower baseline level of plasma micronutrients (vitamin C and carotene) ($P < 0.01$) and higher baseline level of oxidative DNA or protein damage than non-smokers ($N = 5$; $P < 0.05$). During daily supplementation of antioxidants (200 IU vitamin of E, 9 mg of beta-carotene, 500 mg of vitamin C, or 1.8 g of red ginseng) for 4 weeks, smokers plasma antioxidant concentrations increased linearly, while their mean levels of 8-hydroxydeoxyguanosine (8-OHdG) and carbonyl contents decreased compared with those in smokers supplemented with a placebo ($P < 0.05$). Levels of urinary and plasma cotinine remained steady in smokers regardless of supplementation with antioxidants. 8-OHdG and carbonyl content decreased in a time-dependent manner (as the total intake dose increased) after supplementation with vitamin E (8-OHdG, 33.8%; carbonyl content, 43.6%) or red ginseng (8-OHdG, 31.7%; carbonyl content, 21.3%). These preliminary data suggest that supplementation with antioxidants might protect smokers from oxidative damages and could reduce cancer risk or other diseases caused by free radicals associated with smoking.

Lee CK, Han SS, Mo YK, Kim RS, Chung MH, Park YI, Lee SK, Kim YS. **Prevention of ultraviolet radiation-induced suppression of accessory cell function of Langerhans cells by Aloe vera gel components.** Immunopharmacology 1997;37(2-3):153-62.
The active components of Aloe vera gel that can prevent ultraviolet B (UVB)-induced suppression of accessory cell function of Langerhans cells (LC) were purified by activity-guided sequential fractionation followed by in vitro functional assay. The functional assay was based on the fact that exposure of freshly isolated murine epidermal cells (EC) to UVB radiation resulted in impairment of accessory cell function of LC, as measured by their ability to support anti-CD3 monoclonal antibody (mAb)-primed T-cell mitogenesis. This UVB-suppressed LC accessory cell function was prevented by addition of partially purified Aloe gel components to cultures of UVB-irradiated EC. The Aloe gel components appeared to prevent events occurring within the first 24 h after UVB irradiation that lead to the impairment of accessory cell function. The Aloe gel components did not cause proliferation of anti-CD3 mAb-primed T-cells, nor did induce proliferation of normal EC. The activity-guided final purification of Aloe gel components resulted in the isolation of two components. Both of the components were small molecular weight (MW) substances with an apparent MW of less than 1,000 Da but different from each other in net charge characteristics at pH 7.4. These results suggest that Aloe vera gel contains at least two small molecular weight immunomodulators that may prevent UVB-induced immune suppression in the skin.

Lee CK, Kim H, Moon KH, Shin KH. **Screening and isolation of antibiotic resistance inhibitors from herb materials-resistance inhibition of volatile components of Korean aromatic herbs.** Arch Pharm Res 1998;21(1):62-6.
The resistance inhibitory activities of 54 odorant mixtures(essential oil) from 41 Korean aromatic herbs were tested against multi-drug resistant Staphylococcus aureus SA2, which has resistances

to 10 usual antibiotics including chloramphenicol. As results, combinations of 28 kinds of samples from 21 herbs and chloramphenicol have resistance inhibitory activities in dose dependent manner.

Lee E, Park KK, Lee JM, Chun KS, Kang JY, Lee SS, Surh YJ. **Suppression of mouse skin tumor promotion and induction of apoptosis in HL-60 cells by Alpinia oxyphylla Miquel (Zingiberaceae).** Carcinogenesis 1998;19(8):1377-81.
There have been considerable efforts to search for naturally occurring substances for the intervention of carcinogenesis. Many components from dietary or medicinal plants have been identified that possess substantial chemopreventive properties. An example is curcumin (Curcuma longa Linn., Zingiberaceae), which has been shown to inhibit tumor promotion in experimental carcinogenesis. Alpinia oxyphylla Miquel, another plant of the ginger family used in oriental herbal medicine, contains diarylheptanoids whose structures are analogous to that of curcumin. In the present study, we have tested A.oxyphylla for its ability to suppress tumor promotion. Thus, topical application of the methanolic extract of dried fruits of A.oxyphylla significantly ameliorated 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced skin tumor promotion as well as ear edema in female ICR mice. In another study, treatment of HL-60 cells with the methanolic extract of A.oxyphylla significantly reduced the viability of the cells and also inhibited DNA synthesis. Microscopic examination of the treated cells showed characteristic morphology of apoptosis. Furthermore, cells treated with the extract of A.oxyphylla exhibited internucleosomal DNA fragmentation in time- and concentration-dependent manners. TPA-stimulated generation of superoxide anion in differentiated HL-60 cells was also blunted by A.oxyphylla. Taken together, these findings suggest that A.oxyphylla possesses potential chemopreventive and antitumorigenic activities.

Leutner V. **[When the soul screams: pharmacotherapy of depression].** Pharm Ztg 1998 Apr 30;143:11-8, 21. (Ger)
IPA COPYRIGHT: ASHP An overview of the history, epidemiology, classification, symptoms and signs, and diagnostic methods of the various types of depression in man, including drug therapeutic strategies such as Hypericum perforatum L. (St. John's Wort) and the modern antidepressive agents, is presented.

Li CX, Li L, Lou J, Yang WX, Lei TW, Li YH, Liu J, Cheng ML, Huang LH. **The protective effects of traditional Chinese medicine prescription, han-dan-gan-le, on CCl4-induced liver fibrosis in rats.** Am J Chin Med 1998;26(3-4):325-32.
Han-Dan-Gan-Le, a Chinese medicine preparation composed of Salvia miltorrhiza, Radix paeoniae, Astragalus membranaceus, Stephania tetrandra, and dried leaves of Ginkgo biloba, has been used successfully to treat human liver fibrosis and cirrhosis for years. This study was designed to examine the mechanisms of the protection. Male Wistar rats were given CCl4 (1.2 ml/kg, 2 times/week), 20% fat diet, and 30% alcohol in drinking water (every other day) for 6 weeks. Han-Dan-Gan-Le (0.5 and 1.0 g/kg, p.o., daily for 6 weeks) was administered to rats simultaneously to examine the protective effects against CCl4-induced liver fibrosis. The experimentally-induced liver fibrosis and other morphological alterations were significantly ameliorated by Han-Dan-Gan-Le. Han-Dan-Gan-Le treatments decreased CCl4-induced hepatic collagen accumulation by more than 50%, and significantly increased urinary excretion of

hydroxyproline. The CCl4-induced lipid peroxidation in liver and serum was ameliorated as a result of Han-Dan-Gan-Le treatment, possibly by restoring the activity of superoxide dismutase activity in liver and erythrocytes, In conclusion, Han-Dan-Gan-Le is effective in protecting against liver fibrosis. The mechanisms of the protection appear to be due to its antioxidant properties and the modulation of hepatic collagen metabolism.

Li H, Miyahara T, Tezuka Y, Namba T, Nemoto N, Tonami S, Seto H, Tada T, Kadota S. **The effect of Kampo formulae on bone resorption in vitro and in vivo. I. Active constituents of Tsu-kan-gan.** Biol Pharm Bull 1998;21(12):1322-6.
Four water extracts of Kampo formulae (Yi-kkan-sen, Dai-ho-in-gan, Ni-chi-gan, Tsu-kan-gan) were screened for their inhibitory activities on bone resorption induced by parathyroid hormone (PTH) in organ culture using neonatal mouse parietal bones. Among the Kampo formulae, Tsu-kan-gan (TKG) showed the most potent inhibitory activity. We further fractionated the TKG water extract by monitoring the inhibitory activity on bone resorption stimulated by PTH in vitro. The MeOH fraction of the water extract inhibited PTH-stimulated bone resorption, and its inhibitory activity was more potent than those of other fractions. The MeOH fraction was then subjected to Sephadex LH-20 column chromatography to give fractions I, II and III, which were examined for bone resorption activity. Fraction I inhibited PTH-stimulated bone resorption, and its inhibitory activity was more potent than those of the other fractions. Upon oral administration of the three fractions (100 mg/kg/d) to ovariectomized (OVX) mice, fractions I and III prevented the decrease of bone mineral density (BMD) of the lumbar vertebra. Eleven compounds isolated from the MeOH fraction were examined for their inhibitory effect on PTH-stimulated bone resorption. Among them, berberine (1), syringin (3), limonin (4) and mangiferin (10) showed a significant inhibitory effect on bone resorption. In the formation assay of osteoclast-like cells, these compounds decreased the number of tartrate-resistant acid phosphatase (TRAP)-positive multinucleated cells (MNCs). The inhibitory effect of TKG on bone resorption may be at least partly due to the inhibitory action of these compounds.

Lieberman S. **Nutriceutical review of St. John's wort (Hypericum perforatum) for the treatment of depression.** J Womens Health 1998;7(2):177-82.

Lin MH, Hsu SY, Sheih MJ, Chen TF, Chen CY. **Studies on antiulcer Chinese herbs. Part 1.** Chin Pharm J (Taiwan) 1998;50(1):55-66.
IPA COPYRIGHT: ASHP The effects of 5 extracts of Chinese herbal drugs on 5 experimental models of acute ulcers and 2 experimental models of chronic ulcers in rats were studied following oral administration or intraduodenal injection of the extracts at 1/2, 1/4, and 1/8 of the median lethal doses. Atractylodes macrocephala exhibited significant protective effects against acute and chronic experimental ulcers. The other extracts also displayed statistically significant activities.

Lipsky PE, Tao XL. **A potential new treatment for rheumatoid arthritis: thunder god vine.** Semin Arthritis Rheum 1997;26(5):713-23.
Various extracts of the vinelike plant Tripterygium wilfordii Hook f have been widely used in China to treat patients with a number of autoimmune diseases. Although most of the clinical experience has derived from uncontrolled trials, one placebo-controlled double-blind trial has

clearly demonstrated efficacy in rheumatoid arthritis. Studies in laboratory animals have indicated that extracts of Tripterygium wilfordii Hook f suppress both immune and inflammatory responses and also effectively treat a number of models of autoimmune disease. More detailed in vitro analysis has indicated that components of Tripterygium wilfordii Hook f suppress immune responses by inhibiting transcription of cytokine genes, including interleukin-2 and gamma interferon. The current status of knowledge of the potential clinical benefit of this herbal remedy and possible mechanisms accounting for its utility are considered in this review.

Loniewski I, Musial HD, Korwin-Piotrowska K, Krysiukiewicz A. **[Antiemetic activity of ginger rhizome extract (Zingiber officinale roscoe) and eleuterococ root extract (Eleuthrococcus senticosus Maxim)].** Herba Pol 1998;44(1):39-44. (Pol)
IPA COPYRIGHT: ASHP The anti-emetic effects of an extract of the rhizome of Zingiber officinale (ginger) and an extract of the root of Eleuthrococcus senticosus (eleuterococ), alone and in combination, were studied. The substances exhibited anti-emetic activity without affecting the CNS or cholinergic system.

Lowe FC. **Saw palmetto berry in the treatment of benign prostatic hyperplasia.** Clin Res Regul Aff 1997;14(1):53-66.
IPA COPYRIGHT: ASHP Characteristics of Serenoa repens (saw palmetto) berry and the results of clinical studies of the efficacy of S. repens berry extract for the treatment of benign prostatic hyperplasia are discussed. It was noted that there is much controversy concerning the efficacy of the extract. The double blind trials, although usually favorable, do not show the usual placebo response as seen in other benign prostatic hyperplasia studies.

Lu MC. **Effects of Jen-San-Yaung-Jung-Tang on scopolamine-induced amnesia in rats.** Am J Chin Med 1998;26(2):117-25.
The effect of Jen-San-Yaung-Jung-Tang (YJT) on scopolamine (SCOP)-induced amnesia was investigated in a step-through passive avoidance task in rats. It was observed that YJT (0.5 and 1.0 g/kg) significantly improved SCOP-induced amnesia and did not change the horizontal activity and pain threshold. YJT at 0.5 and 1.0 g/kg also did not change SCOP-treated horizontal activity and pain threshold. Furthermore, the antiamnesic effect of YJT at 1.0 g/kg on the SCOP-induced amnesia was augmented by physostigmine, but was not altered by neostigmine or scopolamine N-methylbromide. These results suggest that the antiamnesic effect of YJT could only be related to the memory-related process, and to an increase in central cholinergic neuronal activity.

Lulin M, Yantang L. **Comparison of the immunosuppressive and toxic effects of TII and azathioprine.** Transplant Proc 1998;30(7):3517-8.

Luper S. **A review of plants used in the treatment of liver disease: part 1.** Altern Med Rev 1998;3(6):410-21.
Botanicals have been used traditionally by herbalists and indigenous healers worldwide for the prevention and treatment of liver disease. Clinical research in this century has confirmed the efficacy of several plants in the treatment of liver disease. Basic scientific research has uncovered the mechanisms by which some plants afford their therapeutic effects. Silybum

marianum (milk thistle) has been shown to have clinical applications in the treatment of toxic hepatitis, fatty liver, cirrhosis, ischemic injury, radiation toxicity, and viral hepatitis via its antioxidative, anti-lipid peroxidative, antifibrotic, anti-inflammatory, immunomodulating, and liver regenerating effects. Picrorhiza kurroa, though less well researched than Silybum, appears to have similar applications and mechanisms of action. When compared with Silybum, the hepatoprotective effect of Picrorhiza was found to be similar, or in many cases, superior to the effect of Silybum.

Mack RB. **"A bunch of the boys were whooping it up".** Echinacea for what ails ya. N C Med J 1998;59(4):236-7.

Mack RB. **"Goodbye to the life I used to live" St. John's wort.** N C Med J 1998;59(1):27-9.

Mahabir D, Gulliford MC. **Use of medicinal plants for diabetes in Trinidad and Tobago.** Rev Panam Salud Publica 1997;1(3):174-9.
Use of herbal remedies from medicinal plants (bush medicines) was studied in 622 people with diabetes mellitus attending 17 government health centers on the island of Trinidad, Trinidad and Tobago. Bush medicines were used by 42% of patients surveyed and were used for diabetes by 24%. Bush medicine use was more frequent in Afro-Trinidadians and in those of mixed ethnicity than in Indo-Trinidadians, and was also more prevalent in those with lower educational attainment. Most patients using bush medicines (214/264, or 81%) reported gathering the plants themselves, and 107/264 (41%) took them more frequently than once a week. Patients taking bush medicines mentioned 103 different plants used in remedies. Among the 12 most frequently mentioned, caraili, aloes, olive-bush, and seed-under-leaf were preferentially used for diabetes. Vervine, chandilay, soursop, fever grass, and orange peel were preferentially used for other indications. Patients who reported burning or numbness in the feet or feelings of tiredness, weakness, giddiness, or dizziness used bush medicines for diabetes more frequently than did patients who reported a range of other diabetes-related symptoms. Insulin-treated patients were less frequent users of bush medicines. It is concluded that bush medicines are taken regularly by many patients with diabetes in Trinidad. Plants most frequently used as remedies for diabetes have recognized hypoglycemic activity. Patients' culture, educational background, type of symptoms, and formal medical treatment may also influence the selection and use of bush medicines.

Malagon F, Vazquez J, Delgado G, Ruiz A. **Antimalaric effect of an alcoholic extract of Artemisia ludoviciana mexicana in a rodent malaria model.** Parassitologia 1997;39(1):3-7.
Chloroquine resistance of Plasmodium falciparum first and of P. vivax more recently, stimulated the search for new antimalarics. Chinese investigators have introduced new compounds obtained from extracts of Artemisia annua which possess an antimalaric active principle different from those of the drugs in use. In Mexico eight species of Artemisia have been described and among them just A. ludoviciana has been empirically used in the treatment of intermittent fever. To know whether mexican Artemisia had antimalaric activity several in vivo experiments were performed. Different type of extracts from two Artemisia species were prepared and assayed in five different doses on mice infected by Plasmodium yoelii yoelii, in a four-day test scheme. Here, only the results of the assays on ethanolic extract of A. ludoviciana are presented. The

results of the in vivo experiments showed that the parasite reproduction was inhibited up to 98.6% at the fifth day, as compared with the controls; the ED50 was of 29.2 mg/kg and the SM50 of 28.7. We looked after the presence of artemisinin in the ethanolic extract, without success.

Mashour NH, Lin GI, Frishman WH. **Herbal medicine for the treatment of cardiovascular disease: clinical considerations.** Arch Intern Med 1998;158(20):2225-34.
Herbs have been used as medical treatments since the beginning of civilization and some derivatives (eg, aspirin, reserpine, and digitalis) have become mainstays of human pharmacotherapy. For cardiovascular diseases, herbal treatments have been used in patients with congestive heart failure, systolic hypertension, angina pectoris, atherosclerosis, cerebral insufficiency, venous insufficiency, and arrhythmia. However, many herbal remedies used today have not undergone careful scientific assessment, and some have the potential to cause serious toxic effects and major drug-to-drug interactions. With the high prevalence of herbal use in the United States today, clinicians must inquire about such health practices for cardiac disease and be informed about the potential for benefit and harm. Continuing research is necessary to elucidate the pharmacological activities of the many herbal remedies now being used to treat cardiovascular diseases.

Melchart D, Walther E, Linde K, Brandmaier R, Lersch C. **Echinacea root extracts for the prevention of upper respiratory tract infections: a double-blind, placebo-controlled randomized trial.** Arch Fam Med 1998;7(6):541-5.
OBJECTIVE: To investigate the safety and efficacy of 2 extracts of echinacea for preventing upper respiratory tract infections. DESIGN: Three-armed, randomized, double-blind, placebo-controlled trial. SETTING: Four military institutions and 1 industrial plant. PARTICIPANTS: Three hundred two volunteers without acute illness at time of enrollment. INTERVENTIONS: Ethanolic extract from Echinacea purpurea roots, Echinacea angustifolia roots, or placebo, given orally for 12 weeks. MAIN OUTCOME MEASURE: Time until the first upper respiratory tract infection (time to event). Secondary outcome measures were the number of participants with at least 1 infection, global assessment, and adverse effects. RESULTS: The time until occurrence of the first upper respiratory tract infection was 66 days (95% confidence interval [CI], 61-72 days) in the E angustifolia group, 69 days (95% CI, 64-74 days) in the E purpurea group, and 65 days (95% CI, 59-70 days) in the placebo group (P = .49). In the placebo group, 36.7% had an infection. In the treatment groups, 32.0% in the E angustifolia group (relative risk compared with placebo, 0.87; 95% CI, 0.59-1.30) and 29.3% in the E purpurea group (relative risk compared with placebo, 0.80; 95% CI, 0.53-1.31) had an infection. Participants in the treatment groups believed that they had more benefit from the medication than those in the placebo group (P = .04). Adverse effects were reported by 18 subjects in the E angustifolia group, 10 in the E purpurea group, and 11 in the placebo group. CONCLUSION: In this study a prophylactic effect of the investigated echinacea extracts could not be shown. However, based on the results of this and 2 other studies, one could speculate that there might be an effect of echinacea products in the order of magnitude of 10% to 20% relative risk reduction. Future studies with much larger sample sizes would be needed to prove this effect.

Metori K, Furutsu M, Takahashi S. **The preventive effect of ginseng with du-zhong leaf on protein metabolism in aging.** Biol Pharm Bull 1997;20(3):237-42.
Stimulation of collagen synthesis prevents the aging process. We found such a synergistic effect by using the leaves of Eucommia ulmoides Oliver, Eucomiaceae (Du-Zhong leaf) and the roots of Panax ginseng C. A. MEYER (Ginseng). The formula consists of amounts which exert no effect when used individually. We tested several formula ratios of Ginseng and Du-Zhong leaf, 1:1, 1:2, 1:3 and 1:4, and concluded that the last two formulas were effective. However, we did not observe a significant difference between 1:3 and 1:4. Thus, it was demonstrated that the formula ratio of Ginseng to Du-Zhong leaf of 1:3 was the most effective for the stimulation of collagen synthesis and the prevention of decreased protein metabolism in aging.

Mikhin VP. **[The use of alisat for correction of level of lipids and their peroxidation products in blood of patients with atherosclerosis].** Biull Eksp Biol Med 1998;126(9):345-9. (Rus)

Miller AL. **Botanical influences on cardiovascular disease.** Altern Med Rev 1998;3(6):422-31.
Several botanicals, including Crataegus oxycantha, Terminalia arjuna, Inula racemosa, and Astragalus membranaceus, have been found to have therapeutic benefit for the treatment of cardiovascular disease. Crataegus oxycantha has been used traditionally as a cardiac tonic and current uses include treatment for angina, hypertension, arrhythmias, and congestive heart failure. Animal studies have also indicated that Crataegus extracts may also have potential use as anti-ischemic and lipid-lowering agents. The bark of the Terminalia arjuna tree has a long history of use as a cardiac tonic as well, and has been indicated in the treatment of coronary artery disease, heart failure, hypercholesterolemia and for relief of anginal pain. Additionally, it has been found to have antibacterial and antimutagenic properties. Inula racemosa, also known as Pushkarmoola, is another traditional Ayurvedic botanical that has potential cardioprotective benefit. In human trials, a combination of Inula racemosa and Commiphora mukul was shown to be superior to nitroglycerin in reducing the chest pain and dyspnea associated with angina. Astragalus membranaceus, a Chinese herb, is often used as a "Qi tonifier" and has been studied for its therapeutic benefit in treatment of ischemic heart disease, myocardial infarction, heart failure, and relief of anginal pain. Clinical studies have indicated that its in vitro antioxidant activity is the mechanism by which it affords its cardioprotective benefit.

Miller AL. **St. John's Wort (Hypericum perforatum): clinical effects on depression and other conditions.** Altern Med Rev 1998;3(1):18-26.
St. John's Wort (Hypericum perforatum), a perennial flowering plant, has been used medicinally for thousands of years, and has most recently been identified as an effective treatment for mild to moderate depression. Clinical studies on the use of this plant for depression have utilized liquid tinctures and standardized solid extracts (0.3% hypericin--300 mg three times a day). Severe depression may also respond to this botanical, although it appears a larger dose is needed (600 mg solid extract three times a day). Hypericum has been favorably compared to numerous antidepressant drugs, the studies having revealed equivalent results and a much more favorable incidence of side effects. Studies have also demonstrated its efficacy in treating seasonal affective disorder. In vitro investigations of Hypericum show antiviral activity, although there is

evidence these promising results might not occur in vivo. Traditional actions and uses include enhancement of wound healing, as well as anti-inflammatory and analgesic activity.

Min X, Xiaohui Z, Zhaixiang D, Ming O. **Effect of the Yang tonifying herbs on myocardial beta-adrenoceptors of hypothyroid rabbits.** J Ethnopharmacol 1998;60(1):43-51.
IPA COPYRIGHT: ASHP To investigate the effects of Yang herbs on thyroidectomized rabbits, thyroidectomized rabbits received standard care alone and with Yang tonifying herbs and sham thyroidectomized rabbits were used as controls; rabbits were evaluated for myocardial beta-adrenoceptor density and affinity, serum levels of thyroxine and triiodothyronine, and heart rate. Thyroidectomized rabbits treated with Yang tonifying herbs demonstrated insignificant changes from untreated thyroidectomized rabbits.

Mitra SK, Venkataranganna MV, Sundaram R, Gopumadhavan S. **Protective effect of HD-03, a herbal formulation, against various hepatotoxic agents in rats.** J Ethnopharmacol 1998;63(3):181-6.
HD-03 is a polyherbal formulation containing plant drugs which are known for their hepatoprotective properties in the Ayurvedic system of medicine. In the present study, the formulation was evaluated for its protective effect against diverse hepatotoxic agents viz., paracetamol, thioacetamide and isoniazid. Treatment with HD-03 led to significant amelioration of toxin-induced changes in the biochemical parameters. Since the protective effect of HD-03 was observed in all three types of intoxication, which are different in their primary mechanism of inducing hepatotoxicity, a protective mode of action of HD-03, not specific to the hepatotoxin, is suggested.

Miyamura M, Ono M, Kyotani S, Nishioka Y. **Effects of sho-saiko-to extract on fibrosis and regeneration of the liver in rats.** J Pharm Pharmacol 1998;50(1):97-105.
Sho-saiko-to, one of the most widely used Chinese herbal preparations, has long been used for the treatment of chronic liver diseases. We have investigated its effect in retarding the process of liver fibrosis and accelerating liver regeneration, especially its effect on Ito cells that are thought to be deeply involved with liver fibrosis. Sho-saiko-to extract and its active constituents were orally administered to rats with dimethylnitrosamine-induced liver-injury. After treatment with sho-saiko-to extract hepatic function improved, histopathological results confirmed repair of liver tissue, and retinoid levels increased. On the other hand, when active constituents of sho-saiko-to extract were administered alone, liver retinoid levels remained low, implying that interaction among active constituents of the extract was suppressing Ito cell activation. When sho-saiko-to extract was administered to 70% hepatectomized normal and liver-injured rats, liver weight, the number of S-phase-cells and retinoid levels increased with time. However, these changes were different for normal and liver-injured rats, suggesting that the site of action of sho-saiko-to extract in regenerating liver is different for normal and liver-injured rats. These results show that sho-saiko-to extract was useful for suppressing the activation of Ito cells.

Motoo Y, Taga H, Su SB, Sawabu N. **Effect of gegen-tang on painful gynecomastia in patients with liver cirrhosis: a brief report [published erratum appears in Am J Chin Med 1998;26(1):114].** Am J Chin Med 1997;25(3-4):317-24.
Four patients with liver cirrhosis and complaining of painful gynecomastia were treated with oral

administration of Gegen-Tang (TJ-1). Pain disappeared in 3 patients in one week, and in one patient in 4 weeks. The size of gynecomastia did not change significantly on mammography, but palpable induration diminished or disappeared. The patients had been treated with Chaihu (saiko) group drugs for liver diseases, and TJ-1 was used in combination with these drugs. Serum levels of estrogen, progesterone, testosterone, and other sex hormones did not change significantly after TJ-1 treatment. These results suggest that TJ-1 could be used for the painful gynecomastia that is occasionally seen in cirrhotic patients.

Motoo Y, Taga H, Yamaguchi Y, Watanabe H, Okai T, Sawabu N. **Effect of niuche-shen-qi-wan on painful muscle cramps in patients with liver cirrhosis: a preliminary report.** Am J Chin Med 1997;25(1):97-102.
Twelve patients with liver cirrhosis complaining of painful muscle cramps were treated with Niuche-Shen-Qi-Wan (TJ-107). Three patients were at the decompensated state. Muscle cramps disappeared in 4 weeks on the average after oral administration of TJ-107 in all 12 patients. During the period of TJ-107 administration, there was no significant improvement of hepatic function. One patient complained of mild epigastric discomfort after taking TJ-107, but there were no other adverse effects. Our results indicate that TJ-107 is useful for treatment of painful muscle cramps in cirrhotic patients.

Nagasawa H, Wu G, Sakamoto S, Yamamoto K, Inatomi H. **Effects of guan-mu-tong (Caulis aristolochiae manshuriensis) in combination with other natural products on normal and preneoplastic mammary gland growth in mice.** Am J Chin Med 1997;25(1):79-88.
The effects of combined treatment with Guan-mu-tong (Gmt: Caulis aristolochiae manshuriensis) and other major components of Shi-Liu-Wei-Liu-Qi-Yin (SLWLQY), a Chinese herbal medicine prescribed for breast diseases, on normal and preneoplastic mammary gland growth were investigated. SHN virgin mice were divided into 6 groups at 3 months of age and treated with the samples in drinking water as shown in Table 2 for 8 weeks. Each sample was extracted repeatedly with hot water, dried in vacuo and dissolved with tap water at the concentration indicated in Table 2. Normal and preneoplastic mammary gland growth and thymidylate synthetase activity in the mammary gland were inhibited by Gmt alone; but its effect was affected slightly by the further addition of other products. However, the excretion of urinary components, which is abnormally low in SHN mice, was gradually enhanced by the addition of other products to Gmt and was highest by SLWLQY. The elongated estrous/metestrous stage of the estrous cycle induced by Gmt+Zq was returned to the control level by further addition of other products and by SLWLQY. The normal parameters in this strain during this age period such as body weight change, food and water intake and immune system were affected little by all treatments. All these findings strongly suggest that one of the principles of prescribing Chinese herbal medicines is to normalize the physical conditions, which, in turn, contributes to therapy and protection from diseases.

Nakano M, Nakashima H, Itoh Y. **Anti-human immunodeficiency virus activity of oligosaccharides from rooibos tea (Aspalathus linearis) extracts in vitro.** Leukemia 1997;11(Suppl 3):128-30.
The active substances, acid polysaccharides, were extracted with 1% sodium hydroxide from the leaves of rooibos tea (Aspalathus linearis), Du Zhong Cha (Eucommia ulmoides Oliv.) and

Japanese tea leaves (Camellia sinensis var. sinensis). The alkaline extracts of Rooibos tea and Du-Zhong tea leaves, but not Japanese tea leaves suppressed the HIV-induced cytopathicity using HIV (HTLV-III) infected MT-4 cells, having extremely low cytotoxicity: Its 50% effective concentration (EC50) was 12-67 micrograms/mL, white 50% cytotoxic concentration (CC50) was higher than 1.0 mg/mL. The active substances were purified with ethanol precipitation. The substances were composed of 27% of reducing sugar, 46% of neutral sugars and 22% of uronic acid. A LD50 of the alkaline extracts from rooibos tea was higher than 1.2 g/kg body weight. Acid degradated substances composed of disaccharides and trisaccharides, were also suppressed the HIV-induced cytopathicity. From these results, it is probable that acid polysaccharides from rooibos tea were extremely safe, and that HIV infection may be suppressed by daily intake of the alkaline extracts of rooibos tea and Du-Zhong tea.

Nakata H, Kikuchi Y, Tode T, Hirata J, Kita T, Ishii K, Kudoh K, Nagata I, Shinomiya N. **Inhibitory effects of ginsenoside Rh2 on tumor growth in nude mice bearing human ovarian cancer cells.** Jpn J Cancer Res 1998;89(7):733-40.
Ginsenoside Rh2 (Rh2), isolated from an ethanol extract of the processed root of Panax ginseng CA Meyer, inhibits the growth of B16 melanoma cells. This study was designed to evaluate the ability of Rh2 to inhibit growth of human ovarian cancer cells (HRA) in vitro and in nude mouse. Rh2 inhibited proliferations of various established human ovarian cancer cell lines in a dose-dependent manner between 10 and 60 microM in vitro and induced apoptosis at around the IC50 dose. When HRA cells were inoculated s.c. into the right flank of nude mice, all mice formed a palpable tumor within 14 days. Although i.p. administration of Rh2 alone hardly inhibited the tumor growth, when Rh2 was combined with cis-diamminedichloroplatinum(II) (CDDP) the tumor growth was significantly inhibited, compared to treatment with CDDP alone. When mice were treated p.o. with Rh2 daily (but not weekly), the tumor growth was significantly (P

Nathan A. **Products for motion sickness and temporary sleep disturbance.** Pharm J 1997 Dec 6;259:929-32.
IPA COPYRIGHT: ASHP The use of antihistamines and scopolamine hydrobromide (hyoscine hydrobromide) for motion sickness and the use of antihistamines and herbal products as sleep aids, including their mechanisms of action, dosage, adverse effects, interactions, and product selection points, are presented.

Oh TY, Ryu BK, Ko JI, Ahn BO, Hahm KB, et al . **Protective effect of DA-9601, an extract of Artemisiae herba, against naproxen-induced gastric damage in arthritic rats.** Arch Pharmacal Res 1997;20(5):414-9.

Ohnishi Y, Fujii H, Hayakawa Y, Sakukawa R, Yamaura T, Sakamoto T, Tsukada K, Fujimaki M, Nunome S, Komatsu Y, et al. **Oral administration of a Kampo (Japanese herbal) medicine Juzen-taiho-to inhibits liver metastasis of colon 26-L5 carcinoma cells.** Jpn J Cancer Res 1998;89(2):206-13.
We have investigated the inhibitory effect of oral administration of Juzen-taiho-to, a Kampo Japanese herbal medicine, on liver metastasis by the inoculation of a liver-metastatic variant (L5) of murine colon 26 carcinoma cells into the portal vein. Oral administration of Juzen-taiho-to for 7 days before tumor inoculation resulted in dose-dependent inhibition of liver tumor colonies and

significant enhancement of survival rate as compared with the untreated control, without side effects. We also found that liver metastasis of L5 cells was enhanced in BALB/c mice pretreated with anti-asialo GM1 serum or 2-chloroadenosine, and in BALB/c nu/nu mice, compared to normal mice. This indicates that NK cells, macrophages, and T-cells play important roles in the prevention of metastasis of tumor cells. Juzen-taiho-to significantly inhibited the experimental liver metastasis of colon 26-L5 cells in mice pretreated with anti-asialo GM1 serum and untreated normal mice, whereas it did not inhibit metastasis in 2-chloroadenosine-pretreated mice or T-cell-deficient nude mice. Oral administration of Juzen-taiho-to activated peritoneal exudate macrophages (PEM) to become cytostatic against the tumor cells. These results show that oral administration of Juzen-taiho-to inhibited liver metastasis of colon 26-L5 cells, possibly through a mechanism mediated by the activation of macrophages and/or T-cells in the host immune system. Thus, Juzen-taiho-to may be efficacious for the prevention of cancer metastasis.

Ohta Y, Nishida K, Sasaki E, Kongo M, Hayashi T, Nagata M, Ishiguro I. **Comparative study of oral and parenteral administration of sho-saiko-to (xiao-chaihu-tang) extract on D-galactosamine-induced liver injury in rats.** Am J Chin Med 1997;25(3-4):333-42.
The preventive effect of Sho-saiko-to (Xiao-Chaihu-Tang) extract (TJ-9) on the progression of D-galactosamine (GaIN)-induced liver injury was examined in five week-old male Wistar rats with oral (p.o.) or intraperitoneal (i.p.) administration of the same dose of TJ-9. Rats treated once with GaIN (500 mg/kg body weight, i.p.) received TJ-9 at a dose of 1.0 g/kg body weight (p.o. or i.p.) 2 hours after GaIN treatment at which time an apparent liver injury occurred. Both p.o. and i.p. administration of TJ-9 showed similar significant prevention against the progression of liver injury 24 hours after GaIN injection. Although total protein and albumin concentrations in serum and protein concentration in the liver decreased with the progression of GaIN-induced liver injury, oral or i.p. administration of TJ-9 prevented these decreases in similar degree. However, decreases in serum and liver triglyceride concentration with the progression of liver injury were not attenuated after p.o. or i.p. administration of TJ-9. The activities of liver 5'-nucleotidase and glucose-6-phosphatase, marker enzymes of liver plasma and microsomal membranes, respectively, decreased during the progression of liver injury. A similar preventive effect on the decrease of both enzyme activities was found after p.o. or i.p. administration of TJ-9. These results indicate that the preventive effect on progression of GaIN-induced liver injury by oral or i.p. administration is approximately equal, and that the effect may be through improving the impaired liver protein synthesis and disrupted liver plasma and microsomal membranes in a similar degree.

Ohta Y, Sasaki E, Nishida K, Hayashi T, Nagata M, Ishiguro I. **Preventive effect of oren-gedoku-to (huanglian-jie-du-tang) extract on progression of carbon tetrachloride-induced acute liver injury in rats.** Am J Chin Med 1997;25(1):57-68.
The effect of oral administration of Oren-gedoku-to (Huanglian-Jie-Du-Tang) extract (TJ-15) on the progression of acute liver injury was examined in rats intoxicated with carbon tetrachloride (CCl_4). When TJ-15 at a dose of 500 mg/kg body weight (b.w.) was administered to male Wistar rats aged seven weeks 6 hours after i.p. injection of CCl_4 (1.0 ml/kg b.w.), an apparent liver injury occurred. Significant prevention against the progression of liver injury was found 24 hours after the injection judging from the activities of serum transaminases and other indices of liver cell damage. An increase in lipid peroxide level and decreases in reduced glutathione level and

superoxide dismutase (SOD) activity occurred in the liver at 6 and 24 hours after CCl4 injection. Serum SOD activity increased 24 hours after CCl4 injection. Post-oral TJ-15 administration significantly ameliorated all these changes found at 24 hours after CCl4 injection. An increase in liver triglyceride level and a decrease in serum triglyceride level also occurred 6 and 24 hours after CCl4 injection. Post-oral TJ-15 administration prevented the increase in liver triglyceride level at 24 hours after CCl4 injection. Although the activity of liver tryptophan 2,3-dioxygenase (TDO), a marker of the inhibition of liver protein synthesis by CCl4, decreased 6 and 24 hours after injection of the toxicant, post-oral TJ-15 administration had no effect on this decrease in TDO activity at 24 hours after the injection. These results indicate that oral TJ-15 administration can prevent the progression of acute liver injury in CCl4-injected rats, and suggest that this prevention could be due to the action of TJ-15 to scavenge free radicals formed in the liver and to inhibit triglyceride accumulation in the liver.

Ostrow MJ, Cornelisse PG, Heath KV, Craib KJ, Schechter MT, O'Shaughnessy M, Montaner JS, Hogg RS. **Determinants of complementary therapy use in HIV-infected individuals receiving antiretroviral or anti-opportunistic agents.** J Acquir Immune Defic Syndr Hum Retrovirol 1997;15(2):115-20.
OBJECTIVE: To identify sociodemographic and clinical characteristics of persons using complementary therapy in an HIV/AIDS drug treatment program and to evaluate the associations between complementary therapy use and participant characteristics. METHODS: A cross-sectional study using program participants who completed an annual participant survey between 09/95 and 06/96. Surveys gathered data on use and motivations for use of complementary therapies. Complementary therapies included dietary, medicinal, tactile, and relaxation therapies. Statistical analyses were carried out using parametric and nonparametric measures and multivariate logistic analyses. Multivariate modeling considered age, income, education, time spent out of bed, and degree of pain as independent variables against complementary therapy use (Yes versus No). All reported p values are two-sided. RESULTS: A total of 657 participants completed an annual participant survey within the study period. Of these, 256 participants (39%) had ever used complementary therapies. Univariate analysis indicated that 195 patients (30%) had used dietary supplements, 141 (22%) had used herbal and other medicinal therapies, 145 (22%) had used tactile therapies, and 128 (20%) had used mental relaxation techniques. Multivariate analysis indicated that complementary use was independently associated with younger median age (p = .003), income >$7,300 U.S. (p = .014), having greater physical pain (p = .003), and a university education (p = .002). CONCLUSION: Use of complementary therapies in conjunction with HIV/AIDS medications appears to be most prevalent in young and highly educated individuals and to be associated with the debilitating and chronic nature of HIV disease.

Oubre AY, Carlson TJ, King SR, Reaven GM. **From plant to patient: an ethnomedical approach to the identification of new drugs for the treatment of NIDDM.** Diabetologia 1997;40(5):614-7.

Ozturk Y. **Testing the antidepressant effects of Hypericum species on animal models [published erratum appears in Pharmacopsychiatry 1998 Jan;31(1):37].** Pharmacopsychiatry 1997;30(Suppl 2):125-8.

This paper summarizes the antidepressant effects of certain Hypericum species on animal models. Although there are many drugs in clinical use for the management of human depression, most of the antidepressant drugs have undesirable side effects, some of which may limit the daily life of patients, and therefore, more specific agents with lesser side effects are necessary as a new therapeutic modality for the rational treatment of depression. In our laboratory, we observed antidepressant activity with the alcoholic extract of H. calycinum whose effects on the central nervous system of mice are almost equal to the extract prepared from St. John's wort, H. perforatum. Other species, H. hyssopifolium ssp. elongatum var. elongatum seems to have no antidepressant activity. From these data, it can be concluded that at least some of Hypericum species may have a potential use for the treatment of depression.

Pang L, Hoult JR. **Cytotoxicity to macrophages of tetrandrine, an antisilicosis alkaloid, accompanied by an overproduction of prostaglandins [published erratum appears in Biochem Pharmacol 1997 Jun 15;53(12):1946].** Biochem Pharmacol 1997;53(6):773-82.
Tetrandrine, an anti-inflammatory immunosuppressive bisbenzylisoquinoline alkaloid of Chinese herbal origin, is widely used to treat silicosis and interferes with the regulation of calcium in many cell types. We investigated its effect on the cellular integrity of macrophages and on their ability to generate prostaglandins and nitric oxide, mediators of inflammation with immunomodulatory roles. Tetrandrine at 10(-7) M to 10(-4) M caused dose- and time-dependent loss of cell viability of mouse peritoneal macrophages, guinea-pig alveolar macrophages and mouse macrophage-like J774 cells. Loss of viability (50%) occurred within 1-3 hr and required approximately 5 x 10(-6) M tetrandrine. Loss of macrophage viability after tetrandrine treatment was accompanied by the generation of large amounts of prostaglandin E2 (PGE2), to levels 285-877% of control. Coincubation with indomethacin abolished PGE2 generation, but did not prevent cell death. Tetrandrine did not cause generation of nitric oxide. Verapamil also reduced the viability of mouse peritoneal macrophages and J774 cells, but did not cause PGE2 overproduction, except at 10(-4) M in mouse peritoneal macrophages. In macrophages cultured with lipopolysaccharide and interferon-gamma to induce the generation of large amounts of both PGE2 and nitric oxide, tetrandrine reduced mediator release and their forming enzymes (cyclo-oxygenase-2 and inducible nitric oxide synthase), secondary to cytotoxicity. The predominant action of tetrandrine is to exert a cytotoxic effect on macrophages, perhaps by interfering with calcium homeostasis; this leads to overproduction of immunomodulatory but proinflammatory prostaglandin. This may be relevant to its protective actions in human fibrosing silicosis, in which there is alveolar macrophage involvement.

Park KK, Chun KS, Lee JM, Lee SS, Surh YJ. **Inhibitory effects of [6]-gingerol, a major pungent principle of ginger, on phorbol ester-induced inflammation, epidermal ornithine decarboxylase activity and skin tumor promotion in ICR mice [published erratum appears in Cancer Lett 1998 Sep 25;131(2):231].** Cancer Lett 1998;129(2):139-44.
A wide array of phytochemicals have been shown to possess potential cancer chemopreventive properties. Ginger contains pungent phenolic substances with pronounced antioxidative and antiinflammatory activities. In the present study, we have determined the antitumor promotional activity of [6]-gingerol, a major pungent principle of ginger, using a two-stage mouse skin carcinogenesis model. Topical application of [6]-gingerol onto shaven backs of female ICR mice prior to each topical dose of 12-O-tetradecanoylphorbol-13-acetate (TPA) significantly inhibited

7,12-dimethylbenz[a]anthracene-induced skin papillomagenesis. The compound also suppressed TPA-induced epidermal ornithine decarboxylase activity and inflammation.

Parry BL. **45-Year-old woman with premenstrual dysphoric disorder.** JAMA 1999 Jan 27;281:368-73.
IPA COPYRIGHT: ASHP An overview of the symptoms, pathophysiology, diagnosis, and treatment of premenstrual dysphoric disorder (premenstrual syndrome; PDD) is presented, including the use of vitamins, hormones, evening primrose oil, diuretics, antidepressants, and light therapy; the case of a 45-yr-old PDD patient is presented, and her treatment with sedatives, vitamins, exercise, oral contraceptives, diet, fluoxetine hydrochloride, and Hypericum perforatum (St. John's wort) is discussed. The patient's experiences with side effects of the psychotherapeutic agents are emphasized.

Pepeljnjak S, Kustrak D, Vukusic I. **Investigation of the antimycotic activity of Solidago virgaurea and Solidago gigantea extracts.** Pharm Pharmacol Lett 1998;8(2):85-6.
IPA COPYRIGHT: ASHP The antimycotic activity of ethanolic extracts of Solidago virgaurea and Solidago gigantea against strains of Candida species and dermatophytes was investigated. Although neither plant was found to possess a broad spectrum of activity against the various fungal species, they may be useful in combination with other plants with antimycotic activity.

Peppercorn MA. **66-Year-old woman with ulcerative colitis.** JAMA 1998 Mar 25;279:949-53.
IPA COPYRIGHT: ASHP An overview of the etiology, diagnosis, and treatment of ulcerative colitis is presented, including the efficacy and side effects of oral and rectal corticosteroids and mesalamine (5-ASA) and related drugs, herbs, nicotine, immunosuppressive agents, and surgery; the case of a 66-yr-old female patient with ulcerative colitis is presented, and her therapy with hydrocortisone (Cortenema) as a rectal enema and the limitations to further therapy due to allergies to salicylates and concerns regarding immunosuppression are discussed. The costs of diagnostic procedures, drug therapy, and surgical interventions are summarized.

Pepping J. **Echinacea.** Am J Health Syst Pharm 1999;56(2):121-2.

Pereira F, Santos R, Pereira A. **Contact dermatitis from chamomile tea.** Contact Dermatitis 1997;36(6):307.

Perry EK, Pickering AT, Wang WW, Houghton P, Perry NS. **Medicinal plants and Alzheimer's disease: integrating ethnobotanical and contemporary scientific evidence.** J Altern Complement Med 19998;4(4):419-28.
The use of complementary medicines such as plant extracts in dementia therapy, varies according to the different cultural traditions. In orthodox Western medicine, contrasting with that in China and the Far East for example, pharmacological properties of traditional cognitive or memory enhancing plants have not been widely investigated in the context of current models of Alzheimer's disease. An exception is Ginkgo biloba in which the ginkgolides have antioxidant, neuroprotective, and cholinergic activities relevant to Alzheimer's disease mechanisms. The therapeutic efficacy of Ginkgo biloba extracts in Alzheimer's disease in placebo-controlled clinical trials is reportedly similar to currently prescribed drugs such as tacrine or donepezil and,

importantly, undesirable side effects of Ginkgo biloba are minimal. Old European reference books (eg, medical herbals) document a variety of other plants such as Salvia officinalis (sage) and Melissa officinalis (balm) with memory improving properties, and cholinergic activities have recently been identified in extracts of these plants. Precedents for modern discovery of clinically relevant pharmacological activities in plants with long-established medicinal use include, for example, the interaction of alkaloid opioids in Papaver somniferum (Opium poppy) with endogenous opiate receptors in the brain. With recent major advances in understanding the neurobiology of Alzheimer's disease, and as yet limited efficacy of so-called rationally designed therapies, it may be timely to re-explore historical archives for new directions in drug development. This article considers not only the value of an integrative traditional and modern scientific approach to developing new treatments for dementia, but also in the understanding of disease mechanisms. Long before the current biologically based hypothesis of cholinergic derangement in Alzheimer's disease emerged, plants now known to contain cholinergic antagonists were recorded for their amnesic and dementia-inducing properties.

Perumal Samy R, Ignacimuthu S, Sen A. **Screening of 34 Indian medicinal plants for antibacterial properties.** J Ethnopharmacol 1998;62(2):173-82.
A total of 34 plant species belonging to 18 different families, selected on the basis of folklore medicinal reports practised by the tribal people of Western Ghats, India, were assayed for antibacterial activity against Escherichia coli, Klebsiella aerogenes, Proteus vulgaris, and Pseudomonas aerogenes (gram-negative bacteria) at 1000-5000 ppm using the disc diffusion method. Of these 16 plants showed activity; among them Cassia fistula, Terminalia arjuna and Vitex negundo showed significant antibacterial activity against the tested bacteria. Our findings confirm the traditional therapeutic claims for these herbs.

Phan TT, Hughes MA, Cherry GW. **Enhanced proliferation of fibroblasts and endothelial cells treated with an extract of the leaves of Chromolaena odorata (Eupolin), an herbal remedy for treating wounds.** Plast Reconstr Surg 1998;101(3):756-65.
Burns are a major problem in many developing countries. Eupolin ointment is a topical agent used in the treatment of soft-tissue wounds and burns in Vietnam and is made from an aqueous extract of the leaves of Chromolaena odorata (formerly Eupatorium odoratum). Clinical studies using this extract have shown antimicrobial and anticoagulation effects as well as the promotion of tissue remodeling in the wound healing process. However, the mechanism by which this agent affects cells involved in the wound healing process is unknown. In our research, fibroblasts and endothelial cells, two cell types that play a crucial role in wound healing, were used to investigate some of the effects of Eupolin extract in vitro. Cell growth was estimated by a colorimetric assay at different time intervals. Enhanced growth of fibroblasts and endothelial cells was found at concentrations of 10 microg/ml and 100 microg/ml of Eupolin extract. This was particularly evident in medium supplemented with only 0.5% fetal calf serum where the cells were quiescent. Toxicity of the extract to fibroblasts was observed at 250 microg/ml in Dulbecco's modified Eagle's medium/0.5% fetal calf serum, but there was no significant damage at this dose to the endothelial cells. The results of the study demonstrated that Eupolin extract increased fibroblast and endothelial cell growth, and this could explain in part the beneficial clinical effects that have been observed.

Philipov S, Istatkova R, Ivanovska N, Denkova P, Tosheva K, Navas H, Villegas J. **Phytochemical study and antiinflammatory properties of Lobelia laxiflora L.** Z Naturforsch [C] 1998;53(5-6):311-7.
Three new piperidine alkaloids were isolated from stems, leaves and flowers of Lobelia laxiflora L. (Campanulaceae). The structures of racem. cis-8,10-diethyl-3,4-dehydrolobelidiol (1), racem. trans-8-ethyl-10-phenyl-3,4-dehydrolobelidiol (2) and racem. cis-8-ethyl-10-phenyl-3, 4-dehydrolobelidiol (3) were established by spectral analyses. The residues obtained from the ethanol extracts from stems (S), leaves (L), and flowers (F) were applied in carrageenan (Car)- and cobra venom (CV)-induced acute inflammation in mice. A suppression of paw edema formation at a dose of 100 mg kg-1 was established. In this study the antiinflammatory potential of Lobelia l. was regarded in connection with the complement system. The sequential activation and assembly into functional units of complement components can proceed via two different pathways, named classical (CP) and alternative (AP). The ability of the residues, nonalkaloid fractions, alkaloid fractions and the three alkaloids at a concentration from 0.125 to 1.0 mg ml-1 to inhibit complement activation and thus to prevent inflammatory process was estimated in vitro in human serum via both pathways. All of them inhibited complement activity with a predominant action on CP.

Phillipson JD. Ne**w drugs from nature--it could be yew.** Phytother Res 1999;13(1):2-8.

Piras G, Makino M, Baba M. **Sho-saiko-to, a traditional Kampo medicine, enhances the anti-HIV-1 activity of lamivudine (3TC) in vitro.** Microbiol Immunol 1997;41(10):835-9.
Sho-saiko-to (SST), a traditional Kampo medicine, has been examined for its inhibitory effect on human immunodeficiency virus type 1 (HIV-1) replication in peripheral blood mononuclear cells (PBMCs). SST alone moderately inhibited HIV-1 replication at a concentration of 25 microg/ml. When SST was combined with zidovudine (AZT), lamivudine (3TC) or AZT plus 3TC, SST enhanced the anti-HIV-1 activity of 3TC. In contrast, SST slightly enhanced the anti-HIV-1 activity of AZT plus 3TC but did not enhance the activity of AZT alone. These results suggest that the combination of SST and 3TC has potential as a chemotherapeutic modality of HIV-1 infection.

Plohmann B, Bader G, Hiller K, Franz G. **Immunomodulatory and antitumoral effects of triterpenoid saponins.** Pharmazie 1997;52(12):953-7.
Genuine saponins of Solidago virgaurea L., Heteropappus altaicus (Willd.) Novopokr., Heteropappus biennis (Ldb.) Tamamsch. and Helianthus annuus L. (Asteraceae) as well as related carbohydrate modified glycosides of polygalacic acid and echinocystic acid and some commercial available triterpenoid saponins were investigated in view of their immunomodulating and antitumoral effects. Mitogeneic effects on murine spleen and thymus cells, as well on human mononuclear cells in vitro could be demonstrated. The activity of murine bone marrow macrophages was stimulated in a chemoluminescence assay, and further an induction of cytotoxic macrophages and a TNF alpha release from murine macrophages was observed. The mitogeneic and TNF alpha releasing virgaureasaponin E (1) showed in vivo antitumoral effects in the allogeneic sarcoma 180 tumor model and in the syngeneic DBA/2-MC.SC-1 fibrosarcoma tumor model. In mice, treated with 1, phagocytosis of bone marrow cells

and proliferation of spleen and bone marrow cells were stimulated in an ex vivo assay whereby the TNF alpha concentration in blood considerably increased compared to the control group.

Polasa K, Krishnaswamy K. **Reduction of urinary mutagen excretion in rats fed garlic.** Cancer Lett 1997;114(1-2):185-6.
Naturally occurring substances of plant origin are known to possess antimutagenic potential. Garlic (Allium sativum) was fed to rats in dried powdered form at 0.1%, 0.5% and 1% concentrations in their diet for 4 weeks. At the end of the experiment benzo[a]pyrene (1 mg/rat) was injected intraperitoneally and 24-h urine was collected from the rats. Urinary mutagens were quantitated by the Salmonella typhimurium assay. There was a significant reduction in the excretion of urinary mutagens by carcinogen-exposed rats fed garlic. Further, there was a stimulation in the activities of liver cytosolic glutathione-S-transferase and liver and lung quinone reductases. The study suggested that the antimutagenic potential of garlic may be mediated through induction of detoxification enzymes in target tissues.

Powers JE. **That pesky prostate and the saw palmetto.** S D J Med 1997;50(12):453-4.

Rabe T, Van Staden J. **Antibacterial activity of South African plants used for medicinal purposes.** J Ethnopharmacol 1997;56(1):81-7.
Crude extracts from 21 South African medicinal plants, traditionally used for ailments of an infectious or septic nature, were screened for in vitro antibacterial activity using the agar diffusion and dilution methods. Almost all the activity exhibited was against Gram-positive bacteria, with 12 of the 21 plant species tested showing some activity against Bacillus subtilis. Only the Warburgia salutaris methanol extract inhibited the growth of Escherichia coli. None of the extracts had any activity against Klebsiella pneumoniae. The highest activity was found in the methanol extracts from Bidens pilosa, Psidium guajava, Artemisia afra and Warburgia salutaris. The majority of the antibacterial activity was present in the methanolic, rather than the aqueous extracts.

Ramesh PR, Kumar KS, Rajagopal MR, Balachandran P, Warrier PK. **Managing morphine-induced constipation: a controlled comparison of an Ayurvedic formulation and senna.** J Pain Symptom Manage 1998;16(4):240-4.
Constipation is a frequent cause of distress in advanced cancer. A palliative care unit in Kerala, a southern state of India, conducted a controlled trial comparing a liquid Ayurvedic (herbal) preparation (Misrakasneham) with a conventional laxative tablet (Sofsena) in the management of opioid-induced constipation in patients with advanced cancer. Although there was no statistically significant difference in the apparent degree of laxative action between the two, the results indicate that the small volume of the drug required for effective laxative action, the tolerable taste, the once-daily dose, the acceptable side effect profile, and the low cost make Misrakasneham a good choice for prophylaxis in opioid-induced constipation. There is a need for further studies of Ayurvedic medicines in palliative care.

Randal J. **Diagnosis, Tibetan style, underlies small herbal study of advanced breast cancer [news].** J Natl Cancer Inst 1999;91(7):587-8.

Riggs DR, Dehaven JI, Lamm DL. **Allium sativum (garlic) treatment for murine transitional cell carcinoma.** Cancer 1997;79(10):1987-94.
BACKGROUND: Currently, immunotherapy with Bacillus Calmette-Guerin (BCG) is the most effective treatment for superficial bladder carcinoma, but treatment-related toxicity may limit its use in some patients. Alternative treatments are needed for patients who fail to respond to BCG immunotherapy. Allium sativum (AS), or garlic, is known to have a broad range of biologic activities, including immune stimulation and reported antitumor activity. For these reasons, the authors conducted a series of experiments designed to explore the possible therapeutic effects of AS in the MBT2 murine bladder carcinoma model. METHODS: C3H/HeN mice were randomized prior to initiation of each experimental protocol. Mice received 1 x 10(3) MBT2 cells in 0.1 mL RPMI-1640, administered subcutaneously into the right thigh, on Day 0 of the experiment. AS was injected at the site of tumor transplantation on Day 1 and at 2- to 7-day intervals up to Day 28. To evaluate the effects of oral AS in this model, treatment was initiated 30 days prior to tumor inoculation and continued for 30 days after tumor inoculation. Animals in all experiments were followed for tumor incidence, tumor growth, and survival. RESULTS: In the initial experiments, subcutaneous AS significantly reduced tumor volume compared with the saline control ($P < 0.05$). Unfortunately, treatment-related death was also observed, requiring reduction in the total dose of AS. Animals that received 5 weekly immunizations of AS (5 mg, 5 mg, 1 mg, 1 mg, and 1 mg; cumulative dose = 13 mg) had significantly reduced tumor incidence, tumor growth, and increased survival when compared with animals that received the saline control. No treatment-related deaths were observed with this treatment schedule. To determine whether systemic AS administration might be effective, orally administered AS was tested at doses of 5 mg, 50 mg, and 500 mg per 100 mL of drinking water. Mice that received 50 mg oral AS had significant reductions in tumor volume ($P < 0.05$) when compared with animals that received the saline control, and mice that received 500 mg oral AS had significant reductions in both tumor volume and mortality ($P < 0.05$). CONCLUSIONS: The significant antitumor efficacy of subcutaneous and oral AS warrants further investigation and suggests that AS may provide a new and effective form of therapy for transitional cell carcinoma of the bladder.

Roberge RJ, Leckey R, Spence R, Krenzelok EJ. **Garlic burns of the breast [letter].** Am J Emerg Med 1997;15(5):548.

Robinson M. **Medical therapy of inflammatory bowel disease for the 21st century.** Eur J Surg Suppl 1998;(582):90-8.
Inflammatory bowel disease therapy can be considered in several subcategories, and this review is designed to provide selective updates for some of the most important therapeutic entities currently marketed or soon to be available for the medical management of IBD. Although conventional corticosteroids have been a major component of acute inflammatory bowel disease management, steroids have many serious disadvantages; and toxicity is heightened with chronic steroid therapy. Newer corticosteroids, particularly budesonide, may be less toxic than older agents such as prednisone. Budesonide may be used as an enema in active distal ulcerative colitis (UC) or as delayed release tablets in Crohn's disease (CD). However, budesonide is not completely free from steroid side effects, and may share in some of the toxicity of older corticosteroids, particularly when high dose budesonide is administered. Topical and oral aminosalicylates are widely utilized for the treatment of mild to moderate active UC and mild

active CD, and they also are efficacious for maintenance of IBD remission. Recent data continue to support the concept that higher doses and prolonged use of mesalamine-based drugs are therapeutically superior to lower doses and short term treatment. In addition, the combination of oral and rectal aminosalicylate formulations often succeeds in patients refractory to either used alone. The immunomodulatory drugs azathioprine and 6-mercaptopurine are particularly effective in treating both CD and UC, and methotrexate has also shown some promise in CD therapy. Immunosuppressive therapy for inflammatory bowel disease initially met with strong physician resistance. However, views have shifted in response to positive data on the utility of immunosuppressive agents in many cases of IBD. Although cyclosporine may be used as a 'rescue' medication in some severe IBD cases, it has been associated with severe toxic reactions. Possible candidates for cyclosporine treatment should be offered such therapy only in academic centers highly experienced with the nuances of this modality. Clinical trials of the newer entities IL-10, IL-11, tacrolimus, and anti-TNFalpha, have demonstrated variable efficacy in refractory IBD patients. Anti-TNFalpha has been very impressive, particularly in the presence of fistulizing Crohn's disease. Many physicians have utilized various antibiotics empirically as part of their 'general' management of IBD. Only metronidazole has been adequately studied in controlled CD trials, but other antibiotic studies are pending. Further exploration of antimicrobial treatment for IBD is clearly warranted. Many other investigational agents in disparate pharmaceutical categories have been employed in IBD therapy; and some of these also show varying degrees of promise, including the aloe vera derivative acemannan, several formulations of heparin, and both transdermal and intra-rectal nicotine. Despite the growing list of medications and formulations promoted for the treatment of IBD, no single drug or recognized combination has yet been confirmed as dependably clinically effective. Many additional investigations of IBD medical therapy are needed, including permutations of conventional medications, along with newer agents that may be more precisely targeted to specific aspects of IBD pathophysiology. All physicians who care for UC and CD patients enthusiastically await more optimal regimens for these challenging disorders.

Rosenblatt M, Mindel J. **Spontaneous hyphema associated with ingestion of Ginkgo biloba extract.** N Engl J Med 1997 Apr 10;336:1108.
IPA COPYRIGHT: ASHP A case of spontaneous hyphema associated with ingestion of Ginkoba tablets, an OTC supplement containing 40 mg of concentrated (50:1) extract of the Ginkgo biloba tree, is reported in a 70-yr-old man who took the herbal medication 2 times/day for 1 wk; the potential mechanism for this adverse event is also briefly discussed. The patient's only other medication was aspirin (325 mg tablet/day), taken for 3 yr after coronary artery bypass surgery with no history of eye trauma, ischemia, or vascular occlusion. The patient stopped taking the ginkgo extract but continued to take daily aspirin, and there was no recurrence of bleeding over a 3-month follow-up period.

Rui H. **Research and development of cancer chemopreventive agents in China.** J Cell Biochem Suppl 1997;27:7-11.
Since the late 1970s, a comprehensive search for cancer chemopreventive agents has been established in our Institute. A series of new retinoids have been synthesized and screened on the basis of established methodologies of experimental chemoprevention in vitro as well as in vivo. Pharmacological studies demonstrated that N-4-(carboxyphenyl)retinamide (RII) induces cell

differentiation of HL-60 cells and inhibits dimethylnitrosamine-induced carcinogenesis of the forestomach in mice, 7,12-dimethylbenz[a]anthracene (DMBA)-induced papilloma in mouse skin, and DMBA-induced carcinogenesis of the buccal pouch in Syrian golden hamsters. It significantly promoted lymphoblastic transformation and activated macrophages. In further studies, RII significantly inhibited ornithine decarboxylase activity. After 6 months of chronic toxicological studies in rats and dogs, RII was recommended for clinical trial. Phase II studies found that RII is effective in treating oral and vulvar leukoplakia. It is also effective in treating myelodysplastic syndrome and dysplasia of uterine cervix. The chalcone retinoidal compounds were discovered when the search for new retinoids with less toxicity and higher potency led to third-generation retinoids, which were synthesized and screened. Structure-activity relationship studies found that 3,5-di-tert-butyl-4-methoxy-4-carboxyl chalcone (R9158) is the most active inhibitor of a variety of cancer cells. It has no effect on the Colony Forming Unit-Granulocyte/Macrophage (CFU-GM) of bone marrow in mice. In in vivo studies, R9158 showed a remarkable inhibition of chondrosarcoma in rats. It had no cross-resistance to vincristine, but was cross-resistant to all-trans retinoic acid. Red ginseng, a processed Panax ginseng, is considered a typical tonic in traditional Chinese medicine. Our studies demonstrated that red ginseng extract inhibited DMBA-induced skin papilloma significantly. Experiments showed that glycyrrhetinic acid inhibited croton oil-induced ear edema in mice. It also inhibited epidermal ornithine decarboxylase as well as the rapid DNA damage induced by the carcinogen benzo[a]pyrene (B[a]P). Our pharmacological studies demonstrated that Chinese gallotannin inhibited the malignant transformation of B[a]P-induced V79 cells in vitro and B[a]P-induced pulmonary adenoma in A/J mice in vivo significantly.

Saitoh K, Kase Y, Ishige A, Komatsu Y, Sasaki H, Shibahara N. **Effects of Keishi-ka-shakuyaku-to (Gui-Zhi-Jia-Shao-Yao-Tang) on diarrhea and small intestinal movement.** Biol Pharm Bull 1999;22(1):87-9.
The present study was conducted to determine the characteristics of the effects of Keishi-ka-shakuyaku-to (Gui-Zhi-Jia-Shao-Yao-Tang; TJ-60) on diarrhea. Significant repression was noted by TJ-60 at 1000 mg/kg, p.o. for diarrhea induced by pilocarpine, barium chloride or castor oil. Under normal conditions, TJ-60 did not influence small intestinal transit by its oral treatment even at 1000 mg/kg, however, it dose-dependently improved the acceleration of such transit caused by neostigmine. TJ-60 did not influence the resting tonus in isolated small intestine, but did selectively inhibit low frequency electrostimulated contractions. These results indicate that the antidiarrheal effects of TJ-60 may be due to the inhibition of excessively accelerated small intestinal movement, and that the inhibition of acetylcholine release by parasympathetic nerves is partly involved in the mechanism of this antidiarrheal action.

Sakamoto S, Mitamura T, Iwasawa M, Kitsunai H, Shindou K, Yagishita Y, Zhou YF, Sassa S. **Conservative management for perimenopausal women with uterine leiomyomas using Chinese herbal medicines and synthetic analogs of gonadotropin-releasing hormone.** In Vivo 1998;12(3):333-7.
The effects of a long-term intranasal administration of each of the gonadotropin-releasing hormone analogs, buserelin and nafarelin on uterine leiomyomas after conservative treatment using Chinese herbal medicines, Keishi-bukuryo-gan and Shakuyaku-kanzo-to were investigated in 30 perimenopausal women with leiomyomas. Hypermenorrhea and/or dysmenorrhea as a chief

complaint was moderately improved by the treatment using Chinese herbal medicines in more than 60% of the patients with less than fist-sized leiomyomas, but not the over fist-sized. Afterwards, continuous treatment using analogs produced a long-term reduction in leiomyomas (less than 60%) along with decreases in the serum levels of luteinizing hormone, follicle-stimulating hormone, estradiol, and the tumor marker CA-125, and adverse effects including slight boneloss. Long-term treatment using Chinese herbal medicines and gonadotropin-releasing hormone analogs for the management of uterine leiomyomas could be beneficial for patients a few years before menopause, though possible side effects of this treatment should be monitored.

Sakuragawa N. **Regulation of thrombosis and hemostasis by antithrombin.** Semin Thromb Hemost 1997;23(6):557-62.
In this article, three cases, with antithrombin (AT) abnormality "Toyama" (type IIb), AT abnormality "Aomori" (type IIa), and congenital AT deficiency (type I) with pregnancy and delivery managed with administration of both AT concentrates and low-molecular-weight heparin, are described. Additionally, a case of AT-producing hepatocellular carcinoma, the first case in the world literature, is reported. Following these clinical reports, the development of AT studies on heparin cofactor II, characteristics of the vessel wall related to coagulation-fibrinolysis, and the development of the treatment of thrombosis with low-molecular-weight heparin and herbal drugs are discussed.

Sanae F, Hayashi H, Chisaki K, Komatsu Y. **Effects of Saiko-ka-ryukotsu-borei-to, a Japanese Kampo medicine, on tachycardia and central nervous system stimulation induced by theophylline in rats and mice.** Jpn J Pharmacol 1999;79(3):283-8.
Effects of Saiko-ka-ryukotsu-borei-to (SRBT) on theophylline-induced tachycardia in anesthetized rats and theophylline-induced locomotion and convulsions in mice were examined. An intraduodenal administration of SRBT (1 g/kg) prevented theophylline (5 mg/kg, i.v.)-induced tachycardia in rats. SRBT also attenuated an increase in arterial blood pressure with a slow reduction in heart rate of rats treated with theophylline, with no influence on the plasma level of theophylline. However, SRBT did not change the beating rate of right atrium isolated from rats in the absence or presence of theophylline or isoproterenol. The locomotor activity of theophylline in mice was reduced by the treatment with SRBT. Furthermore, the latency of convulsions in mice induced by administration of theophylline at a higher dose (240 mg/kg, i.p.) was prolonged by treatment with SRBT (1 g/kg, p.o.) and seven out of fifteen mice were saved from death due to convulsions. These results suggest that theophylline-induced tachycardia and central nervous stimulation are suppressed by SRBT and that SRBT may reduce the undesirable actions of theophylline on the cardiovascular and central nervous systems.

Sanyaolu AO, Fagbenro-Beyioku AF, Oyibo WA. **Induced immunity to Plasmodium yoelli nigeriensis in albino mice by antigenic mice organs.** East Afr Med J 1997;74(9):566-9.
Antigenic materials prepared from parasite infected and non-infected tissue (blood), organs (spleen, liver, lung) and whole mouse burnt with or without Aframomum melegmeta (Alligator Pepper) were tested whether they could elicit immune response to Plasmodium yoelli nigeriensis in albino mice. This investigation is in line with the practice of traditional medicine in the western part of Nigeria where burnt herbal preparation are introduced into patient through body cuts known as "Gbere" for protection and therapy against infection. Results from the study

unexpectedly showed that immune response was elicited against malaria parasite by the uninfected antigenic material prepared from spleen and whole mouse. Aframomum melegmeta on its own lysed the red blood cells and played a doubtful role in inducing immunity.

Sata N, Matsunaga S, Fusetani N, Nishikawa H, Takamura S, Saito T. **New antifungal and cytotoxic steroidal saponins from the bulbs of an elephant garlic mutant.** Biosci Biotechnol Biochem 1998;62(10):1904-11.
BIOSIS COPYRIGHT: BIOL ABS. Saponins in bulbs of a mutant of elephant garlic were investigated, and three new steroidal saponins named yayoisaponins A-C were obtained together with the known dioscin and aginoside. Their structures, including the relative stereochemistry, were elucidated by spectral data interpretation, while the absolute stereochemistry of the sugar moieties was assigned on the basis of a chiral gas chromatographic analysis of the acid hydrolysates. Yayoisaponins A-C and aginoside exhibited not only in vitro cytotoxicity against P388 cells at 2.1 mug/ml, but also antifungal activity against Mortierella ramanniana at 10 mug/disk.

Satyan KS, Jaiswal AK, Ghosal S, Bhattacharya SK. **Anxiolytic activity of ginkgolic acid conjugates from Indian Ginkgo biloba.** Psychopharmacology (Berl) 1998;136(2):148-52.
Ginkgolic acid conjugates (GAC) (6-alkylsalicylates, namely n-tridecyl-, n-pentadecyl-, n-heptadecyl-, n-pentadecenyl- and n-heptadecenylsalicylates) isolated from the leaves of Indian Ginkgo biloba Linn., (IGb) were tested for their putative role in anxiety in rats. Elevated plus maze, open-field behaviour, novelty-induced feeding latency and social interaction were the rodent behavioural models used in this study. GAC (0.3 and 0.6 mg/kg, each, p.o.) on single acute administration, showed dose-related changes in the behaviour. GAC (0.6 mg/kg) and DZ augmented open arm entries, the open arm/closed arm entries ratio and increased time spent in the open arm on the elevated plus maze. In the open field, GAC (0.6 mg/kg) and DZ significantly increased ambulation and reduced the immobility time. EGb 761 showed a similar profile. GAC (0.6 mg/kg) and DZ significantly attenuated the increased latency to feed in novel environment. By contrast, EGb 761 and Ginkocer further augmented feeding latency. None of the drugs tested showed any significant effect in the social interaction test. GAC showed consistent and significant anxiolytic activity in all the variables investigated. By contrast, EGb 761 and Ginkocer, which are devoid of GAC, did not evoke significant activity. However, increased rearing and decreased immobility time only in open field behaviour shown by EGb 761 may be due to some antianxiety activity of a lesser degree. Our observations suggest that GAC may be the active constituents of Ginkgo biloba responsible for the anxiolytic activity.

Schaffer EM, Liu JZ, Milner JA. **Garlic powder and allyl sulfur compounds enhance the ability of dietary selenite to inhibit 7,12-dimethylbenz[a]anthracene-induced mammary DNA adducts.** Nutr Cancer 1997;27(2):162-8.
These studies examined the ability of garlic powder or allyl sulfur compounds to modify selenite protection against 7,12-dimethylbenz[a]anthracene (DMBA)-induced mammary epithelial cell DNA adducts. In Study 1, female rats (n = 5) were fed diets containing sodium selenite at 0.1, 0.5, or 1.0 mg Se/kg and garlic powder at 0, 20, or 40 g/kg diet. Total DNA adducts correlated inversely with selenite or garlic powder intake. Garlic powder enhanced the selenite inhibition of mammary DNA adducts. In Study 2, selenite (2.0 mg Se/kg diet), garlic powder (20 g/kg diet),

water-soluble S-allyl cysteine (SAC; 5.2 mumol/kg diet), and oil-soluble diallyl disulfide (DADS; 5.2 mumol/kg diet) inhibited ($p < 0.05$) total DNA adducts by 45%, 40%, 80%, and 75%, respectively. Combining selenite with garlic powder, SAC, or DADS further inhibited DNA adducts. Selenite, but not garlic powder, SAC, or DADS, enhanced liver glutathione S-transferase and uridine diphosphate-glucuronosyltransferase activities. Selenite, garlic powder, SAC, or DADS did not affect liver cytochrome P-450 1A1 activities. The present studies provide evidence that synergistic protection against the initiation of DMBA carcinogenesis occurs when selenite is supplemented in conjunction with garlic or its allyl sulfur components.

Schoepp G. **Is St. John's wort effective for the treatment of depression, and how should patients be counselled on its use?** Pharm Pract 1998 Aug;14:25-7.
IPA COPYRIGHT: ASHP Information on the use of St. John's wort (Hypericum perforatum) for the treatment of depression is provided, including an overview of clinical studies of H. perforatum in the treatment of depression, side effects associated with H. perforatum, possible drug interactions, dosage and administration information, and advice for pharmacists in selecting H. perforatum products and in counseling patients using this herbal product for the treatment for depression.

Scibilia J, Galdi E, Biscaldi G, Moscato G. **Occupational asthma caused by black henna.** Allergy 1997;52(2):231-2.

Segars LW. **Saw palmetto extracts for benign prostatic hyperplasia.** J Fam Pract 1999;48(2):88-9.

Seth SD, Maulik M, Katiyar CK, Maulik SK. **Role of Lipistat in protection against isoproterenol induced myocardial necrosis in rats: a biochemical and histopathological study.** Indian J Physiol Pharmacol 1998;42(1):101-6.
A test drug (Lipistat) comprising of equal-proportions of extracts of Terminalia arjuna, Inula racemosa Hook, latex of Commiphora mukul, in three different doses (225 mg/kg; 350 mg/kg; 450 mg/kg) were administered orally daily for 6 days a week for 60 days in rats. Thereafter, the rats were subjected to isoproterenol (ISO) induced (85 mg/kg, s.c. for 2 days) myocardial necrosis. Gross and microscopic examinations (histopathology) were done along with estimations of myocardial tissue high energy phosphates (HEP) stores and lactate content. Gross examination showed significant ($P < 0.05$) cardioprotection in Lipistat treated animals. On microscopic examination no statistically significant reduction in myocardial damage by 350 and 450 mg/kg of Lipistat were observed although loss of myocardial HEP stores and accumulation of lactate were significantly prevented. The results of the present study suggest the potential usefulness of Lipistat in the prevention of ischemic heart disease.

Shamaan NA, Kadir KA, Rahmat A, Ngah WZ. **Vitamin C and aloe vera supplementation protects from chemical hepatocarcinogenesis in the rat.** Nutrition 1998;14(11-12):846-52.
The effects of vitamin C and aloe vera gel extract supplementation on induced hepatocarcinogenesis in male Sprague-Dawley rats (120-150 g) by diethylnitrosamine (DEN) and 2-acetylaminofluorene (AAF) was investigated. The severity of the carcinogenesis process was determined by measuring gamma-glutamyl transpeptidase (GGT) and the placental form of

glutathione S-transferase (GSTP) histochemically in situ and in plasma and liver fractions. In addition, plasma alkaline phosphatase (ALP) and liver microsomal uridine diphosphate glucuronyl transferase (UDPGT) activity were also determined. Administration of DEN/AAF caused an increase in the surface area and number of enzyme-positive foci (both GGT and GSTP) compared with control. Supplementation of vitamin C or aloe vera gel extract to the cancer-induced rats suppressed this increase significantly ($P < 0.05$; $P < 0.001$). Increases in liver UDPGT, GGT, and GSTP activities were also observed with cancer induction that were again suppressed with either vitamin C or aloe vera gel supplementation. Plasma GGT in the DEN/AAF rats were determined monthly for the duration of the experiment and found to be reduced as early as 1 mo with aloe vera gel supplementation and 2 mo with vitamin C supplementation. In conclusion, vitamin C and aloe vera gel extract supplementation were found to be able to reduce the severity of chemical hepatocarcinogenesis.

Shamosh JA. **Herbal first aid.** J Emerg Nurs 1998;24(6):553-4.

Sharma OP, Dawra RK, Kurade NP, Sharma PD. **A review of the toxicosis and biological properties of the genus Eupatorium.** Nat Toxins 1998;6(1):1-14.
Eupatorium genus grows wild in many parts of the world. A number of species of Eupatorium are toxic to grazing animals. Milk sickness in humans is caused by ingestion of milk of the animals reared on the pastures infested with Eupatorium rugosum (white snakeroot). While some information is available on the toxins in various species of Eupatorium, ambiguities still persist in extrapolation of the data to field incidence of toxicosis. Eupatorium genus has been used for its medicinal properties for many decades. A number of bioactive natural products have been reported in the extracts of Eupatorium spp. and the genus is a promising bioresource for preparation of drugs and value-added products.

Sharma SS, Gupta YK. **Reversal of cisplatin-induced delay in gastric emptying in rats by ginger (Zingiber officinale).** J Ethnopharmacol 1998;62(1):49-55.
Cisplatin causes nausea, vomiting and inhibition of gastric emptying. We have demonstrated the antiemetic effect of the acetone and ethanolic extract of ginger (Zingiber officinale, Roscoe, Zingiberacae) against cisplatin-induced emesis in dogs. In the present study, the acetone and 50% ethanolic extract of ginger in the doses of 100, 200 and 500 mg/kg (p.o.) and ginger juice, in the doses of 2 and 4 ml/kg, were investigated against cisplatin effect on gastric emptying in rats. All three ginger preparations significantly reversed cisplatin-induced delay in gastric emptying. The ginger juice and acetone extract were more effective than the 50% ethanolic extract. The reversal produced by the ginger acetone extract was similar to that caused by the 5-HT3 receptor antagonist ondansetron; however, ginger juice produced better reversal than ondansetron. Therefore, ginger, an antiemetic for cancer chemotherapy, may also be useful in improving the gastrointestinal side effects of cancer chemotherapy.

Sharma SS, Kochupillai V, Gupta SK, Seth SD, Gupta YK. **Antiemetic efficacy of ginger (Zingiber officinale) against cisplatin-induced emesis in dogs.** J Ethnopharmacol 1997;57(2):93-6.
Effect of ginger (Zingiber officinale Roscoe, Zingiberaceae) extracts (acetone, 50% ethanolic and aqueous) were investigated for antiemetic activity against emesis induced by 3 mg/kg

cisplatin (the 100% emetic dose i.v.) in-healthy mongrel dogs. The acetone and 50% ethanolic extract at the doses of 25, 50, 100 and 200 mg/kg p.o. exhibited significant protection while aqueous extract at these doses was ineffective against cisplatin emesis. The acetone extract was more effective than ethanolic extract. However, both were less effective when compared to 5-HT3 receptors antagonist-granisetron. Neither of the ginger extract was effective against apomorphine-induced emesis. The findings suggest that ginger could be an effective and cheap antiemetic adjunct to cancer chemotherapy.

Sharpley AL, Mcgavin CL, Whale R, Cowen PJ. **Antidepressant-like effect of Hypericum perforatum (St John's wort) on the sleep polysomnogram.** Psychopharmacology (Berl) 1998;139(3):286-7.
We studied the effect of two doses (0.9 mg and 1.8 mg) of Hypericum perforatum (St John's wort) on the sleep polysomnogram of healthy subjects using a placebo-controlled, cross-over design. Both doses of hypericum significantly increased the latency to rapid eye movement (REM) sleep without producing any other effect on sleep architecture. Our data are consistent with the proposed clinical antidepressant efficacy of hypericum, and raise the possibility that its pharmacological mechanism of action may be similar to that of conventional antidepressant medication.

Shimada H, Tyler VE, McLaughlin JL. **Biologically active acylglycerides from the berries of saw-palmetto (Serenoa repens).** J Nat Prod 1997;60(4):417-8.
Brine shrimp lethality-directed fractionation of the 95% EtOH extract of the powdered, dried berries of Serenoa repens (Bart.) Small (saw-palmetto) (Palmae) led to the isolation of two monoacylglycerides, 1-monolaurin (1) and 1-monomyristin (2). Compounds 1 and 2 showed moderate biological activities in the brine shrimp lethality test and against renal (A-498) and pancreatic (PACA-2) human tumor cells; borderline cytotoxicity was exhibited against human prostatic (PC-3) cells. The fruits and extracts of saw-palmetto are taken orally as an herbal medicine to prevent prostatic hyperplasias.

Shimizu T, Tomioka H, Sato K, Sano C, Akaki T, Dekio S, Yamada Y, Kamei T, Shibata H, Higashi N. **Effects of the Chinese traditional medicine mao-bushi-saishin-to on therapeutic efficacy of a new benzoxazinorifamycin, KRM-1648, against Mycobacterium avium infection in mice.** Antimicrob Agents Chemother 1999;43(3):514-9.
The Chinese traditional medicine mao-bushi-saishin-to (MBST), which has anti-inflammatory effects and has been used to treat the common cold and nasal allergy in Japan, was examined for its effects on the therapeutic activity of a new benzoxazinorifamycin, KRM-1648 (KRM), against Mycobacterium avium complex (MAC) infection in mice. In addition, we examined the effects of MBST on the anti-MAC activity of murine peritoneal macrophages (M phi s). First, MBST significantly increased the anti-MAC therapeutic activity of KRM when given to mice in combination with KRM, although MBST alone did not exhibit such effects. Second, MBST treatment of M phi s significantly enhanced the KRM-mediated killing of MAC bacteria residing in M phi s, although MBST alone did not potentiate the M phi anti-MAC activity. MBST-treated M phi s showed decreased levels of reactive nitrogen intermediate (RNI) release, suggesting that RNIs are not decisive in the expression of the anti-MAC activity of such M phi populations. MBST partially blocked the interleukin-10 (IL-10) production of MAC-infected M phi s without

affecting their transforming growth factor beta (TGF-beta)-producing activity. Reverse transcription-PCR analysis of the lung tissues of MAC-infected mice at weeks 4 and 8 after infection revealed a marked increase in the levels of tumor necrosis factor alpha, gamma interferon (IFN-gamma), IL-10, and TGF-beta mRNAs. KRM treatment of infected mice tended to decrease the levels of the test cytokine mRNAs, except that it increased TGF-beta mRNA expression at week 4. MBST treatment did not affect the levels of any cytokine mRNAs at week 8, while it down-regulated cytokine mRNA expression at week 4. At week 8, treatment of mice with a combination of KRM and MBST caused a marked decrease in the levels of the test cytokines mRNAs, especially IL-10 and IFN-gamma mRNAs, although such effects were obscure at week 4. These findings suggest that down-regulation of the expression of IL-10 and TGF-beta is related to the combined therapeutic effects of KRM and MBST against MAC infection.

Shuster J. **Herbal remedies and seizures.** Nursing 1997;27(4):75.

Siegers CP, Steffen B, Robke A, Pentz R. **The effects of garlic preparations against human tumor cell proliferation.** Phytomedicine 1999;6(1):7-11.
Epidemiological studies in China provide reason to suspect that a rich garlic content in the diet might reduce the proliferation of tumors in humans. We conducted experiments on human tumor cell lines and determined the influence of a garlic powder preparation, a garlic extract (reported as 8-10% L(+)-alliin enriched), and a combination thereof, on cellular proliferation in cell cultures, employing the widely used indirect neutral red procedure. Garlic powder failed to inhibit the growth of human hepatoma HepG2 or human colorectal carcinoma Caco2 cells at concentrations of up to 1000 micrograms/ml. Garlic extract, in which the alliin content was highly enriched was also unable to inhibit the growth of these cells. However, when the garlic extract was supplemented with garlic powder (to 10% final concentration) there was a concentration-dependent clear inhibition of tumor cell growth (IC50 values of 330 micrograms/ml for HepG2 and 480 micrograms/ml for Caco-2 cells). The growth of the human lymphatic leukemia cell line CCRF CEM was significantly inhibited in a dose-dependent manner by both garlic powder and garlic extract at concentrations as low as 30 micrograms/ml. However, no potentiation of this effect occurred upon mixing of the two preparations. Our results suggest that the antiproliferative effects of garlic may be due to breakdown products of alliin, such as allicin or polysulfides, rather than alliin itself, since the addition of an alliinase system (garlic powder) to an alliin enriched preparation without alliinase (garlic extract) potentiated the effects observed with the two preparations alone.

Sigounas G, Hooker JL, Li W, Anagnostou A, Steiner M. **S-allylmercaptocysteine, a stable thioallyl compound, induces apoptosis in erythroleukemia cell lines.** Nutr Cancer 1997;28(2):153-9.
The antiproliferative potential of S-allylmercaptocysteine (SAMC), a stable organosulfur compound of aged garlic extract, has been investigated using two erythroleukemia cell lines, HEL and OCIM-1. It induces a dose-dependent inhibition of cell growth with a 50% lethal dose of 0.046 mM for OCIM-1 cells and 0.093 mM for HEL cells. [3H]thymidine incorporation was reduced in cells treated with this thioallyl compound, and analysis of high-molecular-weight DNA showed fragmentation compatible with apoptosis. Flow cytometric analyses of DNA

revealed an abnormal cell cycle progression in both types of erythroleukemia cells, with the major portion of the unsynchronized cells in the G2/M phase. Measurement of acid-soluble free sulfhydryl groups showed an initial increase in response to SAMC followed by a progressive dose-dependent decrease with extended incubation of cells. We conclude from these studies that SAMC is an effective antiproliferative agent against erythroleukemia cells that induces cell death by apoptosis.

Sigounas G, Hooker J, Anagnostou A, Steiner M. **S-allylmercaptocysteine inhibits cell proliferation and reduces the viability of erythroleukemia, breast, and prostate cancer cell lines.** Nutr Cancer 1997;27(2):186-91.
Organosulfur compounds are the biologically active components of allium vegetables. Many health benefits have been ascribed to them, including inhibition of carcinogenesis. Inasmuch as several of these thioallyl compounds are quite unstable and others are rapidly inactivated in the body, we have investigated one of the stable components present in aged garlic extract, S-allylmercaptocysteine (SAMC), in an effort to determine whether it can inhibit proliferation of cancer cells. Proliferation and viability of two erythroleukemia cell lines, HEL and OCIM-1, two hormone-responsive breast and prostate cancer cell lines, MCF-7 and CRL-1740, respectively, and normal human umbilical vein endothelial cells in response to different concentrations of SAMC were studied for up to two weeks. There were variations in sensitivity to this organosulfur compound in the different cell lines examined, but the two hormone-responsive cancer cell lines of breast and prostate clearly were far more susceptible to the growth-inhibitory influence of the thioallyl compound. The antiproliferative effect of SAMC was limited to actively growing cells. Human umbilical vein endothelial cells that had reached confluence escaped the reduction in viability so noticeable in the cancer cell lines tested. Our studies thus give evidence of a direct effect of SAMC on established cancer cells.

Silva O, Barbosa S, Diniz A, Valdeira ML, Gomes E. **Antiviral activity of plant extracts against Herpes simplex virus type 1 and African swine fever virus.** Int J Pharmacogn 1997;35(1):12-6.
IPA COPYRIGHT: ASHP Twenty-eight extracts prepared from plants used in traditional African medicine and from the Portuguese plant Rhamnus glandulosa Ait. were screened in order to assay their possible antiviral activity against Herpes simplex virus type 1 (HSV-1) and/or African swine fever virus (ASFV). Twelve of these extracts exhibited virucidal activity against HSV-1 and 6 against ASFV. Further studies showed that 13 of the tested extracts inhibited HSV-1 infection, some having a significant effect upon this virus, e.g. Senna podocarpa and Rhamnus glandulosa Ait. Four of the 21 tested extracts inhibited ASFV infection.

Simpson D. **Buchu--South Africa's amazing herbal remedy.** Scott Med J 1998;43(6):189-91.
Buchu leaves and oil of buchu were used by the indigenous people of South Africa for hundreds of years. The medicinal use of buchu was taken up by the early Dutch settlers and later introduced into the pharmaceutical industry in the UK. Buchu preparations are now used as a diuretic and for a wide range of conditions including stomach aches, rheumatism, bladder and kidney infections and coughs and colds.

Sinclair S. **Chinese herbs: a clinical review of Astragalus, Ligusticum, and Schizandrae.** Altern Med Rev 1998;3(5):338-44.
Although Astragalus, Ligusticum and Schizandrae have a long history of medicinal use within the traditional Chinese system, only recently has the West begun to understand their pharmacological possibilities and clinical applications. Astragalus has demonstrated a wide range of immunopotentiating effects and has proven efficacious as an adjunct cancer therapy. Ligusticum, and its active components, have been investigated for enhancement of the immune system, treatment of ischemic disorders, and as an anti-inflammatory. Clinically, the hepato-protective and antioxidant actions of Schizandrae have proven beneficial in the treatment of chronic viral hepatitis.

Singh A, Shukla Y. **Antitumor activity of diallyl sulfide in two-stage mouse skin model of carcinogenesis.** Biomed Environ Sci 1998;11(3):258-63.
It has been reported that diallyl sulfide (DAS), a sulfur-containing volatile compound in garlic (Allium sativum), exerts anticarcinogenic activity in various rodent tumor models. In the present study, the antitumor property of DAS was tested in Swiss albino mice in the two stage initiation-promotion mouse skin carcinogenesis. Skin cancers were initiated topically with a single subcarcinogenic dose (52 micrograms) of 7, 12-dimethyl benz (a) anthracene (DMBA). Promotion was performed by twice weekly applications of 12-O-tetradecanoyl phorbol-13-acetate (TPA) at a dose of 5 micrograms/animal for 32 weeks. DAS was applied topically (250 micrograms/animal) thrice weekly for 3 weeks for anti-initiating and 1 h prior to each promotion treatment for anti-promoting studies. The results showed that the treatment schedule of DAS can effectively delay the onset of tumorigenesis and reduce the cumulative number of tumors and the average number of tumors per mouse. In groups in which DAS applied prior to initiation or promotion, a significant population of the animals remained tumor-free till the termination of experiment. These findings suggest that DAS can effectively inhibit chemically induced mouse skin carcinogenesis.

Singh A, Shukla Y. **Antitumour activity of diallyl sulfide on polycyclic aromatic hydrocarbon-induced mouse skin carcinogenesis.** Cancer Lett 1998;131(2):209-14.
Diallyl sulfide (DAS), a major flavour component of garlic, is known to modulate xenobiotic metabolism and possess antitoxic, bactericidal, antineoplastic, hypolipidemic and hypocholesteromic effects. In the present study, the anticarcinogenic activity of DAS on a 7,12-dimethylbenzanthracene (DMBA)- or benzo[a]pyrene (B(a)P)-induced mouse skin model of carcinogenesis was evaluated. DAS was applied topically either 1 h prior to or 1 h after the administration of DMBA or B(a)P. A significant protection from neoplasia was observed in DAS- and DMBA/B(a)P-exposed animals when DAS was applied topically compared to the animals exposed only to DMBA/B(a)P. In the animals where DAS was applied 1 h prior to the application of DMBA, a lower magnitude of neoplasia was recorded in terms of the cumulative number of tumours and average number of tumours per mouse during the entire period of study (28 weeks) compared to the animals exposed to DAS 1 h later, while in B(a)P-exposed animals, the antitumorigenic potential of DAS was more evident in the mice treated with DAS 1 h after the B(a)P exposure compared to the animals treated with DAS 1 h prior to B(a)P. The antitumour activity of DAS was of a much higher magnitude in B(a)P-induced carcinogenesis in comparison to animals exposed to DMBA in terms of tumour incidence, cumulative number of tumours and

average number of tumours per mouse. The results suggest that DAS has a protective effect in PAH-induced mouse skin carcinogenesis.

Singh SV, Pan SS, Srivastava SK, Xia H, Hu X, Zaren HA, Orchard JL. **Differential induction of NAD(P)H:quinone oxidoreductase by anti-carcinogenic organosulfides from garlic.** Biochem Biophys Res Commun 1998;244(3):917-20.
This study was undertaken to elucidate the mechanism of organ specificity and differential efficacy of garlic organosulfides (OSCs) [diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATS), dipropyl sulfide (DPS) and dipropyl disulfide (DPDS)] in preventing benzo(a)pyrene (BP)-induced tumorigenesis in mice. The results of the present study reveal a good correlation between chemopreventive efficacies of garlic OSCs and their inductive effects on the expression of NAD(P)H:quinone oxidoreductase (NQO), an enzyme implicated in the detoxification of activated quinone metabolites of BP. Treatment of mice with DADS and DATS, which are potent inhibitors of BP-induced forestomach tumorigenesis, resulted in a statistically significant increase (2.4- and 1.5-fold, respectively) in forestomach NQO activity. In addition, DADS and DATS were much more potent inducers of forestomach NQO activity than DAS, which is a weak inhibitor of BP-induced forestomach tumorigenesis than the former compounds. Propyl-group containing OSCs (DPS and DPDS), which do not inhibit BP-induced tumorigenesis, did not affect forestomach NQO activity. Similar to forestomach, a good correlation was also observed between effects of these OSCs against BP-induced pulmonary tumorigenesis and their effects on NQO expression in the lung. For example, treatment of mice with DAS, which is a potent inhibitor of BP-induced pulmonary tumorigenesis, resulted in about 3.2-fold increase in pulmonary NQO activity. On the other hand, this activity was increased by about 1.5-fold upon DATS administration, which does not inhibit BP-induced cancer of the lung. In conclusion, our results suggest that induction of NQO may be important in anti-cancer effects of garlic OSCs.

Smeaton J. **Changing attitudes toward hysterectomy.** Aust J Pharm 1998 Mar;79:264-7.
IPA COPYRIGHT: ASHP Present attitudes regarding the hysterectomy as a treatment option for various female reproductive conditions are discussed; the various types of hysterectomies, changing attitudes toward the hysterectomy, and the use of various treatment options, including diet, normalization of estrogen levels, and herbal remedies, to prevent the need for a hysterectomy are described.

Soni KB, Lahiri M, Chackradeo P, Bhide SV, Kuttan R. **Protective effect of food additives on aflatoxin-induced mutagenicity and hepatocarcinogenicity.** Cancer Lett 1997;115(2):129-33.
Food additives such as turmeric (Curcuma longa), and active ingredient curcumin (diferuloyl methane), asafoetida (flavouring agent), butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT) and ellagic acid were found to inhibit the mutagenesis induced by aflatoxin B1 (AFB1) (0.5 microg/plate) in Salmonella tester strains TA 98 and TA 100. Turmeric and curcumin, which were the most active, inhibited mutation frequency by more than 80% at concentrations of 2 microg/plate. Other food additives were also significantly effective. Dietary administration of turmeric (0.05%), garlic (0.25%), curcumin and ellagic acid (0.005% each) to rats significantly reduced the number of gammaglutamyl transpeptidase-positive foci induced by AFB1 which is considered as the precursor of hepatocellular neoplasm. These results indicate the

usefulness of antioxidant food additives in ameliorating aflatoxin-induced mutagenicity and carcinogenicity.

Srivastava SK, Hu X, Xia H, Zaren HA, Chatterjee ML, Agarwal R, Singh SV. **Mechanism of differential efficacy of garlic organosulfides in preventing benzo(a)pyrene-induced cancer in mice.** Cancer Lett 1997;118(1):61-7.
The mechanism of differential efficacies of diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATS), dipropyl sulfide (DPS) and dipropyl disulfide (DPDS) in preventing benzo(a)pyrene (BP)-induced cancer in mice has been investigated by determining their effects on the enzymes of BP activation/inactivation pathways. With the exception of DATS, treatment of mice with other organosulfides (OSCs) caused a small but significant increase (37-44%) in hepatic ethoxyresorufin O-deethylase (EROD) activity. However, the forestomach EROD activity did not differ significantly between control and treated groups. Only DAS treatment caused a modest but statistically significant reduction (about 25%) in pulmonary EROD activity. These results suggest that while reduction of EROD activity may, at least in part, contribute to the DAS-mediated inhibition of BP-induced lung cancer, anticarcinogenic effects of OSCs against BP-induced forestomach carcinogenesis seems to be independent of this mechanism. Treatment of mice with DAS, DADS and DATS resulted in a significant increase, as compared with control, in both hepatic (3.0-, 3.2- and 4.4-fold, respectively) and forestomach (1.5-, 2.7- and 2.7-fold, respectively) glutathione transferase (GST) activity toward anti-7beta,8alpha-dihydroxy-9alpha,10alpha-oxy-7,8,9,10-tetrahydr- obenzo(a)pyrene (anti-BPDE), which is the ultimate carcinogen of BP. The pulmonary GST activity was not increased by any of the OSCs. Even though epoxide hydrolase (EH) activity was differentially altered by these OSCs, a correlation between chemopreventive efficacy of OSCs and their effects on EH activity was not apparent. The results of the present study suggest that differences in the ability of OSCs to modulate GST activity toward anti-BPDE may, at least in part, account for their differential chemopreventive efficacy against BP-induced cancer in mice.

Sugiura Y, Ohashi Y, Nakai Y. **The herbal medicine, sairei-to, prevents endotoxin-induced otitis media with effusion in the guinea pig.** Acta Otolaryngol Suppl (Stockh) 1997;531:21-33.
With current pharmacotherapy, otitis media with effusion (OME) is often recurrent and even develops to become chronic. There is now considerable experimental and clinical evidence that the cilia in the tubotympanum play an important part in the prevention of OME. A herbal medicine, sairei-to, has been shown to stimulate the ciliary activity in vitro, and oral administration of the medicine also stimulated the ciliary activity in the tubotympanum rather than physiological states. This study was designed to investigate whether oral administration of sairei-to could prevent experimental OME in the guinea pig. A total of 120 guinea pigs were used. The control group was treated with intratympanic injection of 0.1 ml of physiologic saline solution. The saline-control group was treated with oral administration of physiologic saline solution for 14 successive days. The low-dosage group and the high-dosage group were treated with oral administration of 120 and 600 mg/kg of sairei-to for 14 successive days, respectively. The saline-control group, the low-dosage group and the high-dosage group were then treated with intratympanic injection of 0.1 ml of lipopolysaccharide solution (100 micrograms/ml) derived from Klebsiella pneumoniae. All 10 animals from the 4 groups were sacrificed 1, 3, and 7 days after the intratympanic injection, to examine ciliary activity, mucociliary clearance time,

and mucosal pathology of the tubotympanum. The saline-control group exhibited middle ear effusions and pathologies similar to human OME. The incidence of middle ear effusions in the low-dosage and the high-dosage groups was somewhat reduced compared with the saline-control group. The ciliary activity in the tubotympanum was significantly reduced in the saline-control and low-dosage groups compared with the normal-control group. By contrast, the magnitude of reduction in ciliary activity was much smaller in the high-dosage group. The ciliary activity especially in the Eustachian tube and the middle ear close to the tympanic orifice at 3 and 7 days in the high-dosage group was not significantly different from that in the normal-control group. Mucociliary clearance time in the high-dosage group was not different from that in the normal-control group throughout the observation period. The groups treated with sairei-to, especially the high-dosage group, exhibited much milder pathological changes in the tubotympanum than did the saline-control group. In conclusion, clinical application of sairei-to could be an effective measure to prevent the occurrence of OME and also the recurrence of the disease, especially OME-prone individuals.

Suja V, Sharmila SL, Shyamala Devi C. **Protective effect of Liv.52 and Liv.100, ayurvedic formulations on lipid peroxidation in rat liver homogenate--an in vitro study.** Indian J Exp Biol 1997;35(1):50-2.
Liv.100 is an improvised herbal formulation of Liv.52. Liv.52 is an important component of the ayurvedic system of medicine. This report highlights on the protective effect of Liv.52 and Liv.100 against in vitro peroxidation induced by hydrogen peroxide in rat liver homogenate. Addition of the two herbal formulations reduced the peroxidation effect of hydrogen peroxide in the dose- and time-dependent manner. The protective effect of the drugs is attributed to the enhanced supply of reduced glutathione that inhibit the deleterious process of lipid peroxidation. The results suggest on the antioxidant potential of Liv.52 and Liv.100.

Sun H, Liu W, Xiao K, Dong L, He M, Hu Y, Shen A, Jiang Q. **Study on oxygen supply and protection of bone marrow in acute radiation injured mice.** J Tongji Med Univ 1997;17(4):229-31, 243.
After irradiated by 8 Gy 60Co gamma-ray, mice were intraperitoneally injected immediately with 0.2 ml 100% compound blood-activating soup twice a day for 10 days. The in situ ulnar bone marrow partial pressure of oxygen (PbO2) was determined in vivo before, during and after irradiation respectively. The bone marrow sections in the same part were observed. Our results showed that the normal murine ulnar PbO2 was 12.72 +/- 1.05 kPa. During irradiation, the level of PbO2 decreased to 10.78 +/- 1.17 kPa ($P < 0.001$). And 3 days after irradiation, PbO2 decreased to 9.75 +/- 0.52 kPa, suggesting that the commonly used "blood-activating and stasis-eliminating" Chinese drugs could promote the rehabilitation and proliferation of bone marrow microvessels in the acute radiation injured mice, expand their areas, increase the oxygen supply of bone marrow microenvironment, thereby leading to PbO2 much higher increase than that of control group. It is also helpful in the proliferation and rehabilitation of hematopoietic cells.

Surh YJ, Kim SG, Liem A, Lee JW, Miller JA. **Inhibitory effects of isopropyl-2-(1,3-dithietane-2-ylidene)-2- [N-(4-methylthiazol-2-yl)carbamoyl]acetate (YH439) on benzo[a]pyrene-induced skin carcinogenesis and micronucleated reticulocyte formation in mice.** Mutat Res 1999;423(1-2):149-53.

Recently, a great deal of attention has been devoted to organosulfur compounds with potential cancer chemopreventive properties. Many sulfur-containing substances present in Brassica plants have been reported to possess striking anticarcinogenic and antimutagenic activities. Besides naturally occurring organosulfur compounds, certain synthetic sulfur-containing pharmaceuticals, such as oltipraz and sulindac, are known to exert substantial chemopreventive or chemoprotective effects. Isopropyl-2-(1, 3-dithietane-2-ylidene)-2-[N-(4-methylthiazol-2-yl)carbamoyl]acetate (YH439) was initially developed for its possible use as a hepatoprotectant. The compound has been found to up-regulate the expression of cytochrome P-450 IA1 [I.J. Lee, K.S. Jeong, B.J. Roberts, A.T. Kallarakal, P. Fernandez-Salguero, F.J. Gonzalez, B.J. Song, Transcriptional induction of the cytochrome P-450 1A1 gene by a thiazolium compound YH439, Mol. Pharmacol. 49 (1996) 980-988.] which plays a pivotal role in metabolism of the majority of polycyclic aromatic carcinogens and mutagens, such as benzo[a]pyrene (B[a]P). In the present study, we found that oral administration of YH439 to CD-1 mice significantly suppressed B[a]P-initiated skin tumorigenesis. B[a]P-induced formation of micronuclei in mouse peripheral reticulocytes was also attenuated by YH439 pretreatment. Likewise, diallyl sulfide, a major volatile thioether present in garlic, also protected against B[a]P-induced skin tumorigenesis and micronucleated reticulocyte formation in mice. Copyright 1999 Elsevier Science B.V.

Surh YJ, Lee E, Lee JM. **Chemoprotective properties of some pungent ingredients present in red pepper and ginger.** Mutat Res 1998;402(1-2):259-67.
There has been a substantial body of data, supporting that dietary factors have a profound impact on prevention as well as etiology of human cancer. Capsaicin has been tested by many investigators for its effects on experimental carcinogenesis and mutagenesis. Data in the literature indicate that capsaicin has dual effects on carcinogenic and mutagenic processes. At present, there is no solid evidence that hot red and chili peppers or their principal pungent ingredient capsaicin are carcinogenic in humans although results of early investigations with experimental animals exhibit the moderate tumorigenicity of this compound. In contrast, recent studies reveal substantial antigenotoxic and anticarcinogenic effects of capsaicin, suggesting this compound as another important dietary phytochemical with a potential chemopreventive activity. Some pungent constituents present in ginger and other zingiberaceous plants have potent antioxidant and anti-inflammatory effects, and some of them exhibit anti-tumor promotional activity in experimental carcinogenesis. Copyright 1998 Elsevier Science B.V.

Suvitayavat W, Bunyapraphatsara N, Thirawarapan S, Watanabe K. **Gastric acid secretion inhibitory and gastric lesion protective effects of aloe preparation.** Thai J Phytopharm 1997;4(1):1-11.
IPA COPYRIGHT: ASHP The effect of an Aloe vera formulation on gastric acid secretion in histamine hydrochloride- or bethanechol hydrochloride-induced gastric acid secretion in isolated ddY mouse stomach and in pyrolus ligated Wistar rats and the gastroprotective effect of the A. vera formulation against hydrochloric acid-induced gastric ulcers in Wistar rats were studied. The A. vera formulation inhibited gastric acid secretion in the mouse and rat experiments and also had a gastroprotective effect in the rat experiment.

Suzuki J, Watanabe K, Kobayashi T, Yoshida K, Watanabe Y, Kumada K, Suzuki S, Kume K, Suzuki H. **Effect of sairei-to on prostaglandin E2-induced phosphatidylinositol breakdown**

in aminonucleoside nephrotic rat. Nephron 1997;75(2):208-12.
We describe the effects of Sairei-to, a Chinese herbal medicine, on aminonucleoside-induced nephrotic rats (ANNR), and analyze the urinary excretion of protein and phosphatidylinositol (PI) turnover via prostaglandin E2 (PGE2) receptors in isolated glomeruli. Sairei-to suppressed urinary excretion of protein and PGE2 in ANNR, and inhibited acceleration of PI turnover in isolated nephrotic glomeruli. The affected responsiveness of the PI turnover system to PGE2 in a nephrotic state was presumed to be normalized by Sairei-to. These findings suggest that Sairei-to restores abnormal changes in the PI turnover system in ANNR kidneys, and thereby inhibit excretion of protein into the urine.

Tan D, Xie ZZ, Zhong M, Wu D, Liang X, Li W, Qin Q, Tam G. **[Chinese herbal drugs: sheng-bai-kuai in the treatment of leukopenia caused by chemotherapy].** Hunan I Ko Ta Hsueh Hsueh Pao 1997;22(6):547-9. (Chi)

Tan RX, Tang HQ, Hu J, Shuai B. **Lignans and sesquiterpene lactones from Artemisia sieversiana and Inula racemosa.** Phytochemistry 1998;49(1):157-61.
The aerial parts of Artemisia sieversiana afforded, in addition to beta-sitosterol, stigmasterol and daucosterol, two novel lignans as well as one known and three new guaianolides. The roots of Inula racemosa gave beta-sitosterol, daucosterol and isoalantolactone. The structures were determined by a combination of spectral methods (IR, EIMS, 1H and 13C NMR, DEPT, COSY, NOESY and HETCOR). All isolates were subjected to antifungal tests. Isoalantolactone, a major sesquiterpene lactone of I. racemosa, was found to be active against the human pathogenic fungi. Aspergillus flavus, A. niger, Geotrichum candidum, Candida tropicalis and C. albicans at concentrations of 50, 50, 25, 25 and 25 micrograms/ml, respectively. The taxonomic significance of the characterized constituents is discussed briefly.

Tang X, Edenharder R. **Inhibition of the mutagenicity of 2-nitrofluorene, 3-nitrofluoranthene and 1-nitropyrene by vitamins, porphyrins and related compounds, and vegetable and fruit juices and solvent extracts.** Food Chem Toxicol 1997;35(3-4):373-8.
When 21 vitamins including related compounds haemin, chlorophyllin, chlorophyll, biliverdin and bilirubin, as well as juices from five fruits and 25 vegetables and solvent extracts from the residues of fruits and vegetables were tested for their antimutagenic potencies with respect to mutagenicity induced by 2-nitrofluorene (2-NF), 3-nitrofluoranthene (3-NFA) and 1-nitropyrene(1-NP) in Salmonella typhimurium TA98 the following results were obtained. The tetracyclic nitroarenes 3-NFA and 1-NP were in general more effectively antagonized by potent antimutagenic compounds than the tricyclic 2-NF. beta-Carotene, retinol, retinal, retinoic acid, retinol palmitate, riboflavin 5'-phosphate, alpha-tocopherol, vitamins B12, C, K1 and K3 as well as biliverdin, bilirubin, chlorophyll, chlorophyllin and haemin exerted antimutagenicity against the nitroarenes cited previously. All other vitamins were inactive. While part of the juices were inactive, juices from cauliflower, carrots, chives, radishes and spinach exerted weak antimutagenic activities. However, weak to moderate co-mutagenic effects were seen with grapes, kiwi, pineapple, eggplant, celeriac, chicory greens, fennel leaves and radishes and strong effects with peppers which were not caused by the presence of growth-promoting factors. Most solvent fractions were inactive but fractions containing chlorophyll exerted antimutagenicity.

Taylor M. **Alternatives to conventional hormone replacement therapy.** Compr Ther 1997;23(8):514-32.
Alternative medicines have become "mainstream" in their popularity and economic size. The most highly promoted and popular types of alterative medicines used for menopause are discussed, including mineral and vitamin supplements, phytoestrogens, natural hormones, and botanical/plant medicines.

Taylor RS, Towers GH. **Antibacterial constituents of the Nepalese medicinal herb, Centipeda minima.** Phytochemistry 19998;47(4):631-4.
Centipeda minima, a herb used medicinally to treat sinus infections in Nepal, was found to contain three antibacterial sesquiterpene lactones, identified as 6-O-methylacrylylplenolin, 6-O-isobutyroylplenolin, and 6-O-angeloylplenolin. 6-O-Methylacrylylplenolin had not been previously isolated from C. minima. All three had activity against Bacillus subtilis and Staphylococcus aureus, with 6-O-isobutyroylplenolin being the most active.

Thompson KD. **Antiviral activity of Viracea against acyclovir susceptible and acyclovir resistant strains of herpes simplex virus.** Antiviral Res 1998;39(1):55-61.
Viracea, a topical microbicide, is a blend of benzalkonium chloride and phytochemicals derived from Echinacea purpurea and is a proprietary formula from Destiny BioMediX Corp. Viracea was tested against 40 strains of herpes simplex virus (HSV): 15 strains (five HSV-1 and ten HSV-2) were resistant to acyclovir (ACV-R) and 25 strains (13 HSV-1 and 12 HSV-2) were susceptible to ACV (ACV-S). The median ED50 of Viracea for the five ACV-R strains of HSV-1 was a 1:100 dilution of the drug with a range of 1:50-1:400. The median ED50 of Viracea for the ten ACV-R strains of HSV-2 was 1:200 with a range of 1:50-1:3200. For the ACV-S strains of HSV-1 and HSV-2, the median ED50 of Viracea was 1:100 and 1:200, respectively. The cytotoxicity of Viracea was evaluated in a standard neutral red dye uptake assay in human foreskin fibroblasts. The cytotoxicity of Viracea approached only 50% at the highest concentration of the drug tested, a 1:2 dilution, indicating that Viracea is non-toxic in this cell cytotoxicity assay. Although the active component(s) in Viracea that has anti-HSV activity is not known, it appears that this extract has good antiviral activity against both ACV resistant and ACV susceptible strains of HSV-1 and HSV-2.

Tiwari RK, Geliebter J, Garikapaty VP, Yedavelli SP, Chen S, Mittelman A. **Anti-tumor effects of PC-SPES, an herbal formulation in prostate cancer.** Int J Oncol 1999;14(4):713-9.
Prostate cancer is the most common cancer amongst males in developed countries. Surgical removal of the prostate effectively cures the primary disease but the metastatic disease is refractory to most forms of chemotherapy. There is a clinical need to develop novel treatment strategies that exploit the mode of action of both conventional and alternative drugs/medicinal plants. We have been investigating the anti-proliferative and anti-tumor effects of an herbal preparation termed PC-SPES (patent pending, US serial number 08/697, 920) which is a refined powder of eight different medicinal plants. PC-SPES administered as a food supplement caused a dramatic decrease in prostate specific antigen levels in some prostate cancer patients with advanced disease. These preliminary clinical findings laid the foundation for a program to examine the in vitro and in vivo effects of PC-SPES, and identify the active component in this mixture so that a standardized treatment regimen can be formulated. In this communication, we

report the anti-tumor effects of PC-SPES incorporated in the diet utilizing a well studied Dunning R3327 rat prostate cancer model. Dietary PC-SPES at levels of 0.05% and 0.025% did not exhibit any toxicity and no significant difference in food intake was noted at the end of six weeks. Dose dependent inhibitory effect of dietary PC-SPES was observed on both tumor incidence (P=0. 01) and rate of tumor growth when tumors were induced in syngeneic Copenhagen rats by intradermal injections of MAT-LyLu cells that are known to metastasize in the lung and lymph nodes. The number of pulmonary metastases in animals on PC-SPES that showed no primary tumor growth had no metastatic lesions in the lung, however, in animals that did not respond to PC-SPES, the number of pulmonary metastases was not significantly different from the non-treated controls. The significant anti-tumor effects of PC-SPES on MAT-LyLu induced tumorigenesis and metastasis in Copenhagen rats, in general refractory to most conventional therapy, suggests a therapeutic benefit of this herbal food supplement and may be a useful adjuvant to conventional therapeutic modalities.

Touwaide A, Pollio A, Aliotta G, Piomelli D, De Santo NG. **Medicinal plants for the treatment of urogenital tract pathologies according to Dioscorides' De Materia Medica.** Am J Nephrol 1997;17(3-4):241-7.
The De Materia Medica of the Greek Dioscorides reports about 200 plants used for the treatment of pathologies of the urogenital tract during the 1st century AD. On the basis of explicit and implicit affirmations by Dioscorides, a theoretical system concerning the specific properties of these plants has been attempted. Comparison of the species reported by Dioscorides and Pliny the Elder for renal affections does not support the thesis of a close relationship between De Materia Medica and the Naturalis Historia.

Ulate-Rodriguez J, Schafer HW, Zottola EA, Davidson PM. **Inhibition of Listeria monocytogenes, Escherichia coli O157:H7, and Micrococcus luteus by linear furanocoumarins in a model food system.** J Food Protect 1997;60(9):1050-4.
BIOSIS COPYRIGHT: BIOL ABS. Lime peel, parsnip, lemon peel, dried parsley flakes, cold-pressed lime oil, and distilled lime oil samples were analyzed for the presence and concentration of the linear furanocoumarins (LFs) psoralen, 5-methoxypsoralen (5-MOP), and 8-methoxypsoralen (8-MOP) by thin layer chromatography and gas chromatographymass spectrometry. Cold-pressed lime oil had the highest LF content (psoralen, 67 : 29 mug/ml, 5-MOP, 1,634 : 62 mug/ml, and 8-MOP, 44 : 2 mug/ml). The antimicrobial effectiveness of LFs against Listeria monocytogenes, Escherichia coli O157:H7, and Micrococcus luteus was tested in a model food system consisting of a slurry of 25% commercial "garden vegetables" baby food in 0.1% peptone water. Inhibition required UV activation after the addition of the LFs to the model system. Lime peel extract, cold-pressed lime oil, and a 5-MOP standard inhibited the growth of L. monocytogenes, but not E. coli O157:H7. M. luteus was inhibited only by the cold-pressed lime oil. The minimum LF concentration that caused inhibition of the growth of L. monocytogenes was 32 mug/g and the minimum bactericidal concentration was 43 mug/g. Cold-pressed lime oil inhibited L. monocytogenes even at the lowest concentration added to the model system (10 mug/g), while the corresponding LF standard did not. This suggested the presence of other antimicrobial agents in the oil.

Van Der Weijden GA, Timmer CJ, Timmerman MF, Reijerse E, Mantel MS, Van Der Velden U. **The effect of herbal extracts in an experimental mouthrinse on established plaque and gingivitis.** J Clin Periodontol 1998;25(5):399-403.
The purpose of the present study was to establish in vitro the inhibiting effect of a herbal extract mixture on a selected number of micro-organisms and to test in vivo the effect of a mouthwash containing 6.3 mg/ml herbal extract mixture on plaque and gingivitis as compared to a minus active control mouthrinse. The herbal extract was a mixture of: Juniperus communis (juniper), Urtica dioca (nettle), Achillaea millefolium (yarrow); 1:1:1. In the study, in-vitro, the effect of pure herbal extract mixture on acid production of Streptococcus mutans was tested and the minimum inhibitory concentrations (MIC) of the following micro-organisms were tested: Streptococcus mutans, Streptococcus mitis, Actynomyces viscosus, Actynomyces naeslundii, Actinobacillus actinomycetemcomitans, Prevotella intermedia, Campylobacter rectus, Fusobacterium nucleatum, Veillonella parvula. The MIC-values for A. viscosus and P. gingivalis were 100 mg/ml. The MIC-values for A. naeslundii and A. actinomycetemcomitans were considerably lower (10 mg/ml). S. mitis was the most susceptible of the tested organisms to the extract with a MIC value of 1 mg/ml. S. mutans, C. rectus, V. parvula, and F. nucleatum were not influenced by the extracts. No inhibitory effect of the 6.3 mg/ml herbal extract mixture was observed on the acid production of S. mutans. For the study in-vivo, 45 volunteers were selected on the basis of having moderate gingival inflammation. As efficacy parameters the plaque index, modified gingival index and angulated bleeding index were assessed. The subjects were randomly divided among 3 experimental groups (2x test and 1 'minus active' control). The participants were requested to rinse with 10 ml of mouthwash twice a day for a period of three months. After 6 weeks and 3 months, the same clinical indices as at baseline were recorded. The results show no difference between the two test groups and the control group. In conclusion, the results of the present study have shown that the mixture of the 3 herbal extracts, Juniperus communis, Urtica dioca and Achillaea millefolium when used in a mouthrinse has no effect on plaque growth and gingival health.

Van Rijn J, Van Den Berg J. **Flavonoids as enhancers of x-ray-induced cell damage in hepatoma cells.** Clin Cancer Res 1997;3(10):1775-9.
The nuclear enzyme topoisomerase II, which is involved in replication, transcription, and probably repair of DNA, can be inhibited by a number of flavonoids. In conjunction with X-rays, three of these compounds were tested as to their effects on Reuber H35 hepatoma cells. In this combination, the isoflavone genistein, the flavone apigenin, and the flavonol quercetin caused an enhancement of radiation-induced cell death. This enhanced cytotoxicity was only observed when the flavonoids were applied following an irradiation treatment and is attributed to decreased repair of DNA radiation damage with a concomitant reduction of the rate of cell repopulation. Fractionated irradiations, given as five sequences of 3 Gy each over a period of 5 days, reduced the surviving cell population only by a factor of 20, whereas the continuous presence of genistein during radiation sequences resulted in a reduction of at least a factor of 10,000. Thus, these flavonoids not only seem to act as radiation enhancers but also exhibit potential antitumor activities.

Veit M, Van Rensen E, Blume H, Ihrig M, Morck H, et al . **[Evaluation of phytopharmaceuticals in the therapy of BPH].** Pharm Ztg 1998 Jun 4;143:11-6, 18, 20, 22-3,

26, 28, 30, 32-3. (Ger)
IPA COPYRIGHT: ASHP A review of the efficacy and safety of commercial phytopharmaceutical agents for the therapy of benign prostatic hyperplasia (BPH), based on data from in vitro studies and clinical trials, is presented.

Venkateswaran S, Pari L, Viswanathan P, Menon VP. **Protective effect of Livex, a herbal formulation against erythromycin estolate induced hepatotoxicity in rats.** J Ethnopharmacol 1997;57(3):161-7.
Livex, a compound herbal formulation, was investigated for its possible hepatoprotective effect in Wistar rats against erythromycin estolate induced toxicity. Oral administration of Livex significantly prevented the occurrence of erythromycin estolate induced hepatic damage. The increased level of serum enzymes (aspartate transaminase, alanine transaminase, alkaline phosphatase), bilirubin, serum and tissue cholesterol, triglycerides, phospholipids and free fatty acids observed in rats treated with erythromycin estolate were very much reduced in rats treated with Livex and erythromycin estolate. These biochemical observations were supplemented by histopathological examination of liver sections. Results of this study revealed that Livex could afford a significant protection against erythromycin estolate induced hepatocellular damage.

Vesselago M. **Drugs and herbal preparations: how safe are they? [letter; comment].** Can Fam Physician 1997;43:1047.

Vieregge B, Resch K, Kaever V. **Synergistic effects of the alkaloid sinomenine in combination with the immunosuppressive drugs tacrolimus and mycophenolic acid [letter].** Planta Med 1999;65(1):80-2.
The alkaloid sinomenine extracted from the medicinal plant Sinomenium acutum is used in China for the treatment of various rheumatic diseases. It has immunomodulatory properties in a cardiac allograft transplantation model. Its antiproliferative effect on human mononuclear cells in combination with different immunosuppressive drugs was further analysed in vitro. Sinomenine dose-dependently attenuated thymidine incorporation, interleukin-2 synthesis, and cell cycle progression of activated T-lymphocytes. Cell proliferation was synergistically decreased by addition of sinomenine together with suboptimal concentrations of the established immunosuppressive drugs tacrolimus or mycophenolic acid, respectively.

Vinekar AS, Andrade C, Sriprada VT, George J, Joseph T, Chandra JS. **Attenuation of ECS-induced retrograde amnesia by using an herbal formulation.** J ECT 1998;14(2):83-8.
Earlier research indicated the efficacy of a complex herbal formulation in the attenuation of electroconvulsive shock (ECS)-induced amnestic deficits in rats; this study sought to ascertain whether a simplified herbal formulation (Memorin; Phyto-Pharma, India) also was effective. Rats pretreated for a fortnight with Memorin (200 mg/kg/day) or vehicle were exposed to a passive-avoidance learning paradigm in a shuttle box. The next day, the rats were administered two true or sham ECSs, 5 h apart; recall of the pre-ECS learning was reassessed on the following day. ECS was found to produce significant retrograde amnesia ($p < 0.002$). Memorin attenuated the ECS-induced amnesia ($p = 0.00003$) without influencing the ECS seizure duration. The clinical implications of these findings are discussed.

Visalyaputra S, Petchpaisit N, Somcharoen K, Choavaratana R. **The efficacy of ginger root in the prevention of postoperative nausea and vomiting after outpatient gynaecological laparoscopy.** Anaesthesia 1998;53(5):506-10.
To determine the anti-emetic effect of ginger as compared to droperidol, 120 patients scheduled to have gynaecological diagnostic laparoscopy as day cases were randomly allocated into placebo, droperidol, ginger and ginger plus droperidol groups to receive either 2 g of ginger or 1.25 mg of droperidol or both. There were no significant differences in the incidences of postoperative nausea which were 32%, 20%, 22% and 33%, and vomiting which were 35%, 15%, 25% and 25% in the four groups, respectively. We conclude that ginger powder, in the dose of 2 g, droperidol 1.25 mg or both are ineffective in reducing the incidence of postoperative nausea and vomiting after day case gynaecological laparoscopy.

Volz HP, Kieser M. **Kava-kava extract WS 1490 versus placebo in anxiety disorders--a randomized placebo-controlled 25-week outpatient trial.** Pharmacopsychiatry 1997;30(1):1-5.
101 outpatients suffering from anxiety of non-psychotic origin (DSM-III-R criteria: agoraphobia, specific phobia, generalized anxiety disorder, and adjustment disorder with anxiety) were included in a 25-week multicenter randomized placebo-controlled double-blind trial with WS 1490, a special extract of kava-kava. In the main outcome criterion, the Hamilton Anxiety Scale (HAMA), there was a significant superiority of the test drug starting from week 8 on. WS 1490 was also found to be superior with respect to the secondary outcome variables. HAMA subscores somatic and psychic anxiety, Clinical Global Impression, Self-Report Symptom Inventory-90 Items revised, and Adjective Mood Scale. Adverse events were rare and distributed evenly in both groups. These results support WS 1490 as a treatment alternative to tricyclic antidepressants and benzodiazepines in anxiety disorders, with proven long-term efficacy and none of the tolerance problems associated with tricyclics and benzodiazepines.

Vorbach EU, Arnoldt KH, Hubner WD. **Efficacy and tolerability of St. John's wort extract LI 160 versus imipramine in patients with severe depressive episodes according to ICD-10.** Pharmacopsychiatry 1997;30(Suppl 2):81-5.
The special extract of St. John's wort, LI 160, exhibited a superior antidepressant efficacy compared to placebo in several controlled trials. Two further trials demonstrated a similar reduction of depressive symptomatology under LI 160 compared to tricyclics. All these trials were performed in mildly to moderately depressed patients. The present investigation was a randomized, controlled, multicentre, 6-week trial comparing 1800 mg LI 160/die to 150 mg imipramine/die in severely depressed patients according to ICD-10. The main efficacy parameter, a reduction of the total score of the Hamilton Depression Scale, proved both treatment regimens very effective at the end of the 6 week treatment period (mean values 25.3 to 14.5 in the LI 160 group and 26.1 to 13.6 in the imipramine group), but not statistically equivalent within a a-priori defined 25% interval of deviation. The analysis of subgroups with more than a 33% and 50% reduction of the HAMD total score justified the assumption of equivalence within a 25% deviation interval. This view was also supported by the global efficacy ratings from patients and investigators. Regarding adverse events, the nonrejection of the nonequivalence hypothesis denotes a superiority of the herbal antidepressant. These main result indicate that LI 160 might be a treatment alternative to the synthetic tricyclic antidepressant imipramine in the

majority of severe forms of depressions. However, more studies of this type must be performed before a stronger recommendation can be made.

Voth EA, Schwartz RH. **Medicinal applications of delta-9-tetrahydrocannabinol and marijuana [see comments].** Ann Intern Med 1997;126(10):791-8.
The use of crude marijuana for herbal medicinal applications is now being widely discussed in both the medical and lay literature. Ballot initiatives in California and Arizona have recently made crude marijuana accessible to patients under certain circumstances. As medicinal applications of pure forms of delta-9-tetrahydrocannabinol (THC) and crude marijuana are being considered, the most promising uses of any form of THC are to counteract the nausea associated with cancer chemotherapy and to stimulate appetite. We evaluated the relevant research published between 1975 and 1996 on the medical applications, physical complications, and legal precedents for the use of pure THC or crude marijuana. Our review focused on the medical use of THC derivatives for nausea associated with cancer chemotherapy, glaucoma, stimulation of appetite, and spinal cord spasticity. Despite the toxicity of THC delivered in any form, evidence supports the selective use of pure THC preparations to treat nausea associated with cancer chemotherapy and to stimulate appetite. The evidence does not support the reclassification of crude marijuana as a prescribable medicine.

Wagner J, Wagner ML, Hening WA. **Beyond benzodiazepines: alternative pharmacologic agents for the treatment of insomnia.** Ann Pharmacother 1998;32(6):680-91.
OBJECTIVE: To review the epidemiology, etiology, and classification of insomnia and provide an overview of the pharmacologic therapy of insomnia. Novel nonbenzodiazepine hypnotics including zolpidem, zopiclone, and zaleplon, as well as nonprescription products such as valerian and melatonin, are reviewed in detail. DATA SOURCES: A MEDLINE search was performed to identify relevant clinical studies, case reports, abstracts, and review articles published between April 1992 and December 1997. Key search terms included insomnia, benzodiazepines, zolpidem, zopiclone, zaleplon, Cl 284,846, melatonin, and valerian. Additional references were obtained from the lists of review articles and textbooks. DATA EXTRACTION AND SYNTHESIS: Data concerning the safety and efficacy of the hypnotic agents were extracted from all available clinical trials and abstracts. Background information regarding insomnia, benzodiazepines, and other hypnotics was extracted from the most current literature, including review articles and textbooks. CONCLUSIONS: New developments in benzodiazepine receptor pharmacology have introduced novel nonbenzodiazepine hypnotics that provide comparable efficacy to benzodiazepines. Although they may possess theoretical advantages over benzodiazepines based on their unique pharmacologic profiles, they offer few, if any, significant advantages in terms of adverse effects. Over-the-counter agents such as valerian and melatonin may be useful in alleviating mild, short-term insomnia, but further clinical trials are required to fully evaluate their safety and efficacy.

Wakabayashi C, Hasegawa H, Murata J, Saiki I. **In vivo antimetastatic action of ginseng protopanaxadiol saponins is based on their intestinal bacterial metabolites after oral administration.** Oncol Res 1997;9(8):411-7.
The present study demonstrated in vivo and in vitro antimetastatic activities of a major intestinal bacterial metabolite M1 formed from protopanaxadiol saponins of ginseng (the root of Panax

ginseng C. A. Meyer) in comparison with its whole standardized extract and ginsenosides Rb1, Rb2, and Rc. Although Ginseng extract (1 mg/mouse) and ginsenosides (0.5 mg/mouse) significantly inhibited lung metastasis produced by i.v. injection of B16-BL6 melanoma cells in syngeneic mice (27-61% of untreated control), they hardly inhibited the invasion and migration of B16-BL6 melanoma and HT1080 fibrosarcoma cells in vitro. However, the intestinal bacterial metabolite M1 inhibited lung metastasis of melanoma cells and in vitro tumor cell invasion and migration at nontoxic or marginally toxic concentrations. Additionally, pharmacokinetic studies of ginsenoside Rb1 and M1 after oral administration (2 mg/mouse) revealed that intact Rb1 was not detectable in serum for 24 h by HPLC analysis, whereas the level of M1 in the serum reached maximum at 8 h (8.5 +/- 0.4 micrograms/ml) after Rb1 administration and at 2 h (10.3 +/- 1.0 micrograms/ml) after M1 administration. These findings suggest that the in vivo antimetastatic effect by oral administration of ginsenosides is mediated by their metabolic component M1.

Wang B. **Traditional Chinese medical treatment to invigorate blood and relieve stasis treatment of schizophrenia: comparison with antipsychotics treatment.** Psychiatry Clin Neurosci 1998;52(Suppl):329-30.
In this study, 80 schizophrenic patients, divided into two groups of 40, were treated with traditional Chinese medicine to invigorate the blood and relieve stasis and antipsychotic drugs, and were observed by the rating methods of BPRS,TESS, CGI scale and hemorheology test. The results show that such traditional Chinese medicine to invigorate blood and relieve stasis has fewer side effects on schizophrenic patients than do antipsychotic drugs, and there is objective evidence of hemorheology changes. Traditional Chinese medicine is superior to antipsychotic drugs in the effects of anti-anxiety-depression and antipsychomotor inhibition, but it is less effective in controlling psychomotor excitation compared with antipsychotic drugs.

Wang BH, Zuzel KA, Rahman K, Billington D. **Protective effects of aged garlic extract against bromobenzene toxicity to precision cut rat liver slices.** Toxicology 1998;126(3):213-22.
Precision-cut liver slices from phenobarbital-treated rats were incubated for up to 8 h with the industrial solvent and hepatotoxin bromobenzene at a final concentration of 1 mM. Phenobarbital pretreatment potentiates bromobenzene hepatotoxicity by inducing those P450 isoforms responsible for the formation of the active hepatotoxin, namely bromobenzene-3,4-oxide. A reduction in cell viability was indicated by a decrease in the K+, ATP and glutathione content of the slices and the increased release of the intracellular enzymes, lactate dehydrogenase and alanine aminotransferase, into the medium. Furthermore, levels of lipid peroxidation as judged by the formation of thiobarbituric acid reactive substances, were increased approximately 5-fold. Aged garlic extract (AGE) at concentrations of 1-5% (v/v) reduced the toxicity of bromobenzene in a concentration-dependent manner as judged by all of the parameters of viability studied, with the exception of lipid peroxidation which was reduced to control levels even at the lowest concentration of garlic extract used. AGE was found to cause partial inhibition of cytochrome P450 when assayed as both 7-ethoxycoumarin O-deethylase and 7-pentoxyresorufin O-dependentylase activities, but even the highest concentration used inhibited both activities by less than 50%. It is suggested that the hepatoprotective effects of AGE are due primarily to the reduced glutathione-sparing properties of its constituents, most probably its organosulphur compounds.

Wang C, Kurzer MS. **Effects of phytoestrogens on DNA synthesis in MCF-7 cells in the presence of estradiol or growth factors.** Nutr Cancer 1998;31(2):90-100.
Phytoestrogen effects on estrogen action and tyrosine kinase activity have been proposed to contribute to cancer prevention. To study these mechanisms, a number of phytoestrogens and related compounds were evaluated for their effects on DNA synthesis (estimated by thymidine incorporation analysis) in estrogen-dependent MCF-7 cells in the presence of estradiol (E2), tamoxifen, insulin, or epidermal growth factor. We observed that 1) at 0.01-10 microM, genistein and coumestrol enhanced E2-induced DNA synthesis, as did 10 microM enterolactone. Chrysin at 1.0-10 microM and 10 microM luteolin or apigenin inhibited E2-induced DNA synthesis, as did all compounds at > 10 microM, 2) tamoxifen enhanced genistein-induced DNA synthesis but inhibited DNA synthesis induced by all other compounds, and 3) genistein enhanced insulin- and epidermal growth factor-induced DNA synthesis at 0.1-1.0 and 0.1-10 microM, respectively. At higher concentrations, inhibition was observed. Similar effects were seen with coumestrol. In conclusion, the effects of phytoestrogens in the presence of E2 or growth factors are concentration dependent and variable. At low concentrations, genistein and coumestrol significantly enhanced E2-induced and tyrosine kinase-mediated DNA synthesis; at high concentrations, inhibition was observed. Differing effects were observed with the other compounds. The variable effects of phytoestrogens on DNA synthesis must be considered when their roles in cancer prevention or treatment are evaluated.

Wang WK, Hsu TL, Chiang Y, Wang YY. **Pulse spectrum study on the effect of sie-zie-tang and Radix aconiti.** Am J Chin Med 1997;25(3-4):357-66.
Extracts of the traditional Chinese formula Sie-Zie-Tang as well as one of its main components, Radix Aconiti were injected into rats intraperitoneally to observe pressure wave spectrum changes at the caudate artery. We found that Radix Aconiti decreased the C0 (DC term of the pulse), C5 and C6 (the harmonic proportions of the 5th and the 6th harmonic), but increased C2 and C3 (the harmonic proportions of the second and the third harmonic) significantly. For Sie-Zie-Tang, the increases of C2, C3, and C4 were accompanied by the decreasing of C0. The decreases of C5, C6 were small and not significant. The additional ingredients in the formula reduce toxic side effects (arrhythmia or heart failure caused by faster and stronger heart beat) due to Radix Aconiti. For human subjects, low dose Sie-Zie-Tang tends to normalize the Fourier components of the pressure wave. Orally taking the formula elevates the harmonic proportion of the harmonic that is lower than normal, but suppresses the higher one. Our results provides a possible mechanism for heart meridian related herbs. It strengthens heart beats, and normalizes energy distribution to different meridians. The study on Sie-Zie-Tang reveals another formula construction to reduce toxic side effects.

Watanabe H. **Candidates for cognitive enhancer extracted from medicinal plants: paeoniflorin and tetramethylpyrazine.** Behav Brain Res 1997;83(1-2):135-41.
A traditional Chinese medicine, Shimotsu-to, consisting of four herbs: Japanese angelica root, cnidium rhizome, peony root and rehmannia root, has been reported to improve spatial working memory in rats. The present results indicate that Paeoniflorin and tetramethylpyrazine (TMP) extracted from peony root and cnidium rhizome, respectively, are candidates for cognitive enhancer.

Weihmayer T. **[Control of pain with stimulating and healing plants. Naturopathy series, 15: Therapy of arthroses].** Fortschr Med 1997;115(18):42. (Ger)

Wesnes KA, Faleni RA, Hefting NR, Hoogsteen G, Houben JJ, Jenkins E, Jonkman JH, Leonard J, Petrini O, Van Lier JJ. **The cognitive, subjective, and physical effects of a ginkgo biloba/panax ginseng combination in healthy volunteers with neurasthenic complaints.** Psychopharmacol Bull 1997;33(4):677-83.
We evaluated the effects of a Ginkgo biloba/ginseng combination on cognitive function in this 90-day, double-blind, placebo-controlled, parallel-group study. Sixty-four healthy volunteers (aged 40 to 65 years), selected on the basis of fulfilling the ICD-10 F48.0 criteria for neurasthenia, were assigned randomly to four equal dosing groups, receiving 80, 160, or 320 mg of the combination b.i.d. or placebo. Assessments were performed on the day before dosing, and again at Days 1, 30, and 90 at 1 hour after the morning dose and 1 hour after the afternoon dose. The assessments included the Cognitive Drug Research (CDR) computerized assessment system, the Vienna Determination Unit, cycle ergometry, and various questionnaires. The treatments were well tolerated by all volunteers. On Day 90 at 1 hour post morning dosing, dose-related improvements were seen on the CDR tests, the 320 mg dose being significantly superior to placebo. These effects, however, were reversed 1 hour after the afternoon dose, possibly suggesting that a longer inter-dosing interval would be preferable. The 80-mg dose produced a significant benefit on the ergometry assessment of heart rate at maximum load. There were also several supporting changes from other assessments, including an advantage of 320 mg over placebo on the global score from the Symptom Checklist-90-revised (SCL-90-R) at Day 90.

Westendorf J, Pfau W, Schulte A. **Carcinogenicity and DNA adduct formation observed in ACI rats after long-term treatment with madder root, Rubia tinctorum L.** Carcinogenesis 1998;19(12):2163-8.
Madder root, Rubia tinctorum L., is a traditional herbal medicine used against kidney stones. Recently we reported that lucidin, a hydroxyanthraquinone derivative present in this plant, is mutagenic in bacteria and mammalian cells. We also demonstrated the formation of DNA adducts in tissue culture and mice after treatment with this compound. To elucidate the possible carcinogenicity of madder root, three groups of male and female ACI rats received either a normal diet or a diet supplemented with 1 or 10% drug for a total period of 780 days. Weight gain and morbidity were not different among the three groups. Non-neoplastic lesions related to the treatment were evident in the liver and kidneys of both sexes. Moreover, dose-dependent increases in benign and malignant tumour formation were observed in the liver and kidneys of treated animals. 32P-post-labelling analysis showed an increase in the overall level of DNA adducts observed in the liver, kidney and colon of rats treated with 10% madder root in the diet for 2 weeks. HPLC analysis of 32P-labelled DNA adducts revealed a peak co-migrating with an adduct obtained after in vitro treatment of deoxyguanosine-3'-phosphate with lucidin. These observations suggest that the use of madder root for medicinal purposes is associated with a carcinogenic risk.

Wheatley D. **LI 160, an extract of St. John's wort, versus amitriptyline in mildly to moderately depressed outpatients--a controlled 6-week clinical trial.** Pharmacopsychiatry 1997;30(Suppl 2):77-80.

Up to now, the antidepressant efficacy of the extract of St. John's wort, LI 160, has been compared to imipramine and maprotiline, demonstrating similar antidepressant efficacy in mildly to moderately depressed patients, treated either with LI 160 or the respective synthetic comparator. In the study reported here, LI 160 (total daily dose: 900 mg) was compared with the sedating tricyclic amitriptyline (total daily dose: 75 mg) in a controlled, randomized, multicentre trial. At the end of the 6-week study, the major target variable, the Hamilton Depression Scale response rate, exhibited no statistically significant difference between the groups, although a tendency for a better response rate was seen in the amitriptyline group. The secondary efficacy parameters, decreases in the total Hamilton Depression and Montgomery-Asberg scores, showed a significant advantage for amitriptyline, but only at week 6. With regard to tolerability, LI 160 was clearly superior to amitriptyline, particularly in relation to anticholinergic and Central Nervous System adverse events. Thus, 37% of the LI 160 treated patients reported adverse events, compared to 64% in the amitriptyline group. This considerable superiority in tolerability for LI 160 in relation to amitriptyline, could confer an advantage in improving compliance for antidepressant pharmacotherapy.

Whitmarsh TE, Coleston-Shields DM, Steiner TJ. **Double-blind randomized placebo-controlled study of homoeopathic prophylaxis of migraine.** Cephalalgia 1997;17(5):600-4.
Homoeopathic remedies for migraine are widely available over the counter, statutorily offered by the national health service in the UK, and apparently popular with patients. Do they work? Sixty-three outpatients with migraine with or without aura by IHS criteria entered a 4-month randomized placebo-controlled, double-blind parallel-groups trial of individualized homoeopathic prophylaxis, the first month being baseline with all patients on placebo. Three patients (4.8%) dropped out, leaving 30 in each treatment group. There were chance differences in attack frequency and severity between the groups at baseline (attacks were more frequent but less severe in the placebo group). Both groups improved on therapy, but neither to a great extent on the primary outcome measure of attack frequency (verum: -19%; placebo: -16%). Reduction was mostly in mild attacks on placebo, more in moderate and severe attacks on homoeopathy. Few adverse events were reported. Overall, there was no significant benefit over placebo of homoeopathic treatment. The course of change differed between groups, and suggested that improvement reversed in the last month of treatment on placebo. On this evidence we cannot recommend homoeopathy for migraine prophylaxis, but cannot conclude that it is without effect.

Widy-Tyszkiewicz E, Schminda R. **Randomized double blind study of sedative effects of phytotherapeutic containing valerian, hops, balm and motherwort versus placebo.** Herba Pol 1997;43(2):154-9.

Wildfeuer A, Neu IS, Safayhi H, Metzger G, Wehrmann M, Vogel U, Ammon HP. **Effects of boswellic acids extracted from a herbal medicine on the biosynthesis of leukotrienes and the course of experimental autoimmune encephalomyelitis.** Arzneimittelforschung 1998;48(6):668-74.
Mixed acetylboswellic acids, pentacyclic triterpenes extracted from the gum resin of Boswellia serrata Roxb., significantly inhibited the ionophore-stimulated release of the leukotrienes (LT) B4 and C4 from intact human polymorphonuclear neutrophil leukocytes (PMNLs), with IC50 values of 8.48 micrograms/ml and 8.43 micrograms/ml, respectively. Purified acetyl-11-keto-

beta-boswellic acid was about three times more potent as inhibitor of the formation of both LTB4 (IC50 = 2.53 micrograms/ml) and LTC4 (IC50 = 2.26 micrograms/ml) from human PMNLs in the same assay. The comparative agent MK 886 (3-[1-(4-chlorobenzyl)-3-t-butyl-thio-5-isopropylindol-2-yl]- 2,2-dimethylpropanoic acid, L-663,536, CAS 118, 414-82-7) was about 10 to 100-fold more active than the boswellic acids in inhibiting the formation of 5-lipoxygenase products in human PMNLs, with IC50 values of 0.0068 microgram/ml (LTB4) and 0.49 microgram/ml (LTC4). After daily intraperitoneal dosage the extract of mixed acetylboswellic acids (20 mg/kg) significantly reduced the clinical symptoms in guinea pigs with experimental autoimmune encephalomyelitis (EAE) between days 11 and 21. However, the inflammatory infiltrates in the brain and the spinal cord were not significantly less extensive in the treated animals than in the respective control group. The multiple intraperitoneal application of boswellic acids did not inhibit the ionophore-challenged ex vivo release of leukotrienes B4 and C4 from PMNLs separated from the blood of guinea pigs with EAE. The boswellic acids have thus been characterized as selective, non-redox and potent inhibitors of the biosynthesis of leukotrienes in vitro.

Wincor MZ, Gutierrez MA. **St. John's wort and the treatment of depression.** US Pharm 1997 Aug;22:88, 90, 97.
IPA COPYRIGHT: ASHP An overview of the botanical and chemical properties, pharmacology, clinical trials, adverse effects and toxicity of St. John's wort (Hypericum perforatum) for the treatment of depression is presented, including patient information on the use of St. John's wort for depression therapy, drug interactions, and dosage information.

Wu CZ, Inoue M, Ogihara Y. **Antihypercholesterolemic action of a traditional Chinese medicine (Kampo medicine), Ogi-Keishi-Gomotsu-To-Ka-Kojin.** Biol Pharm Bull 19998;21(12):1311-6.
The effect of Ogi-Keishi-Gomotsu-To-Ka-Kojin (OKGK), a traditional Chinese herbal medicine (Kampo medicine), on cholesterol metabolism was studied in male Sprague-Dawley rats. Intake of OKGK at doses of 1.38 g/kg for 4 weeks significantly reduced total cholesterol levels in the serum and liver of hypercholesterolemia rats fed a cholesterol-enriched diet. OKGK suppressed cholesterol absorption through the intestine and stimulated excretion of cholesterol into feces as bile acids. Biochemical study indicated that OKGK treatment enhanced cholesterol 7alpha-hydroxylase activity the rate limiting enzyme of cholic acid synthesis, in the liver without any effect on the rate limiting enzyme of cholesterol synthesis, 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Further, cholesterol-enriched diet containing cholic acid suppressed cholesterol 7alpha-hydroxylase activity, whereas OKGK administration reversed the suppression. In conclusion, these results supported the idea that OKGK may be an effective agent for treatment of patients with hypercholesterolemia.

Wu Y, Zhang Y, Wu JA, Lowell T, Gu M, Yuan CS. **Effects of Erkang, a modified formulation of Chinese folk medicine Shi-Quan-Da-Bu-Tang, on mice.** J Ethnopharmacol 1998;61(2):153-9.
Shi-Quan-Da-Bu-Tang is a traditional Chinese herbal medicine formula used to increase vital energy, and strengthen health and immunity. Data from previous studies demonstrated that this formula also has the ability to attack tumor tissue. The Erkang capsule is a modified formula of

Shi-Quan-Da-Bu-Tang, with the addition of four other herbs to increase the adaptogen effects and ergogenic properties. Results from this study in mice indicated that the Erkang treated group had significant differences in mortality, body weight change, fatigue, cold temperature endurance, and immune function related organ weight change, compared to the control animals.

Xiaoguang C, Hongyan L, Xiaohong L, Zhaodi F, Yan L, Lihua T, Rui H. **Cancer chemopreventive and therapeutic activities of red ginseng.** J Ethnopharmacol 1998;60(1):71-8.
Red ginseng extract A and B are the active components of Panax ginseng. Red ginseng is a classical traditional Chinese medicine. Among Chinese herbs, red ginseng has been considered as one of the tonics. Many studies indicated that red ginseng could enhance immune function of the human body. The effects of red ginseng extracts on transplantable tumors, proliferation of lymphocyte, two-stage model and rat liver lipid peroxidation were studied. In a two-stage model, red ginseng extracts had a significant cancer chemoprevention. At 50-400 mg/kg, they could inhibit DMBA/Croton oil-induced skin papilloma in mice, decrease the incidence of papilloma, prolong the latent period of tumor occurrence and reduce tumor number per mouse in a dose-dependent manner. Red ginseng extract B could effectively inhibit the Fe2+/cysteine-induced lipid peroxidation of rat liver microsome, suggesting that red ginseng extract B has a stronger antioxidative effect than that of extract A. The results indicated that red ginseng extracts (50 approximately 400 mg/kg) could significantly inhibit the growth of transplantable mouse sarcoma S180 and melanoma B16. Red ginseng extracts A (0.5 mg/ml) and B (0.1 and 0.25 mg/ml) might effectively promote the transformation of T lymphocyte, but there was no influence on lymphocyte proliferation stimulated by concanavalin A. This suggests that red ginseng extracts have potent tumor therapeutic activity and improve the cell immune system.

Xu Q, Yuan K, Lu J, Wang R, Wu F. **A new strategy for regulating the immunological liver injury--effectiveness of DTH-inhibiting agents on DTH-induced liver injury to picryl chloride.** Pharmacol Res 1997;36(5):401-9.
Aqueous extracts from various crude drugs showing a selective inhibition on the induction or effector phase of delayed-type hypersensitivity (DTH) reaction were applied to the new model of liver injury induced in mice by picryl chloride(PCl)-induced DTH. The inhibiting drugs to the induction phase of DTH, Fructus Triburi (FT) and Er-Miao-San (EMS), showed a remarkable improvement against the elevation in serum transaminase levels as well as in histopathological changes when given during this phase. The administration in the effector phase by Rhizoma Smilacis Glabrae (RSG) and Cortex Dictamni (CD), selectively inhibiting the phase of DTH, also significantly improved the liver damage. In addition, RSG and CD showed an almost complete recovery of serum alkaline phosphatase from a persistent decrease in the sustaining process of liver injury when given consecutively for 4 weeks after the elicitation of liver injury. Cyclophosphamide, an immunosuppressive agent, significantly inhibited the enzymatic elevation given in either phase, while it did not affect the ability to sustain liver injury. When the above extracts were given in a combined manner to the same mouse during these two phases, respectively, FT with RSG and EMS with CD showed a distinct synergism against the liver injury. RSG or CD also enhanced the activity of prednisolone in suppressing PCl-induced ear contact sensitivity. These findings suggest that this immunological liver injury may be regulated

by a set of selective suppressants to DTH reaction and the suitable application of such agents may pave the way for a new strategy in treating liver damage.

Yamada K, Kanba S, Yagi G, Asai M. **Effectiveness of herbal medicine (shakuyaku-kanzo-to) for neuroleptic-induced hyperprolactinemia [letter].** J Clin Psychopharmacol 1997;17(3):234-5.

Yamasaki K, Nakano M, Kawahata T, Mori H, Otake T, Ueba N, Oishi I, Inami R, Yamane M, Nakamura M, et al. **Anti-HIV-1 activity of herbs in Labiatae.** Biol Pharm Bull 1998;21(8):829-33.
The anti-HIV-1 activity of aromatic herbs in Labiatae was evaluated in vitro. Forty five extract from among 51 samples obtained from 46 herb species showed significant inhibitory effects against HIV-1 induced cytopathogenicity in MT-4 cells. In particular, the aqueous extracts of Melissa officinalis, a family of Mentha x piperita "grapefruit mint," Mentha x piperita var. crispa, Ocimum basilicum cv "cinnamon," Perilla frutescens var. crispa f. viridis, Prunella vulgaris subsp. asiatica and Satureja montana showed potent anti-HIV-1 activity (with an ED of 16 microg/ml). The active components in the extract samples were found to be water-soluble polar substances, not nonpolar compounds such as essential oils. In addition, these aqueous extracts inhibited giant cell formation in co-culture of Molt-4 cells with and without HIV-1 infection and showed inhibitory activity against HIV-1 reverse transcriptase.

Yang LC, Wang F, Liu M. **A study of an endothelin antagonist from a Chinese anti-snake venom medicinal herb.** J Cardiovasc Pharmacol 1998;31(Suppl 1):249-50.
Because it is well known that endothelin (ET) plays an important role in the pathogenesis of cardiovascular diseases, antagonists of ET for clinical use are very important. Because ET and some snake toxins have a homologous structure and similar biologic actions the effect of Chinese anti-snake venom herbal medicines on ET bioactivity was investigated both in vivo and in vitro. Hong Bei Si Chou [Cissus assamica (Laws.) Craib] is a herbal medicine used to treat snake bite in Guangxi province. It was found that all the different fractions of EtOH extraction, the EtOAc part of the EtOH extraction, and resverotrol (3,4'5-trihydroxytransstilbene) isolated from the EtOAc part could antagonize ET both in vivo and in vitro. These three fractions transiently relaxed ET-contracted isolated rat aortic ring in a dose-dependent manner. They also antagonized the lethal effects of ET-1 in mice and inhibited blood pressure elevation induced by ET-1. The results have shown that it is possible to find ET antagonists in Chinese anti-snake venom medicinal herbs. In the future, our work should shed new light on the treatment of cardiovascular diseases in which ET is involved.

Yap HK, Zuo XJ, Toyoda M, Okada Y, Ang SG, Lai YH, Matloff JM, Marchevsky A, Ramgolam VS, Jordan SC. **Immunosuppressive effect of the hydrophobic extract of a Chinese herb on rat lung allograft rejection.** Transplant Proc 1998;30(4):980-1.

Yim TK, Wu WK, Mak DH, Ko KM. **Myocardial protective effect of an anthraquinone-containing extract of Polygonum multiflorum ex vivo.** Planta Med 1998;64(7):607-11.
An ethyl acetate extract of Polygonum multiflorum Thunb. (PME) was fractionated into an anthraquinone-containing (PME-I) and a non-anthraquinone-containing (PME-II) fraction. The

effects of PME and its related extracts pretreatment on myocardial ischemia-reperfusion (IR) injury in isolated perfused rat hearts were examined. Pretreatment with PME extract or its anthraquinone-containing fraction produced a dose-dependent protection against myocardial IR injury, as evidenced by a significant decrease in the extent of LDH leakage as well as an improvement in contractile force recovery. The myocardial protection was found to be associated with an enhancement in myocardial glutathione antioxidant status, as indicated by significant reductions in both the extent of IR-induced reduced glutathione (GSH) depletion and inhibition of Se-glutathione peroxidase (GPX) and glutathione reductase (GRD) activities. Both alpha-tocopherol acetate (VE) and emodin (EMD) pretreatments protected against IR-induced myocardial injury as assessed by the decrease in the extent of LDH leakage. But the contractile force recovery of the ischemic-reperfused hearts prepared from VE or EMD pretreated animals was not improved. The more complete myocardial protection afforded by the anthraquinone-containing fraction of PME extract may be related to its ability to sustain the glutathione antioxidant status under the condition of IR-induced oxidative stress.

Yokozawa T, Dong E, Liu ZW, Shibata T, Hasegawa M, Watanabe H, Oura H. **Magnesium lithospermate B ameliorates cephaloridine-induced renal injury.** Exp Toxicol Pathol 1997;49(5):337-41.
To determine whether magnesium lithospermate B ameliorates renal injury induced by cephaloridine, the effect of cephaloridine was investigated in rats given magnesium lithospermate B for 20 days preceding cephaloridine administration and in control rats given no magnesium lithospermate B. In the control rats, blood and urinary parameters and the activity of radical-eliminating enzymes in the renal tissue deviated from the normal range, indicating damage to the kidneys. In contrast, rats given magnesium lithospermate B showed decreased urine volume, increased urinary osmotic pressure, and decreased urinary levels of glucose, protein, sodium and potassium, denoting less damage to the kidney. In this group, the urinary nitrite/nitrate ratio, and the activities of superoxide dismutase and catalase in the renal tissue were increased, while the malondialdehyde levels were decreased, suggesting the involvement of radicals in the normalizing of kidney function. The increased levels of urea nitrogen in the blood of rats with induced renal failure were also lowered by administering magnesium lithospermate B.

Yokozawa T, Dong E, Oura H, Kashiwagi H, Nonaka G, Nishioka I. **Magnesium lithospermate B suppresses the increase of active oxygen in rats after subtotal nephrectomy.** Nephron 1997;75(1):88-93.
Subtotally nephrectomized rats were found to have decreased activities of superoxide dismutase (SOD) and catalase, and spin trapping with 5,5-dimethyl-1-pyrroline-N-oxide (DMPO) showed that the amount of hydroxyl radical in the residual kidney tissue was greater than that in normal rat kidney. This indicated both direct and indirect involvement of free radicals in renal failure. In contrast, rats given magnesium lithospermate B (10 mg/kg body weight) orally for 30 days after subtotal nephrectomy showed restoration of SOD and catalase activities to almost normal levels. Hydroxyl radical, which is highly reactive and for which there is no scavenger system in the body, was decreased markedly in kidney homogenates obtained from rats given magnesium lithospermate B and in an experimental system for hydroxyl radical production to which magnesium lithospermate B was directly added. The increased levels of uremic toxins in the

blood were also low in rats given magnesium lithospermate B. This indicates that magnesium lithospermate B helps to inhibit the progression of renal failure by scavenging radicals.

Yoon SR, Nah JJ, Shin YH, Kim SK, Nam KY, Choi HS, Nah SY. **Ginsenosides induce differential antinociception and inhibit substance P induced-nociceptive response in mice.** Life Sci 1998;62(21):319-25.
Ginsenosides are main pharmacoactive molecules of ginseng. The antinociceptive activity of ginsenosides after intrathecal (i.t.) injection was examined in formalin test. We also investigated the effects of ginsenosides on substance P (SP) induced-pain behaviors by i.t. treatment using mice. Pretreatment of ginsenosides by i.t. induced the inhibition of biting and licking of hind paw injected with 1% formalin with dose-dependent manner. The ED50 was 23 (19-28, 95% C.I.) microg/mouse for acute phase and 15 (9-23, 95% C.I.) microg/mouse for tonic phase. Interestingly, cotreatment of ginsenosides with SP also inhibited SP-induced pain behaviors (scratching, licking or biting of hind portion of body) with dose-dependent manner. The ED50 for the inhibition of SP-induced pain behavior by ginsenosides was 30 (11-85, 95% C.I.) microg/mouse. These results suggest that ginsenosides have antinociceptive activity in formalin test and this effect is due to blocking of SP-induced nociceptive information to postsynaptic site(s) at the spinal level.

You KM, Son KH, Chang HW, Kang SS, Kim HP. **Vitexicarpin, a flavonoid from the fruits of Vitex rotundifolia, inhibits mouse lymphocyte proliferation and growth of cell lines in vitro.** Planta Med 1998;64(6):546-50.
Certain flavonoids having a C-2,3-double bond were reported to show an inhibitory activity against T-lymphocyte proliferation, but not against B-lymphocyte proliferation in vitro. In the course of these studies, vitexicarpin (3',5-dihydroxy-3,4',6,7-tetramethoxyflavone) isolated from the fruits of Vitex rotundifolia was found to show potent inhibition against lymphocyte proliferation. Vitexicarpin inhibited T-lymphocyte proliferation as well as B-lymphocyte proliferation at > 0.1 microM. IC50's were approximately 0.7 microM both for T- and B-cell proliferation. The inhibitory activity of vitexicarpin was reversible. Vitexicarpin also inhibited the growth of certain cancer cell lines, EL-4 and P815.9 (IC50 = 0.25-0.3 microM). These results suggest that vitexicarpin may be a potential therapeutic agent involved in inflammatory/immunoregulatory disorders such as rheumatoid arthritis and lymphomas.

Zheng RL, Zhang H. **Effects of ferulic acid on fertile and asthenozoospermic infertile human sperm motility, viability, lipid peroxidation, and cyclic nucleotides.** Free Radic Biol Med 1997;22(4):581-6.
The capacity of human sperm fertilization principally depends on sperm motility and membrane integrity. Reactive oxygen species, such as superoxide anion and hydrogen peroxide, are known to impair sperm motility and membrane integrity by inducing membrane lipid peroxidation (LPO). Ferulic acid (FA), an effective constituent in various medicinal herbs, has recently been shown to scavenge oxygen free radicals and increase the intracellular cAMP and cGMP. The aim of this study is to investigate the effects of FA on human sperm motility, viability, lipid peroxidation, and cyclic nucleotides in fertile and asthenozoospermic infertile individuals in vitro. The sperm samples were obtained from 10 fertile volunteers and 10 asthenozoospermic infertile patients. Washed spermatozoa were incubated at 37 degrees C in Ham's F-10 medium

with 0, 0.1, 0.2, 0.4, 0.8, or 1.6 mM of FA. Samples were analyzed for viability, determined by eosin-Y dye exclusion method at 0, 1, 2, 3, 5, and 6 h of incubation; motility, determined by the trans-membrane migration method within 2 h of incubation; LPO, determined by thiobarbituric acid (TBA) method at 3 h of incubation and the intracellular cAMP and cGMP, determined, respectively, by 3H-cAMP and 125I-cGMP radioimmunoassay at 3 h of incubation. The results showed: in both fertile and infertile spermatozoa, the viability, trans-membrane migration ratio (TMMR) and the levels of intracellular cAMP and cGMP in FA-treated spermatozoa were significantly higher than those of spermatozoa in control groups, while TBA-reactive substances contents in treated spermatozoa were significantly lower than those in control spermatozoa. The effects of FA on these processes were concentration dependent. These data suggested that FA is beneficial to sperm viability and motility in both fertile and infertile individuals, and that reduction of lipid peroxidative damage to sperm membranes and increase of intracellular cAMP and cGMP may be involved in these benefits. It is possible that FA may be used for cure of asthenozoospermic infertility.

Zheng S, Yang H, Zhang S, Wang X, Yu L, Lu J, Li J. **Initial study on naturally occurring products from traditional Chinese herbs and vegetables for chemoprevention.** J Cell Biochem Suppl 1997;27:106-12.
A number of naturally occurring products from vegetables and herbs exert chemopreventive properties against carcinogenesis. In this paper, two such compounds, isolated from garlic and from a traditional Chinese medicinal herb, are described for review. Elemene, isolated from the Chinese medicinal herb Rhizoma zedoariae, was shown to exhibit antitumor activity in human and murine tumor cells in vitro and in vivo. This novel antineoplastic agent has substantial clinical activity against various tumors. The in vitro effect of elemene on the growth of leukemia cells was evaluated by MTT assay. The IC50 values of elemene for promyelocytic leukemia HL-60 cells and erythroleukemia K562 cells were 27.5 micrograms/mL and 81 micrograms/mL, respectively, while IC50 for peripheral blood leukocytes (PBL) was 254.3 micrograms/mL. The inhibitory effect of elemene on proliferation of HL-60 cells was associated with cell cycle arrest from S to G2M phase transition and with induction of apoptosis. The apoptosis of tumor cells was confirmed by DNA ladder formation on gel electrophoresis and characteristic ultrastructural alterations. The results also demonstrated that inhibitory effects of allicin, a natural organosulfide from garlic, on proliferation of tumor cells were associated with the cell cycle blockage of S/G2M boundary phase and induction of apoptosis. These findings suggest that induction of apoptosis may contribute to the mechanisms of antitumor activity of elemene and allicin, which merit investigation as potential chemoprevention agents in humans.

Zhu JS, Halpern GM, Jones K. **The scientific rediscovery of a precious ancient Chinese herbal regimen: Cordyceps sinensis: part II.** J Altern Complement Med 1998;4(4):429-57.
Cordyceps sinensis (Berk.) Sacc. is a time-honored tonic food and herbal medicine in China, where recent research has shown that many of its traditional uses may be viewed from the basis of pharmacological activities. The ongoing exploration of C. sinensis in its wild form and cultured, fermented mycelial products derived from it, are reviewed from English and Chinese literature. Part II concludes the series with a review of C. sinensis in preclinical in vitro and in vivo studies, and open-label and double-blinded clinical trials on the respiratory, renal, hepatic, cardiovascular, immunologic, and nervous systems, and its effects on cancer, glucose

metabolism, inflammatory conditions, and toxicological studies. In Part I, which appeared in the Fall 1998 issue of this journal (4(3):289-303), we discussed the effects of C. sinensis on antisenescence, endocrine and sexual functions, atherosclerosis, hyperlipidemia, and free radicals.

Zhu JS, Halpern GM, Jones K. **The scientific rediscovery of an ancient Chinese herbal medicine: Cordyceps sinensis: part I.** J Altern Complement Med 1998;4(3):289-303.
This review presents Cordyceps sinensis (Berk.) Sacc., a fungus highly valued in China as a tonic food and herbal medicine. The extant records show the continued use of C. sinensis is now centuries old. The major chemical, pharmacological, and toxicological studies on C. sinensis and the various derived, cultured, fermented mycelial products currently in use are reviewed from the English and Chinese literature. Preclinical in vitro and in vivo studies and clinical blinded or open-label trials in to date over 2000 patients are reviewed. These studies show the main activities of the fungus in oxygen-free radical scavenging, antisenescence, endocrine, hypolipidemic, antiatherosclerotic, and sexual function-restorative activities. The safety of the fungus, its effects on the nervous system, glucose metabolism, the respiratory, hepatic, cardiovascular, and immune systems, immunologic disease, inflammatory conditions, cancer, and diseases of the kidney will be reviewed in the second part of this article to be published in the winter issue of this journal.

Ziment I. **Alternative therapies for asthma.** Curr Opin Pulm Med 1997;3(1):61-71.
Many traditional drugs and techniques are gaining popularity in the treatment of asthma, although scientific proof of their value is usually inadequate. Alternative remedies, including herbs and nonmedication management techniques, have not been shown to be useful primary measures, but they still appeal to patients who feel unsatisfied with orthodox medicines. Dietary modification may be worth considering; evidence suggests that salt reduction and magnesium supplementation have value in reducing asthmatic symptoms. The evidence on the role of steroid-sparing agents is not encouraging, but administering steroids once a day in the mid-afternoon may provide benefit. New aerosol techniques are appearing, but judgement is needed to select the best device for each medication as well as for each patient.

Zusy MJ. **Herbal medicines: are your patients treating themselves?** Nurs Spectr 1997;7(11):6.