Annual Bibliography of Significant Advances in Dietary Supplements Research 2001

To raise the level of knowledge on scientific development of dietary supplements as they relate to health promotion, health maintenance, and disease prevention.

OFFICE OF DIETARY SUPPLEMENTS
National Institutes of Health

CHPA
Consumer Healthcare Products Association

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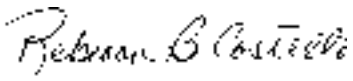
For the third consecutive year, the Office of Dietary Supplements at the National Institutes of Health and the Consumer Healthcare Products Association are pleased to provide you with the *Annual Bibliography of Significant Advances in Dietary Supplement Research*. Published annually, this publication represents research that appeared in scientific journals the previous year. As a new feature of the 2001 issue, in the appendix section we have listed the papers that appeared in the 2000 and 1999 issues. This feature will help you track research developments in the field of dietary supplements.

As with the 2000 and 1999 issues, editors of peer-reviewed journals nominated original research that appeared in their journals the previous year. For this issue, we limited the number of nominations per journal to 24 and we invited scientific reviewers to nominate noteworthy papers as well. This process identified over 250 papers published in 2001, which we then forwarded to internationally recognized scientists to select the top 25 papers. These 25 papers were then annotated and compiled into this bibliography.

We rely on the efforts of many individuals for the continued success of this project. Their outstanding contributions and combined efforts make it possible for us to bring you this publication annually. Please join us in thanking these individuals who include journal editors, scientific reviewers, and staff at the Office of Dietary Supplements, the Consumer Healthcare Products Association, and the National Agricultural Library in the US Department of Agriculture. These individuals are listed in the acknowledgments section of this publication.

Please contact us if you have questions or need multiple copies of this issue, or past issues, to distribute in your classroom, practice, or workplace. We welcome your comments on this publication.

Sincerely,



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About the Office of Dietary Supplements (ODS) at the National Institutes of Health:

ODS was established by the Dietary Supplements Health and Education Act of 1994 (DSHEA, Public Law 103-417). The mission of ODS is to strengthen knowledge and understanding of dietary supplements by evaluating scientific information, stimulating and supporting research, disseminating research results, and educating the public to foster an enhanced quality of life and health for the US population.

About the Consumer Healthcare Products Association (CHPA):

CHPA is a 121-year-old trade organization representing manufacturers and distributors of national and store brand nonprescription medicines and dietary supplements. CHPA's membership includes about 200 companies involved in the manufacture and distribution of these self-care products and their affiliated services, such as raw material suppliers, research testing companies, contract manufacturing companies, and advertising agencies.

Dietary supplements are products intended to supplement the diet and are provided in many forms including tablets, capsules, powders, geltabs, extracts, or liquids. They contain one or more of the following dietary ingredients: (a) a vitamin; (b) a mineral; (c) an herb or other botanical; (d) an amino acid; (e) a dietary substance intended to supplement the diet by increasing the total dietary intake; or (f) a concentrate, metabolite, constituent, extract; or (g) combination of any ingredient listed.

Supplementation of atherogenic diet with B-vitamins does not prevent atherosclerosis or vascular dysfunction in monkeys.

SR Lentz, DJ Piegors, MR Malinow, and DD Heistad. *Circulation* (Circulation) 2001 103:1006-1011.

Elevated blood levels of homocysteine or hyperhomocysteinemia are associated with an increased risk for stroke, myocardial infarction, and venous thrombosis. Folic acid taken in supplements, in fortified foods, or in combination with other B-vitamins has been shown to reduce blood homocysteine levels. The purpose of this study was to determine whether dietary supplementation with B-vitamins would prevent hyperhomocysteinemia and slow the development of vascular dysfunction in monkeys fed a high fat and cholesterol or atherogenic diet. Sixteen adult cynomolgus monkeys, without pre-existing atherosclerosis, were fed an atherogenic diet and received daily B-vitamin supplements (5 mg folic acid, 400 μg vitamin B_{12}, and 20 mg vitamin B_6) or no supplements for 13 to 26 months. After 17 months, blood levels of homocysteine did not increase in the monkeys that received the B-vitamins. The B-vitamins had no effect on blood cholesterol levels or on vascular remodeling of the common carotid artery. In addition, the vitamins did not prevent thickening of the inner wall of the carotid or iliac artery. In this study, supplementation with B-vitamins prevented hyperhomocysteinemia, but this was not sufficient to attenuate the development of vascular dysfunction or atherosclerotic lesions in monkeys with hypercholesterolemia fed an atherogenic diet. These data suggest that controlling the level of fat and cholesterol in the diet may be necessary in order to derive clinical benefits from taking B-vitamin supplements.

Funding: Department of Veterans Affairs, and the National Heart, Lung, and Blood Institute and the National Institute for Diabetes and Digestive and Kidney Diseases, NIH.

Low-dose vitamin B_6 effectively lowers fasting plasma homocysteine in healthy elderly persons who are folate and riboflavin replete.

MC McKinley, H McNulty, J McPartlin, JJ Strain, K Pentieva, M Ward, DG Weir, and JM Scott. *American Journal of Clinical Nutrition* (Am J Clin Nutr) 2001 73:759-764.

Aging is associated with an increase in homocysteine blood levels and a decline in vitamin B_6 status, which may increase the risk for cardiovascular disease in the elderly. The aim of this study was to see if vitamin B_6 would independently lower homocysteine levels in older individuals who were not deficient in folate, riboflavin, or vitamin B_{12}. To ensure that they were not deficient in these B-vitamins, 22 healthy older adults between 62 and 80 years of age were given riboflavin (1.6 mg) daily for 12 weeks followed by a combination of folic acid (400 μg) and riboflavin (1.6 mg) daily for an additional six weeks. Vitamin B_{12} supplements were not provided, as none of the individuals was deficient in vitamin B_{12}. They were then given a low-dose level of vitamin B_6 (1.6 mg) or a placebo daily for an additional 12 weeks while continuing to take the riboflavin and folic acid supplements. Folic acid supplementation lowered fasting blood levels of homocysteine by 19.6 percent. Vitamin B_6 supplementation lowered these levels by an additional 7.5 percent. These data suggest that adding low-dose vitamin B_6 to a B-vitamin supplementation regimen will result in additional reductions in blood levels of homocysteine and thus prove helpful in protecting older individuals from cardiovascular disease.

Funding: European Union (EU) Project and Abbott Germany.

Folic acid fortification increases red blood cell folate concentrations in the Framingham Study.

SF Choumenkovitch, PF Jacques, MR Nadeau, PWF Wilson, IH Rosenberg, and J Selhub. ***Journal of Nutrition*** **(J Nutr) 2001 131:3277-3280.**

In 1996 the US Food and Drug Administration (FDA) mandated that all cereal grain products be fortified with 140 μg folic acid/100 g of product. The benefits of adequate folate intake include protection against the development of neural tube defects as well as a reduction in blood homocysteine levels, a risk factor for cardiovascular disease. This study analyzed data generated from the Framingham Offspring Cohort, the offspring and their spouses from the Framingham Heart Study (FHS), an epidemiologic study of the natural history of heart disease. Specifically, levels of folate in red blood cells (RBC), a measure of folate status, of 872 individuals who were examined before implementation of the FDA fortification program were compared with 626 individuals who were examined after the program. Separate statistical analyses were performed according to the individual's use of B-vitamin supplements. The results show that the introduction of the FDA fortification program significantly improved the folate status in the Framingham Offspring Cohort. Additionally RBC folate levels were 24 percent higher among those also taking B-vitamin supplements. According to the researchers, the FDA fortification program has achieved its goal of eliminating folate deficiency in the general United States population. This study shows that B-vitamin supplements can provide additional benefits over those derived from FDA's mandatory folic acid fortification program.

Funding: US Department of Agriculture, and the National Heart, Lung, and Blood Institute and the National Institute of Diabetes and Digestive and Kidney Diseases, NIH.

Cost-effectiveness of vitamin therapy to lower plasma homocysteine levels for the prevention of coronary heart disease.

JA Tice, E Ross, PG Coxson, I Rosenberg, MC Weinstein, MGM Hunink, PA Goldman, L Williams, and L Goldman. ***Journal of the American Medical Association*** **(JAMA) 2001 286:936-943.**

This study sought to calculate the cost-effectiveness of the US Food and Drug Administration (FDA) folic acid grain fortification program and additional supplementation with B-vitamins to reduce the risk of coronary heart disease (CHD). The researchers used the Coronary Heart Disease Policy Model, a validated, state-transition model of CHD events and its costs among US residents aged 35-84 years. The model was customized to predict an increased intake of 100 μg/day from the folic acid fortification program would result in an 11 percent decrease in blood homocysteine levels. The cost of vitamin supplements, 1.0 mg folic acid and 0.5 mg vitamin B_{12} taken daily, was estimated at $20.29 a year. Based on the model, the grain fortification program was estimated to decrease CHD events by eight percent in women and 13 percent in men. Compared with grain fortification alone, treating all adults with known CHD with folic acid and vitamin B_{12} supplements over a 10-year period would result in 310,000 fewer deaths. The associated projected quality of life adjusted costs among all men 45 years and older and all women over 55 years without CHD were calculated to save over $2 billion over 10 years. As the cost-effectiveness calculations in this model are based on reductions in blood homocysteine levels, clinical data are needed to confirm the calculated decreases in CHD event rates.

Funding: Source not identified.

Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease.

Oxidative processes lead to the development of atherosclerosis, while supplementation with antioxidant vitamins is thought to inhibit these processes and reduce the risk for coronary heart disease. This study was undertaken to evaluate the combined effect of the prescription drug simvastatin and niacin (simvastatin-niacin), with and without a combination of antioxidants on disease progression in individuals with cardiovascular disease and low high-density lipoprotein (HDL) cholesterol levels. One hundred and sixty adult men and women received simvastatin-niacin, antioxidants, simvastatin-niacin plus antioxidants, or placebos over a three-year period. The antioxidant supplement, given twice daily, provided a total daily dose of 800 IU of vitamin E (*d*-α-tocopherol), 1000 mg of vitamin C, 25 mg of natural β-carotene, and 100 μg of selenium. A coronary angiogram was performed at the beginning and at the end of the three-year trial to quantify the degree of atherosclerotic plaque in the coronary arteries. As expected, simvastatin-niacin significantly reduced levels of low-density lipoprotein (LDL) cholesterol and raised levels of HDL cholesterol. At the pharmacological levels used in this study, the antioxidant regimen alone did not alter blood cholesterol levels and was found to blunt the beneficial HDL raising effect and, to a lesser extent, deter the disease regression of simvastatin-niacin. This study suggests that negative interactions can occur between prescription drugs and antioxidant nutrients. As the number of individuals in this study was small, a large-scale study is needed to confirm these interactions using levels of antioxidant nutrients closer to those found in common dietary supplements.

Funding: National Heart, Lung, and Blood Institute and the National Institute of Diabetes and Digestive and Kidney Diseases, NIH, and the University of Washington.

BG Brown, X-Q Zhao, A Chait, LD Fisher, MC Cheung, JS Morse, AA Dowdy, EK Marino, EL Bolson, P Alaupovic, J Frohlich, and JJ Albers. ***New England Journal of Medicine*** **(N Engl J Med) 2001 345:1583-1592.**

FAT-SOLUBLE VITAMINS

Serum carotenoids and breast cancer.

Carotenoids are orange pigments with known antioxidant properties found in plants. Carotenoids may contribute to the prevention of cancer by counteracting oxidative processes that could damage and interfere with the normal functioning of cells. While it is documented that adequate intake of fruits and vegetables protects against some forms of cancer, the evidence in the case of breast cancer is not compelling. This study examined the association between the etiology of breast cancer and blood biochemical markers that indicate intakes of fruits, vegetables, and carotenoids in supplements. Blood concentrations of the carotenoids lutein, zeaxanthin, β-cryptoxanthin, lycopene, α-carotene, and β-carotene were compared to the incidence of breast cancer among 270 women with and 270 women without a history of breast cancer. These 35-65-year-old women were selected from the New York Women's Health Study, a prospective study of 14,275 women. Analyses of the data showed an increased risk of breast cancer with decreasing levels of lutein, β-cryptoxanthin, α-carotene, and β-carotene. The risk of breast cancer for women with blood levels of β-carotene in the lowest quartile was double that of those in the highest quartile. The risk of breast cancer associated with the other carotenoids was similar. The results of this observational study indicate that low intakes of carotenoids, from either foods or supplements, are associated with an increased risk of breast cancer and may have public health relevance for women.

Funding: National Cancer Institute, NIH.

P Toniolo, AL Van Kappel, A Akhmedkhanov, P Ferrari, I Kato, RE Shore, and E Riboli. ***American Journal of Epidemiology*** **(Am J Epidemiol) 2001 153:1142-1147.**

Effects of a short-term vitamin D_3 and calcium supplementation on blood pressure and parathyroid hormone levels in elderly women.

M Pfeifer, B Begerow, HW Minne, D Nachtigall, and C Hansen. ***The Journal of Clinical Endocrinology and Metabolism*** **(J Clin Endocrinol Metab) 2001 86:1633-1637.**

In addition to helping build strong bones, calcium and vitamin D may have beneficial roles in the management of blood pressure. These researchers evaluated the effects of supplementation with calcium and vitamin D on blood pressure in elderly women. Over an eight-week period, 148 women aged 70 and older, took 600 mg calcium as calcium carbonate, or 600 mg calcium plus 400 IU vitamin D_3 twice a day with meals. There was no placebo treatment in this study. Dietary intakes of calcium, vitamin D, and salt, as well as alcohol and nicotine consumption were monitored. Biochemical analyses were conducted on blood and urine samples at the start and at the end of the study. At the end of eight weeks, the combined calcium plus vitamin D_3 treatment was more effective than the calcium alone regimen. The combined treatment reduced systolic blood pressures by 9.3 percent, blood parathyroid levels by 17 percent, and heart rates by 5.4 percent. No difference was observed in diastolic blood pressure levels between the two regimens. This study supports the use of calcium and vitamin D supplements, at currently recommended levels, in the management of blood pressure in older individuals. As this was a short-term study with no placebo treatment, a longer trial with a placebo arm is warranted before public health recommendations are made.

Funding: Strathmann, Inc, Germany.

Chronic administration of pharmacologic doses of vitamin E improves the cardiac autonomic nervous system in patients with type 2 diabetes.

D Manzella, M Barbieri, E Ragno, and G Paolisso. ***American Journal of Clinical Nutrition*** **(Am J Clin Nutr) 2001 73:1052-1057.**

Individuals with type 2 or adult onset diabetes are predisposed to elevated oxidative stress and declines in antioxidant defense. One negative effect of elevated levels of oxidative stress is an imbalance in the activity of the nervous system of the heart. This study evaluated the effects of vitamin E supplementation on components of the cardiac nervous system in individuals with type 2 diabetes and cardiac neuropathy. Fifty individuals received either 600 mg of vitamin E (α-tocopherol) or a placebo daily for four months. Several biochemical and physiological measures were used to evaluate oxidative stress and cardiac function. Vitamin E supplementation reduced blood measures of oxidative stress and improved cardiac autonomic function. Vitamin E modulated insulin resistance, which may explain the observed positive effects on the nervous system. These results suggest that reductions in oxidative stress in type 2 diabetes are associated with a decrease in blood catecholamines and cardiac nervous system activity, which may further contribute to reductions in cardiovascular disease risk. The mechanism of action of how vitamin E affects the nervous system is not known and calls for further research as neuropathy is a common and limiting abnormality in diabetes.

Funding: Second University of Naples, Italy.

A controlled clinical trial of vitamin E supplementation in patients with congestive heart failure.

ME Keith, KN Jeejeebhoy, A Langer, R Kurian, A Barr, B O'Kelly, and MJ Sole. ***The American Journal of Clinical Nutrition*** **(Am J Clin Nutr) 2001 73:219-224.**

Oxidative stress caused by an increase in free radical production or a decrease in cellular antioxidant levels, such as vitamin E, results in increased cell injury and in some cases, heart failure in humans. This study was designed to test whether vitamin E supplementation would affect oxidative stress in individuals with advanced heart failure. Fifty-six clinically stable individuals with advanced heart failure received two 335.6 mg (500 IU) capsules of vitamin E (α-tocopherol) or a placebo daily for 12 weeks. Breath and blood samples were used to measure indicators of heart function and heart disease. Quality of life was measured at the start and the end of the study. Results of the study show that while vitamin E concentration in the blood doubled during the first six weeks of the trial and remained elevated for the full 12 weeks, there was no significant improvement in health status or quality of life among individuals who received the supplements. This study examined the short-term effects of vitamin E in individuals with advanced heart failure and the results do not support the use of vitamin E supplements by these individuals. It is yet to be determined if there is a supportive role for vitamin E in the long-term management of heart failure.

Funding: Medical Research Council of Canada and Bayer Inc, Toronto.

Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomized trial in general practice.

Collaborative Groups of the Primary Prevention Project (PPP). ***The Lancet*** **(Lancet) 2001 357:89-95.**

The Primary Prevention Project (PPP) was a controlled, centrally randomized, open-label clinical trial designed to evaluate whether chronic treatment with aspirin (antiplatelet therapy) and vitamin E (antioxidant therapy) reduces the frequency of cardiovascular events in individuals with one or more cardiovascular risk factors. In addition to taking their prescribed medications, 4,495 individuals over 50-years-old received a daily dose of aspirin (100 mg), vitamin E (300 mg α-tocopherol), or a placebo. These individuals met with their physicians annually and their medications were renewed every four months. This five-year study, however, was stopped mid-way for ethical reasons due to new research supporting the use of aspirin in the primary prevention of heart attacks. Analysis of the data collected after a mean treatment of 3.6 years indicated that vitamin E supplementation did not reduce the risk for a cardiovascular event, however it did lower the incidence of peripheral artery disease. It is possible that the study was not long enough to observe any cardiovascular benefits from vitamin E supplementation. The results of this study show that vitamin E does not provide any additional benefit among individuals with cardiovascular disease who are taking prescription medicine to treat their medical condition.

Funding: Medical Department of Bayer Italy.

Elevated iron status increases bacterial invasion and survival and alters cytokine/chemokine mRNA expression in Caco-2 human intestinal cells.

SL Foster, SH Richardson, and ML Failla. *Journal of Nutrition* (J Nutr) 2001 131:1452-1458.

Iron plays a central role in many biochemical and physiological processes including microbial growth and immune function. High concentrations of iron in cells makes them more susceptible to infections. Using *in-vitro* (in-cell culture) techniques, researchers investigated whether intestinal cells (enterocytes) with elevated iron concentrations were more susceptible to invasion by intestinal pathogens. The enterocyte-like Caco-2 human intestinal cell line (host) and *Salmonella enteritidis* (parasite) were used as models to examine the effect of iron status on the host-parasite interaction. Increased iron levels in uninfected Caco-2 cells resulted in a 25-45 percent decrease in levels of immune modulators indicated by the ratio of cytokine/chemokine mRNA. In contrast, increased iron levels in infected cells resulted in a 21-95 percent increase in cytokine/chemokine mRNA levels compared with infected cells with lower iron levels. These results show that in response to a microbial invasion, intestinal cells with higher iron concentrations are more susceptible to infection. This study provides important information on the role of iron in supporting infections and has implications for iron supplements taken during infectious conditions.

Funding: Source not identified.

Effect of zinc supplementation on malaria and other causes of morbidity in West African children: randomised double blind placebo controlled trial.

O Müller, H Becher, AB van Zweeden, Y Ye, DA Diallo, AT Konate, A Gbangou, B Kouyate, and M Garenne. *British Medical Journal* (BMJ) 2001 322:1-6.

Malaria is widespread in tropical Africa and its effects on the immune system account for the high rate of illness and death observed in this region. Further, children in developing countries are often deficient in zinc, a mineral important in building immunity. In this six-month clinical study, 709 West African children, aged six to 31 months, were given 12.5 mg of zinc as zinc sulfate or a placebo for six days a week. Six hundred and eighty five children completed the study with a 36 percent prevalence rate of malnutrition. The primary outcome of the study was the incidence of symptomatic falciparum malaria, which is malaria caused by one of the four known species of malaria parasites. Other outcomes, such as the severity of malaria episodes, the prevalence of the malaria parasite, the prevalence of other illnesses, and all causes of death also were determined. The scientists found that zinc supplementation reduced incidence of diarrhea, but had no effect on the incidence of malaria or all other causes of death. As observed with other trials conducted in malnourished children in developing countries, single nutrient interventions may not be effective in treating children with multiple nutrient deficiencies.

Funding: The World Health Organization and the Deutsche Forschungsgemeinschaft.

Simultaneous zinc and vitamin A supplementation in Bangladeshi children: randomised double blind controlled trial.

MM Rahman, SH Vermund, MA Wahed, GJ Fuchs, AH Baqui, and JO Alvarez. ***British Medical Journal*** **(BMJ) 2001 323:314-318.**

Adequate vitamin A status reduces the incidence of childhood mortality, but its effect on morbidity is not clear. Other micronutrient deficiencies, such as zinc deficiency, can complicate the observed effects of vitamin A supplementation. As zinc has an interactive effect with vitamin A, this study examined the effects of vitamin A and zinc supplementation on the incidence of diarrhea and acute lower respiratory infections. Eight hundred children aged 12-35 months, residing in economically depressed areas in Bangladesh, were given one of the following four treatments: 1) 5 ml of zinc syrup, containing 20 mg zinc, given once daily for 14 days; 2) a single 200, 000 IU (60 mg) capsule of vitamin A given on day 14; 3) combined zinc and vitamin A; and 4) a placebo syrup daily and placebo capsule on day 14. After this 14-day treatment period the children were studied once a week for six months and morbidity information was collected. The incidence of diarrhea and acute lower respiratory infection were used as measures of morbidity. The study showed that the combination zinc and vitamin A treatment was more effective than either alone in reducing the incidence of diarrhea, including severe diarrhea, or dysentery. Although zinc supplementation alone reduced the incidence of diarrhea compared to the placebo group, there was a twofold increase in the prevalence of lower respiratory illness. The addition of vitamin A, however, reduced this adverse effect. This study adds to the body of knowledge that single nutrient interventions may not have beneficial outcomes and that combined treatments may be more effective when treating malnourished children.

Funding: Thrasher Research Fund.

FIBER AND SOY

The prebiotic effects of biscuits containing partially hydrolysed guar gum and fructo-oligosaccarides: a human volunteer study.

KM Tuohy, S Kolida, AM Lustenberger, and GR Gibson. ***British Journal of Nutrition*** **(Br J Nutr) 2001 86:341-348.**

Prebiotics are non-digestible food ingredients that become food for intestinal bacteria, such as bifidobacteria, clostridia, and lactobacilli when they reach the lower intestine. In recent years, there has been an increased interest in altering levels of these bacteria and studying their relationship to human health. In this 21-day cross-over study, 31 individuals consumed cookies that contained prebiotic dietary fibers that provided 6.6 g/day fructo-oligsaccharides and 3.4 g/day partially hydrolyzed guar gum, or no dietary fiber. These individuals kept daily diaries of stool frequency and consistency, abdominal pain, intestinal bloating, flatulence, and any other adverse effects. The researchers used a fluorescent staining method (FISH) to measure levels of gut bacteria in fecal samples. Intake of fructo-oligsaccharides and guar gum for 21 days resulted in increased bifidobacteria levels, but these levels returned to normal seven days after ceasing the dietary fiber regimen. The greatest increase in bifidobacteria levels was observed in individuals with the lowest starting levels of bifidobacteria. Dietary fiber did not alter levels of other gut bacteria. As bifidobacteria are regarded as beneficial gut bacteria, these results suggest that the ingestion of fructo-oligsaccharides and partially hydrolyzed guar gum could have positive health outcomes. These health outcomes should be identified in future research.

Funding: Novartis Nutrition Research AG, Switzerland.

Inhibition of postmenopausal atherosclerosis progression: a comparison of the effects of conjugated equine estrogens and soy phytoestrogens.

TB Clarkson, MS Anthony, and TM Morgan. ***The Journal of Clinical Endocrinology and Metabolism*** **(J Clin Endocrinol Metab) 2001 86:41-47.**

Plants such as soy contain isoflavones also called phytoestrogens, since they bind to estrogen receptors. This animal study was conducted to examine the effect of soy phytoestrogens on atherosclerosis and to compare these effects with conjugated equine estrogens (estrogen replacement therapy). One hundred and eighty-nine premenopausal cynomolgus monkeys consumed a moderately atherogenic diet for 26 months and then their ovaries were removed (ovariectomy) to induce menopause. For 36 months following ovariectomy, the monkeys were given one of the following three diets: 1) soy protein with soy phytoestrogens; 2) conjugated equine estrogen in soy protein with no soy phytoestrogens; or 3) a control diet consisting of soy protein with no soy phytoestrogens. Compared with the control diet, the two treatment diets significantly lowered total cholesterol levels. In addition, soy with phytoestrogens increased high-density lipoprotein (HDL) cholesterol. Conjugated equine estrogen increased triglyceride levels, while soy with phytoestrogens had no effect on triglyceride levels. Measurements of atherosclerosis, as determined by plaque size, showed that both treatment diets inhibited atherosclerosis, although soy with phytoestrogens was not as effective as conjugated equine estrogen. The results from this study suggest that soy protein with phytoestrogens may improve lipid profiles, inhibit atherosclerosis, and may be an alternative to hormone replacement therapy for some women.

Funding: National Heart, Lung, and Blood Institute, NIH.

Dietary soy has both beneficial and potentially adverse cardiovascular effects: a placebo-controlled study in men and postmenopausal women.

HJ Teede, FS Dalais, D Kotsopoulos, Y-L Liang, S Davis, and BP McGrath. ***The Journal of Clinical Endocrinology and Metabolism*** **(J Clin Endocrinol Metab) 2001 86:3053-3060.**

Diets high in soy have been associated with a lower risk for cardiovascular disease. The mechanism of action of soy is similar to that of estrogen, but it is not known if soy can similarly influence endothelial tissues in blood vessels. Endothelial dysfunction is an early marker of cardiovascular disease. To evaluate the cardiovascular effects of soy, 213 healthy individuals (108 men and 105 postmenopausal women) were given a soy protein isolate (40 g soy protein and 118 mg isoflavones) or a casein placebo daily for three months. Individuals were monitored for blood pressure, lipids, sex hormones, indices of vascular function, and endothelial function. Dietary soy supplementation resulted in significant lowering of systolic and diastolic blood pressures, triglycerides, and low-density lipoprotein/high-density lipoprotein (LDL/HDL) cholesterol ratio in both men and postmenopausal women. Vascular compliance (as measured by pulse wave velocity and brachial artery flow mediated dilatation) was unchanged by the soy treatment, reinforcing previous research that suggests soy may act through pathways other than those that are estrogen dependent. An unexpected adverse finding was a 15 percent increase in Lp(a) lipoprotein, a marker of cardiac risk. The results of this study suggest that while soy failed to improve indices of vascular function, it may have other cardioprotective properties by improving both blood pressure and lipid profiles. Further research is needed to understand the effects of soy on the cardiovascular system in individuals with existing cardiac risk factors.

Funding: National Heart Foundation, Australia.

High dietary phytoestrogen intake is associated with higher bone mineral density in postmenopausal but not premenopausal women.

Phytoestrogens such as isoflavones, the active components in soy, are hypothesized to have estrogen-like actions on hormone-sensitive tissues in the body. Because the incidence of hip fractures has tripled in China in the last 30 years and because of the side effects associated with hormone replacement therapy, these researchers wanted to determine whether high intakes of soy would be associated with a lower risk for osteoporosis. This retrospective study compared past intakes of dietary phytoestrogen, assessed by a food frequency questionnaire, with bone mineral density in 650 Chinese women between the ages of 19 and 86. Findings in postmenopausal women revealed that bone mineral density measurements at the lumbar spine and hip were significantly higher in women with the highest isoflavone intake compared with women with the lowest isoflavone intake. High isoflavone intake also was associated with lower levels of blood parathyroid hormone, osteocalcin, and urinary N-telopeptide (all measurements of bone turnover) in postmenopausal women. In premenopausal women, no associations were found between bone mineral density and isoflavone intake. These findings suggest that high intakes of dietary isoflavones may increase bone mineral density in postmenopausal women and thus reduce their risk for osteoporosis. Additional research is needed to understand the effects of phytoestrogen consumption on bone health in other population groups.

Funding: University of Hong Kong, China

J Mei, SSC Yeung, and AWC Kung. ***The Journal of Clinical Endocrinology and Metabolism*** **(J Clin Endocrinol Metab) 2001 86:5217-5221.**

AMINO ACIDS AND FATTY ACIDS

Endothelium-dependent vasodilation is independent of the plasma L-arginine/ADMA ratio in men with stable angina.

L-arginine is an amino acid found naturally in the body that serves as a substrate for nitric oxide, a potent vasodilator. The beneficial effects of L-arginine are thought to result from increased nitric oxide production. These effects include improved endothelial (blood vessel) function, reduced oxidative stress, and decreased blood platelet aggregation. The study examined whether the L-arginine to ADMA ratio (ADMA is an inhibitor of L-arginine) affects endothelium-dependent vasodilation. In addition, the researchers wanted to test whether supplementation with L-arginine decreases oxidative stress and improves endothelium-dependent vasodilation in men with coronary artery disease. Forty men with stable angina and mild hypercholesterolemia received either L-arginine (15 g) or a placebo daily for two weeks. After two weeks of oral supplementation, blood levels of L-arginine increased and resulted in a 62 percent increase in the L-arginine/ADMA ratio; however, an improvement in vascular function was not observed. Blood levels of 8-epi-prostaglandin $F_{2\alpha}$ (a marker of oxidative stress), exercise performance, and EKG monitoring also were unchanged by supplementation. The investigators concluded that elevating the L-arginine/ADMA ratio with oral L-arginine does not improve endothelium-dependent vasodilation. Additionally, L-arginine did not appear to possess significant antioxidant or anti-anginal activities in these individuals. These findings do not agree with some previous animal and human research, indicating the need for definitive research.

Funding: British Heart Foundation.

HA Walker, E McGing, I Fisher, RH Böger, SM Bode-Böger, G Jackson, JM Ritter, and PJ Chowienczyk. ***Journal of the American College of Cardiology.*** **(J Am Coll Cardiol) 2001 38:499-505.**

Dietary supplementation with γ-linolenic acid or fish oil decreases T lymphocyte proliferation in healthy older humans.

F Thies, G Nebe-von-Caron, JR Powell, P Yaqoob, EA Newsholme, and PC Calder. *Journal of Nutrition.* (J Nutr) 2001 131:1918-1927.

Animal and human research shows that dietary polyunsaturated fatty acids (PUFAs) may alter immune function. This study investigated whether moderate intakes of PUFAs affect the production of lymphocytes and select immune factors such as interleukin-2 and interferon-γ, which are important defenses against invading bacteria, viruses, and fungi. Forty-eight healthy adults received daily for 12 weeks an encapsulated placebo oil blend, in addition to five other oil blends, which provided varying levels and types of PUFAs. These five oil blends provided: 1) 2 g of α-linolenic acid (ALNA); 2) 770 mg of γ-linolenic acid (GLA); 3) 680 mg of arachidonic acid (ARA); 4) 720 mg of docosahexaenoic acid (DHA); or 5) 720 mg of eicosapentaenoic (EPA) plus 280 mg of DHA from fish oils. Blood samples were analyzed for peripheral blood mononuclear cell (PBMC) phospholipid composition, lymphocyte production in PBMC cultures, and production of cytokines by PBMC cultures. The fatty acid composition of PBMC phospholipids was significantly altered by intake of GLA, ARA, DHA, and fish oil. Lymphocyte production was decreased with GLA and fish oils, but was not affected by ALNA, ARA, or DHA. The production of interleukin-2 or interferon-γ by PBMC was unchanged. The authors concluded that moderate intakes of GLA or EPA, but not other PUFAs, could decrease lymphocyte proliferation without affecting the production of interleukin-2 or interferon-γ. These data suggest that adverse immunological effects are unlikely at the level of EPA and DHA provided in this study. However additional research is needed to identify the mechanism of action and to confirm these effects on immune function and on rates of infection in humans at levels of EPA and DHA used in this study.

Funding: AgriFood LINK Programme, UK.

BOTANICALS

Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomised, placebo-controlled study.

R Schellenburg for the study group. *British Medical Journal* (BMJ) 2001 322:134-137.

The fruits of *Vitex agnus castus* or chaste tree are used in traditional medicine because it is thought to relieve premenstrual syndrome (PMS) symptoms. As these effects had not been scientifically validated in a clinical trial, these German-based researchers studied the effects of chaste tree on PMS, in 178 women with a mean age of 36 years. These women were given daily, for three consecutive cycles, a 20 mg chaste tree (dry berry extract) tablet, standardized for casticin (a marker compound in chaste tree) or a placebo tablet. Women who received chaste tree had significant decreases in PMS symptoms compared with those who received a placebo. Self-evaluation by the women was corroborated by a physician's own evaluation using the Clinical Global Impression Scale. There was improvement in five of the six self-assessment items. Improvements were seen for irritability, mood alterations, anger, headache, and breast fullness, but not for bloating. No adverse events related to use of chaste tree were observed in this study. According to the researchers, acceptance of chaste tree by women was high and the side effects were few and mild. This study lends support to the traditional use of chaste tree in the management of PMS symptoms.

Funding: Clinical Research Organization Praxis Klinische Arzneimittelforschung Polheim, Germany.

Determination of ephedrine-type alkaloids in dietary supplements by LC/MS using a stable-isotope labeled internal standard.

In traditional Chinese medicine, ephedra, or *Ma Huang,* is used for the management of asthma. In the United States, it is marketed primarily for weight loss and enhancing athletic performance. This paper describes an analytical method that was developed to quantify the various ephedrine-type alkaloids present in two ephedra-containing products, a gel capsule and a high-protein, chocolate-flavored drink. The researchers modified a liquid chromatographic (LC) method developed by Hulburt *et al* in 1998 to allow detection by mass spectrometry (MS). The MS method had advantages over the original method, as it was more sensitive and less susceptible to interference by other ingredients typically used in ephedra containing dietary supplements. As the reproducibility of the method under different conditions was not determined, this method is now being tested by different laboratories to determine if it meets the requirements of a full-collaborative study as outlined by AOAC INTERNATIONAL. When these studies are complete, this method will become an official method of analysis for the qualitative and quantitative determination of ephedrine-type alkaloids in ephedra products.

Funding: US Food and Drug Administration.

ML Gay, KD White, WR Obermeyer, JM Betz, and SM Musser.
Journal of AOAC INTERNATIONAL
(J AOAC Int) 2001 84:761-769.

Ginger for nausea and vomiting in pregnancy: randomized, double-masked, placebo-controlled trial.

Some women use ginger to manage their symptoms of nausea and vomiting during early pregnancy. Although not debilitating, these symptoms are unpleasant and can result in lost days from work. Given the scarcity of clinical studies, these researchers conducted this study to confirm the effects of ginger in managing nausea and vomiting among pregnant women. Seventy Thai women in the early stages of pregnancy with nausea and vomiting were given either a 250 mg capsule of ginger or a placebo four times a day for four days. The women were asked to record the severity and number of vomiting episodes. In addition, the severity of their nausea was assessed using a five-item Likert scale. The number of vomiting episodes was significantly reduced in women taking ginger. Using the Likert scales, 28 of the 32 women in the ginger treated group had improvement in their nausea symptoms compared with 10 out of 35 in the placebo group. No adverse effect of ginger on pregnancy outcomes was detected, although the study was of very short duration. This study shows that ginger may be effective in managing nausea and vomiting occurring during the early stages of pregnancy.

Funding: Source not identified.

T Vutyavanich, T Kraisarin, and R-A Ruangsri.
Obstetrics and Gynecology
(Obstet Gynecol) 2001 97:577-582.

Caffeine intake increases the rate of bone loss in elderly women and interacts with vitamin D receptor genotypes.

PB Rapuri, JC Gallagher, HK Kinyamu, and KL Ryschon. ***American Journal of Clinical Nutrition*** **(Am J Clin Nutr) 2001 74: 694-700.**

The role of caffeine, a ubiquitous ingredient found in beverages, foods and some medication, as a risk factor for bone loss is controversial. This study examined the association between caffeine intakes and bone mineral density, and the interaction between caffeine intakes, vitamin D receptor gene (VDR) polymorphism, and bone mineral density. There were two groups in this study, 443 women in the cross-sectional analysis and 96 in the three-year longitudinal analysis. The women from these two groups were selected from Sites Testing Osteoporosis Prevention or Intervention (STOP IT) program, which was a study designed to compare the effects of hormone replacement and vitamin D analogue therapies in reversing bone loss. High caffeine intakes were defined as >300mg/day and low as ≤300mg/day. High intakes were associated with high rates of bone loss at the spine. When analyzed according to VDR genotype, women with the *tt* genotype had higher rates of bone loss at the spine as compared to women with the *TT* genotype. These results suggest that high caffeine intakes may increase the risk of osteoporosis in elderly women. As this effect depends on an individual's genotype and diet-gene interactions, and because elderly people have diminished ability to increase calcium absorption to compensate for increased urinary losses, a prudent recommendation would be to ensure adequate calcium intake with moderate caffeine consumption.

Funding: National Institute on Aging, NIH.

Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomized, placebo-controlled clinical trial.

JY Reginster, R Deroisy, LC Rovati, RL Lee, E Lejeune, O Bruyere, G Giacovelli, Y Henrotin, JE Dacre, and C Gossett. ***The Lancet.*** **(Lancet) 2001 357:251-256.**

Osteoarthritis is among the most frequent forms of musculoskeletal disorders and is a major cause of disability. Nonsteroidal anti-inflammatory drugs are used to treat the symptoms of osteoarthritis; however, they do not modify joint structure or lessen the progression of this condition. Glucosamine sulfate, a sulfate derivative of the naturally occurring aminosugar glucosamine, has been shown to have positive effects on articular cartilage and joint tissues. The aim of this study was to establish whether glucosamine sulfate could affect the progression of symptoms and produce changes in joint structure of individuals with osteoarthritis. Two hundred and twelve individuals, aged 50 and over with primary knee osteoarthritis, received either 1500 mg glucosamine sulfate or placebo once daily for three years. Several measures were used to determine improvements of the knee joint. Symptoms of osteoarthritis were assessed using the Western Ontario and McMaster Universities (WOMAC) osteoarthritis questionnaire. After three years, there was no change in knee joint space among those taking glucosamine sulfate, while those taking the placebo experienced a significant narrowing of the joint space. Individuals who completed treatment with glucosamine sulfate had a 20-25 percent improvement in symptoms, compared with a slight worsening of symptoms in the placebo group. These findings are consistent with those seen in previous studies of glucosamine and suggest that glucosamine sulfate could play an important role in the long-term management of osteoarthritis in older adults.

Funding: Rotta Research Group, Monza, Italy.

Melatonin treatment for age-related insomnia.

Older individuals frequently experience insomnia, which may be related to a decreased production of melatonin that occurs with aging. This study examined whether physiological doses of melatonin would restore nighttime melatonin levels and improve sleep in older individuals. Over a nine-week period, 30 men and women aged 50 and over (half of whom reported having insomnia) received three dose levels of melatonin (0.1 mg, 0.3 mg, or 3.0 mg) or a placebo half an hour before bedtime. Results showed that melatonin had no effect on sleep efficiency in individuals with normal sleep patterns. In individuals with insomnia, melatonin significantly improved sleep at all three doses, with the greatest effect seen with the 0.3 mg dose. Melatonin administration at all three doses also significantly increased circulating melatonin levels at night. The 3.0 mg dose elevated melatonin levels during the day, resulting in decreased core body temperatures and hypothermia. According to this study, older individuals with insomnia may benefit from a 0.3 mg dose of melatonin taken 30-minutes before going to sleep.

Funding: National Institute on Aging and National Center for Research Resources, NIH, and the Center for Brain Sciences and Metabolism Charitable Trust.

IV Zhdanova, RJ Wurtman, MM Regan, JA Taylor, JP Shi, and OU Leclair. ***The Journal of Clinical Endocrinology and Metabolism*** **(J Clin Endocrinol Metab) 2001 86:4727-4730.**

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Appendix

Citations of papers that appeared in *the Annual Bibliography of Significant Advances in Dietary Supplement Research 2000*

Night blindness during pregnancy and subsequent mortality among women in Nepal: effects of vitamin A and β-carotene supplementation. P Christian, KP West Jr, SK Khatry, E Kimbrough-Pradhan, SC LeClerq, J Katz, SR Shrestha, SM Dali, and A Sommer. *American Journal of Epidemiology* (Am J Epidemiol) 2000 152:542-547.

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Improved vascular endothelial function after oral B vitamins: an effect mediated through reduced concentrations of free plasma homocysteine. JC Chambers, PM Ueland, OA Obeid, J Wrigley, H Refsum, and JS Kooner. *Circulation* (Circulation) 2000 102:2479-2483.

Multivitamin/mineral supplementation improves plasma B-vitamin status and homocysteine concentration in healthy older adults consuming a folate-fortified diet. DL McKay, G Perrone, H Rasmussen, G Dallal, and JB Blumberg. *The Journal of Nutrition* (J Nutr) 2000 130:3090-3096.

Effect of calcium or 25OH vitamin D_3 dietary supplementation on bone loss at the hip in men and women over the age of 60. M Peacock, G Liu, M Carey, R McClintock, W Ambrosius, S Hui, and CC Johnston. *The Journal of Clinical Endocrinology and Metabolism* (J Clin Endocrinol Metab) 2000 85:3011-3019.

Lack of hemoglobin response to iron supplementation in anemic Mexican preschoolers with multiple micronutrient deficiencies. LH Allen, JL Rosado, JE Casterline, P López, E Muñoz, OP Garcia, and H Martinez. *The American Journal of Clinical Nutrition* (Am J Clin Nutr) 2000 71:1485-1494.

Oral magnesium therapy improves endothelial function in patients with coronary artery disease. M Shechter, M Sharir, MJP Labrador, J Forrester, B Silver, and CNB Merz. *Circulation* (Circulation) 2000 102:2353-2358.

Prospective study of serum selenium levels and incident esophageal and gastric cancers. SD Mark, Y-L Qiao, SM Dawsey, Y-P Wu, H Katki, EW Gunter, JF Fraumeni Jr, WJ Blot, Z-W Dong, and PR Taylor. *The Journal of the National Cancer Institute* (J Natl Cancer Inst) 2000 92:1753-1763.

Effect of docosahexaenoic acid supplementation of lactating women on the fatty acid composition of breast milk lipids and maternal and infant plasma phospholipids. CL Jensen, M Maude, RE Anderson, and WC Heird. *The American Journal of Clinical Nutrition* (Am J Clin Nutr) 2000 71(suppl):292S-299S.

Supplementation of postmenopausal women with fish oil rich in eicosapentaenoic acid and docosahexaenoic acid is not associated with greater *in vivo* lipid peroxidation compared with oils rich in oleate and linoleate as assessed by plasma malondialdehyde and F_2-isoprostanes. JV Higdon, J Liu, S-H Du, JD Morrow, BN Ames, and RC Wander. *The American Journal of Clinical Nutrition* (Am J Clin Nutr) 2000 72:714-722.

Highly unsaturated (n-3) fatty acids, but not α-linolenic, conjugated linoleic or γ-linolenic acids, reduce tumorgenesis in $Apc^{Min/+}$ mice. MBH Petrik, MF McEntee, BT Johnson, MG Obukowicz, and J Whelan. *The Journal of Nutrition* (J Nutr) 2000 130:2434-2443.

Plant stanol esters affect serum cholesterol concentrations of hypercholesterolemic men and women in a dose-dependent manner. MA Hallikainen, ES Sarkkinen, and MIJ Uusitupa. *The Journal of Nutrition* (J Nutr) 2000 130:767-776.

Cholesterol reduction by glucomannan and chitosan is mediated by changes in cholesterol absorption and bile acid and fat excretion in rats. CM Gallaher, J Munion, R Hesslink Jr, J Wise, and DD Gallaher. *The Journal of Nutrition* (J Nutr) 2000 130:2753-2759.

Isoflavone-rich soy protein isolate attenuates bone loss in the lumbar spine of perimenopausal women. D Lee Alekel, A St Germain, CT Peterson, KB Hanson, JW Stewart, and T Toda. *The American Journal of Clinical Nutrition* (Am J Clin Nutr) 2000 72:844-852.

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Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia Fangchi*) JL Nortier, M-CM Martinez, HH Schmeiser, VM Arlt, CA Bieler, M Petein, MF Depierreux, L De Pauw, D Abramowicz, P Vereerstraeten, and J-L Vanherweghem. *The New England Journal of Medicine* (N Engl J Med) 2000 342:1686-1692.

Adverse cardiovascular and central nervous system events associated with dietary supplements containing ephedra alkaloids. CA Haller and NL Benowitz. *The New England Journal of Medicine* (N Engl J Med) 2000 343:1833-1838.

American ginseng (*Panax quinquefolis L*) reduces postprandial glycemia in nondiabetic subjects and subjects with type 2 diabetes mellitus. V Vuksan, JL Sievenpiper, VYY Koo, T Francis, U Beljan-Zdravhovic, Z Xu, and E Vidgen. *Archives of Internal Medicine* (Arch Intern Med) 2000 160:1009-1013.

St. John's wort induces hepatic drug metabolism through activation of the pregnane X receptor. LB Moore, B Goodwin, SA Jones, GB Wisely, CJ Serabjit-Singh, TM Wilson, JL Collins, and SA Kilewer. *Proceedings of the National Academy of Sciences* (Proc Natl Acad Sci USA) 2000 97:7500-7502.

Comparison of St. John's wort and imipramine for treating depression: randomized controlled trial. H Woelk for the Remotiv/Imipramine Study Group. *British Medical Journal* (BMJ) 2000 321:536-539.

The Andro Project. Physiological and hormonal influences of androstenedione supplementation in men 35 to 65 years old participating in a high-intensity resistance training program. CE Broeder, J Quindry, K Brittingham, L Panton, J Thomson, S Appakondu, K Breuel, R Byrd, J Douglas, C Earnest, C Mitchell, M Olson, T Roy, and C Yarlagadda. *Archives of Internal Medicine* (Arch Intern Med) 2000 160:3093-3104.

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Glucosamine and chondroitin for treatment of osteoarthritis. TE McAlindon, MP LaValley, JP Gulin, and DT Felson. *Journal of the American Medical Association* (JAMA) 2000 283:1469-1475.

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Entrainment of free-running circadian rhythms by melatonin in blind people. RL Sack, RW Brandes, AR Kendall, and AJ Lewy. *The New England Journal of Medicine* (N Engl J Med) 2000 343:1070-1077.

Citations of papers that appeared in *the Annual Bibliography of Significant Advances in Dietary Supplement Research 1999*

Fortification with low amounts of folic acid makes a significant difference in folate status in young women: implications for the prevention of neural tube defects. GJ Cuskelly, H McNulty, and JM Scott. *American Journal of Clinical Nutrition* (Am J Clin Nutr) 1999 70:234-239.

The effect of folic acid fortification on plasma folate and total homocysteine concentrations. PF Jacques, J Selhub, AG Bostom, PWF Wilson, and IH Rosenberg. *The New England Journal of Medicine* (N Engl J Med) 1999 340:1449-1454.

Antioxidant supplementation effects on low-density lipoprotein oxidation for individuals with type 2 diabetes mellitus. JW Anderson, MS Gowri, J Turner, L Nichols, VA Diwadkar, CK Chow, and PR Oeltgen. *Journal of the American College of Nutrition* (J Am Coll Nutr) 1999 18:451-461.

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Effect of long-term beta-carotene and vitamin A on serum cholesterol and triglyceride levels among participants in the Carotene and Retinol Efficacy Trial (CARET). CA Redlich, JS Chung, MR Cullen, WS Blaner, AM Van Bennekum, and L Berglund. *Atherosclerosis* (Atherosclerosis) 1999 143:427-434.

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Moderate supplementation with natural α-tocopherol decreases platelet aggregation and low-density lipoprotein oxidation. L Mabile, KR Bruckdorfer, and C Rice-Evans. *Atherosclerosis* (Atherosclerosis) 1999 147:177-185.

Vitamin E improves arterial compliance in middle-aged men and women. P Mottram, H Shige, and P Nestel. *Atherosclerosis* (Atherosclerosis) 1999 145:99-404.

Effect of dietary supplementation with black currant seed oil on the immune response of healthy elderly subjects. D Wu, M Meydani, LS Leka, Z Nightingale, GJ Handelman, JB Blumberg, and SN Meydani. *American Journal of Clinical Nutrition* (Am J Clin Nutr) 1999 70:536-543.

Conjugated linoleic acid-enriched butter fat alters mammary gland morphogenesis and reduces cancer risk in rats. C Ip, S Banni, E Angioni, G Carta, J McGinley, HJ Thompson, D Barbano, and D Bauman. *Journal of Nutrition* (J Nutr) 1999 129:2135-2142.

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Fish oil supplementation prevents diabetes-induced nerve conduction velocity and neuroanatomical changes in rats. A Gerbi, J-M Maixent, J-L Ansaldi, M Pierlovisi, T Coste, J-F Pelissier, P Vague, and D Raccah. *Journal of Nutrition* (J Nutr) 1999 129:207-213.

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Influence of prenatal iron and zinc supplements on supplemental iron absorption, red blood cell iron incorporation, and iron status in pregnant Peruvian women. KO O'Brien, N Zavaleta, LE Caulfield, D-X Yang, and SA Abrams. *American Journal of Clinical Nutrition* (Am J Clin Nutr) 1999 69:509-515.

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The chemical form of selenium influence 3,2'-dimethyl-4-aminobiphenyl-DNA adduct formation in rat colon. CD Davis, Y Feng, DW Hein, and JW Finley. *Journal of Nutrition* (J Nutr) 1999 129:63-69.

Impact of trace elements and vitamin supplementation on immunity and infections in institutionalized elderly patients. F Girodon, P Galan, A-L Monget, M-C Boutron-Ruault, P Brunet-Lecomte, P Preziosi, J Arnaud, J-C Manuguerra, S Hercberg, and the MIN.VIT.AOX. Geriatric network. *Archives of Internal Medicine* (Arch Intern Med) 1999 159:748-754.

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Cholesterol-lowering effects of dietary fiber: a meta-analysis. L Brown, B Rosner, WW Willett, and FH Sacks. *American Journal of Clinical Nutrition* (Am J Clin Nutr) 1999 69:30-42.

Comparison of melatonin products against USP's nutritional supplements standards and other criteria. H Hahm, J Kujawa, and L Augsburger. *Journal of the American Pharmaceutical Association* (J Am Pharm Assoc) 1999 39:27-31.

Acknowledgments

2001 List of Journals and Journal Editors

The Office of Dietary Supplements and the Consumer Healthcare Products Association thank the following journals and their editors for their contributions in nominating scientific papers that appeared in their journals in 2001.

- **The American Journal of Clinical Nutrition,** Charles H Halsted, MD
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- **Archives of Internal Medicine,** James E Dalen, MD, MPH
- **Biochemical Pharmacology,** Alan C Sartorelli, PhD
- **The British Journal of Nutrition,** Paul Trayhurn, DSc
- **British Medical Journal,** Richard Smith, CBE, BSc, MB, ChB
- **Cancer Epidemiology, Biomarkers, and Prevention,** Frederick P Li, MD
- **Circulation,** James T Willerson, MD
- **International Journal for Research and Investigation on Atherosclerosis and Related Diseases,** Professor James Shepherd, PhD
- **International Journal of Pharmacognosy/Pharmaceutical Biology,** John M Pezzuto, PhD
- **Journal of AOAC INTERNATIONAL,** Robert Rathbone
- **Journal of Agricultural and Food Chemistry,** James Seiber, PhD
- **The Journal of Alternative and Complementary Medicine,** Kim A Jobst, DM, MRCP
- **Journal of the American College of Cardiology,** Anthony N DeMaria, MD, MACC
- **Journal of the American College of Nutrition,** David M Klurfeld, PhD
- **Journal of The American Dietetic Association,** Elaine R Monsen, PhD, RD
- **The Journal of the American Medical Association,** Catherine D DeAngelis, MD, MPH
- **The Journal of Clinical Endocrinology and Metabolism,** John P Bilezikian, MD
- **Journal of the National Cancer Institute,** Barnett S Kramer, MD, MPH
- **Journal of Natural Products,** A Douglas Kinghorn, PhD, DSc
- **The Journal of Nutrition,** John W Suttie, PhD
- **The Lancet,** Richard Horton, MB
- **Life Sciences,** HI Yamarura, PhD
- **Medicine and Science in Sports and Exercise,** Kent B Pandolf, PhD, MPH
- **The New England Journal of Medicine,** Jeffery M Drazen, MD
- **Phytochemistry (International Journal of Plant Biochemistry),** Norman G Lewis, PhD
- **Phytomedicine,** Norman R Farnsworth, PhD
- **Planta Medica,** Adolf Nahrstedt
- **Proceedings of the National Academy of Sciences,** Nicholas Cozzarelli, PhD
- **Science Magazine,** Katrina Kelner, PhD

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