

## HERBAL MEDICINES

**Year 2003**

Medicinal herbs are some of our oldest medicines and their increasing use in recent years is evidence of a public interest in having alternatives to conventional medicine. Herbal medicines continue to be a major market in U.S. pharmacies and constitute a multi-billion dollar industry. Although approximately 1500 botanicals are sold as dietary supplements or ethnic traditional medicines, herbal formulations are not subject to **U.S. Federal Drug Administration (US FDA)** premarket toxicity testing to assure their safety or efficacy.

In response to concerns regarding the use and efficacy of medicinal herbs and to recent nominations of these products for study by the **National Toxicology Program (NTP)**, a workshop on herbal medicines was held in 1998. Recommendations from the workshop included a call for more research on herbals, the identification and standardization of product ingredients by industry, and increased consumer education through package inserts.

In follow-up to this workshop, the NTP staff is working with the **National Institutes of Health (NIH)** Office of Dietary Supplements, the US FDA, the academic community, and others to define further and to implement research that addresses deficiencies in our knowledge about herbal medicines and their potential toxicities. Herbs and active or toxic ingredients found in some herbs, continue to be nominated and selected for study by the NTP. Studies have been designed for many of these herbal products and several studies are in progress. These studies focus on characterization of potential adverse health effects including reproductive toxicity, neurotoxicity, and immunotoxicity as well as those associated with acute high dose exposure and chronic exposure to lower doses. In addition, special attention is being given to the potential for herb/herb and herb/drug interactions and the responses of sensitive subpopulations (e.g. pregnant women, the young, the developing fetus, the elderly, etc). NTP studies include both traditional toxicological research and molecular mechanistic considerations. The NTP welcomes comments from the public and others regarding NTP research in this area. Comments should be forwarded to the NTP Liaison and Scientific Review Office ([liaison@starbase.niehs.nih.gov](mailto:liaison@starbase.niehs.nih.gov)).

### Herbals and Herbal Components under Study by the NTP\*

Aloe vera gel	Widely used herb, both as a dietary supplement and component of cosmetics. Ninth highest in sales in U.S. (2002). The gel has been used for centuries as a treatment for minor burns and is increasingly being used in products for internal consumption.
Black Cohosh	Used to treat symptoms of pre-menstrual syndrome, dysmenorrhea and menopause. Ranked eleventh in sales in 2002.
Bladderwrack	A source of iodide used in treatment of thyroid diseases and also used as a component of weight-loss preparations.
Comfrey	Herb consumed in teas and as fresh leaves for salads; however, it contains pyrrolizidine alkaloids (e.g., symphatine), which are known to be toxic. Used externally as an anti-inflammatory agent in the treatment of bruises, sprains, and other external wounds. Based in part on NTP studies on the alkaloid components of comfrey, the FDA has recommended that manufacturer of dietary supplements containing this herb remove them from the market.

<i>Echinacea purpurea</i> extract	The most commonly used medicinal herb in the United States (2002). Used as an immunostimulant to treat colds, sore throat, and flu.
Ephedra	Also known as Ma Huang: 21st in sales in 2002. Traditionally used as a treatment for symptoms of asthma and upper respiratory infections. Often found in weight loss and "energy" preparations, which usually also contain caffeine. Use has been associated with side effects such as heart palpitations, psychiatric and upper gastrointestinal effects, and symptoms of autonomic hyperactivity such as tremor and insomnia, especially when take with other stimulants.
<i>Ginkgo biloba</i> extract	Fourth highest in sales (2002). Ginkgo fruit and seeds have been used medicinally for thousands of years. The extract of green-picked leaves has shown increasing popularity in the United States. Ginkgo biloba extract promotes vasodilatation and improved blood flow and appears beneficial, particularly for short-term memory loss, headache, and depression.
Ginseng and Ginsenosides	Ginseng ranked 13th in sales of medicinal herbs in 2002 down from 4 <sup>th</sup> in 1996. Ginsenosides are thought to be the active ingredients. Ginseng has been used as a treatment for a variety of conditions: hypertension, diabetes, and depression, and been associated with various adverse health effects.
Goldenseal	Seventeenth in sales (2002); Traditionally used to treat wounds, digestive problems, and infections. Current uses include as a laxative, tonic, and diuretic. Mistakenly thought to disguise the presence of other drugs in drug tests.
Green Tea Extract	Used for its antioxidative properties, fifteenth in sales in 2002.
Kava kava	The 25 <sup>th</sup> most widely used medicinal herb (2002), has psychoactive properties, and is sold as a calmative and antidepressant. A recent report of severe liver toxicity has led to restrictions of its sale in Europe and apparently affected sales in the United States. Some components may alter efficacy/toxicity of therapeutic agents.
Milk Thistle Extract	Ranked 8 <sup>th</sup> in sales in 2002. Used to treat depression and several liver conditions including cirrhosis and hepatitis and to increase breast milk production.
Pulegone	A major terpenoid constituent of the herb, Pennyroyal, is found in lesser concentrations in other mints. Pennyroyal has been used as a carminative insect repellent, emmenagogue, and abortifacient. Pulegone has well-recognized toxicity to the liver, kidney, and central nervous system.
Senna	Laxative with increased use due to the removal of one of the widely used chemical-stimulant type laxatives from the market. Study in p53+/- transgenic mice in progress.
Thujone	Terpenoid found in a variety of herbs, including sage and tansy, and in high concentrations in wormwood. Suspected as the causative toxic agent associated with drinking absinthe, a liqueur flavored with wormwood extract.

\* Sales Ranking are from The American Herb Association Vol. 18:3, 2002 p.7.

[Those entries without ranking are not in the top 36 in sales for 2002.]

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