

Herbal Remedies and Children: Do They Work? Are They Harmful?

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ABSTRACT. More parents are considering the use of herbal remedies to maintain their children's good health and to treat their illnesses. They look to pediatricians and other primary care clinicians for advice concerning the safety and efficacy of herbal products for children. This article reviews principles for the clinician to keep in mind while investigating the literature on herbal medicine and addressing the use of herbal medicines with parents. *Pediatrics* 2003;112:240–246; herbs, dietary supplements, herbal remedy, pediatric herbs, children's herbs, complementary and alternative medicine.

ABBREVIATIONS. CAM, complementary and alternative medicine; DSHEA, Dietary Supplement Health and Education Act; FDA, Food and Drug Administration.

Complementary and alternative medicine (CAM) refers to diagnostic and therapeutic systems that are not encompassed within the practice of allopathic medicine. The National Center for Complementary and Alternative Medicine at the National Institutes of Health defines CAM as “a broad domain of healing resources that encompasses all health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period.”¹ CAM is widely practiced in the United States. In a 1990 telephone survey of 1539 US adults, 34% reported using at least 1 unconventional therapy within the previous year.² Extrapolations of the data suggested that Americans make 425 million visits annually to providers of unconventional therapies (but only 388 million visits to primary care clinicians), spending approximately \$13.7 billion, of which \$10.3 billion was out-of-pocket, on alternative remedies. By 1997, a comparable study found that 42% of Americans made >629 million visits to providers of unconventional therapy (as opposed to 387 million visits to primary care clinicians) and spent >\$27 billion on CAM, much of it out-of-pocket.³

Among US adults in 1997 who reported the frequent use of prescription medications, 1 in 5 concurrently took herbal remedies or high-dose vitamins. Estimated out-of-pocket expenditures for high-dose

vitamins rose from \$0.9 billion in 1990 to \$3.3 billion in 1997. Americans spent more than \$5.1 billion on herbal products and \$1.7 billion on dietary supplements in 1997.³ Such products are now being marketed to parents for the treatment of their children.

In this review, only 1 modality within CAM—the use of herbal products to treat children's health conditions—is addressed. Herbal medicines are touted to the public as less toxic and more effective than conventional drugs for various ailments because they are “natural” and their efficacy is based on knowledge gained over thousands of years. Although one can dispute the theory, pediatricians and other primary care clinicians cannot afford to ignore the reality, which is that herbal medicines, having potential benefits and toxicities, are a newly emerging growth industry in the United States. In Europe, Asia, and elsewhere, their use has long been more accepted.

HERBAL DEFINITIONS

Herbs that are used for medicinal purposes come in a variety of forms. Active parts of a plant may include leaves, flowers, stems, roots, seeds, and berries. They may be taken internally as pills or powders, dissolved into tinctures or syrups, or brewed in teas and decoctions. Salves, ointments, shampoos, or poultices may be applied to the skin, scalp, or mucous membranes.

Many plants contain essential oils that are distilled, packaged, and sold unregulated to the public for medicinal purposes. Essential oils include any of a class of volatile oils composed of a mixture of complex hydrocarbons (often terpenes, alkaloids, and other large molecular weight compounds) extracted from a plant.⁴ Essential oils give the plant its characteristic aroma and will evaporate quickly from the skin or another surface; they are so concentrated that, if applied directly to the skin, they will often cause inflammation and dermatitis. Fixed oils are nonvolatile oils made of long-chain fatty acids, such as mineral oil or safflower oil. These are often used as carriers into which a few drops of the very concentrated essential oil are diluted during their application. Resins are solid or semisolid organic substances found in plant secretions; they are usually applied topically as creams or ointments.

There are several terms used in the context of herbal therapy that are useful to know. Aromatherapy involves the inhalation of volatile oils to treat certain health problems. A carminative is an agent that aids in expelling gas from the gastrointestinal tract. A rubefacient reddens the skin via cuta-

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neous vasodilation. An emmenagogue influences menstruation; an abortifacient induces abortion. The “discipline of signatures” is a historical term suggesting that the appearance of a plant or its extract gives a clue as to its medicinal value. For example, because the extract in St John’s wort is red, this would imply that it is restorative for conditions involving the blood.

CHARACTERISTICS OF PATIENTS USING HERBAL REMEDIES

The use of herbs has been popularized with saturation marketing such that they are available in pharmacies, grocery stores, and other outlets. Families with children who have chronic medical conditions, such as autism, cystic fibrosis, rheumatoid arthritis, or asthma, may be particularly likely to pursue herbal remedies as part of their treatment regimen. The American Academy of Pediatrics’ Committee on Children with Disabilities recently issued guidelines for discussing such issues with parents of children with chronic health problems, acknowledging the frequency with which such families may seek alternative treatments.⁵

In 1 survey, 11% (or 208 children) of families ($n = 1911$) that used the outpatient clinics of the University of Montreal for their children’s care sought CAM for medical conditions.⁶ This is probably an underestimate, because the study was conducted years ago and surveyed a selected population. The families indicated that they sought help from a variety of practice types, including chiropractic (36%), homeopathy (25%), naturopathy (11.5%), acupuncture (11.5%), osteopathy (9%), oligotherapy (4%), and other (3%). They used CAM for respiratory tract illnesses (37%); ear, nose, and throat conditions (24%); musculoskeletal conditions (15%); skin conditions (6%); gastrointestinal conditions (6%); allergies (6%); prevention (5%); and other conditions (11%).

A profile of adult CAM users found that they were highly educated individuals of a high socioeconomic status who often were treating their own chronic medical problems refractory to conventional medical management.⁷ Many reasons were put forward as to why these adults choose to seek CAM. They may hold values systems that emphasize natural, holistic, and organic products or may have had a transformational experience that changed the way they view the world. They often prefer a humanistic, unhurried approach to their medical care. They may hold specific, culturally dictated therapeutic preferences. They demand empowerment in any treatment plan regarding health issues. In the above study, researchers found that a significant number of people used CAM in the context of self-diagnosis and self-treatment. They may be generally suspicious of conventional allopathic medical authority or technology. They sometimes express a deep dissatisfaction with mainstream medicine.

EFFICACY OF HERBAL REMEDIES

That many pharmaceuticals used today were originally derived from plant sources (eg, salicylates from willow bark, quinine from cinchona, digitalis

from foxglove leaves) suggests that some herbs may prove to be effective remedies for treating medical diseases. Angell and Kassirer⁸ stated that there is no such thing as an “alternative” medicine but only that for which effectiveness has been confirmed using the scrutiny of evidence-based science. Thus, any claims of health benefits from an herbal remedy should be subjected to the scrutiny of evidence-based medicine. The scientific criteria for causal associations include biological plausibility, consistency of research results, dose-response effects, reproducibility of the research in different contexts using different methodologies, the strength of the association, and a correct temporality between cause and effect. Using this level of scientific precision, studies of some herbal remedies have revealed promising results. For example, tea tree oil has been found to inhibit the growth of certain dermatophytes and may be useful for fungal skin conditions.⁹ In laboratory studies, some essential oils have been demonstrated to have antimicrobial actions.^{10,11} *Artemisia* species have compared favorably with chloroquine in the treatment of some types of malaria.^{12,13} *Astragalus membranaceus* extracts enhanced the antibody response to a T cell-dependent antigen in immunosuppressed mice.¹⁴ In 1 study, herbal teas that contained chamomile seemed to have a favorable effect on infantile colic.¹⁵ St John’s wort (*Hypericum perforatum*) may affect serotonin receptor expression in the brain; such actions might underlie the efficacy of *H perforatum* extract in alleviating mild depression in adults.¹⁶ Whereas a recent randomized, controlled trial showed no effect of St John’s wort on depression,¹⁷ such controlled studies of the beneficial effects of St John’s wort in children with depression or other conditions are lacking. Echinacea (*Echinacea purpurea*) has been found to be a potent activator of the immune system. It increases the number and phagocytic performance of granulocytes,¹⁸ activates macrophages¹⁹ and T lymphocytes,²⁰ causes elaboration of cytokines,²¹ and has ill-defined antiviral properties.²² Such immune changes may explain why echinacea has been advocated to shorten the course and severity of upper respiratory infections in adults; some controlled studies are promising.^{23,24} The usefulness of echinacea for alleviating symptoms of respiratory infections in children has yet to be demonstrated.

Most herbal medicines have not been subjected to rigorous clinical trials. The lack of standardization and regulation of many products complicates the testing of their clinical utility. As a result, there remains a dearth of knowledge concerning how children are affected by taking herbal products. Inevitably, the clinician must read critically the peer-reviewed studies on efficacy of herbal remedies and form his or her own conclusions. There have been several recent reviews of herbal remedies in the treatment of childhood health conditions.^{25–27} The review by Gardiner and Kemper²⁶ includes tables on toxicities of herbs as well as adverse drug-herbal interactions. Web sites and other resources are included at the end of this report.

TOXICITY OF HERBS

There are general and herb-specific concerns regarding herbal products and their ability to produce toxicity and adverse effects. A confusing nomenclature and issues of quality control and the accurate identification of plants are important concerns. There are no international conventions for naming plants, and there are many confusing synonyms. The common names of plants and herbal remedies can be archaic and variable depending on the geographic region. For example, "cohosh" can refer to several species of plants depending on geographic location. There is no governmental regulation on the manufacture, purity, concentration, or labeling claims of herbal remedies and dietary supplements. Thus, it is always "buyer beware" in this marketplace. Errors in labeling may be inadvertent, but intentional mislabeling has also been problematic. For example, 1 study revealed that products sold as ginseng contained such substitutes as scopolamine and reserpine.²⁸ The concentration of active ingredients and other chemicals in plants varies by the part of the plant harvested and sold; the maturity of the plant at the time of harvest; the time of year during harvest; geography and soil conditions; soil composition and its contaminants; and year-to-year variations in soil acidity, water, weather conditions, and other growth factors.

Because of the variability in herbal product ingredients, the actual dose of active ingredients being consumed is often variable, unpredictable, or simply unknown. When compared with adults, children may be particularly susceptible to the effects of such dosage variations by virtue of their smaller size and different capacity for detoxifying chemicals. Finally, foragers seeking herbal remedies may mistakenly collect one plant confusing it for another. This can be a lethal error if, for example, water hemlock is harvested and eaten after mistakenly being identified as wild ginseng.²⁹

The safety of herbal products may be related to the mixtures of active chemicals that they contain; their interactions with other herbs and drugs, contaminants, or adulterants; or their inherent toxicity. Plants have complex mixtures of terpenes, alkaloids, saponins, and other chemicals, increasing the risk of adverse reactions to any one of them or to the additive or synergistic effects of chemical interactions. For example, >100 chemicals have been identified in tea tree oil.³⁰

Active ingredients in herbs and dietary supplements can cause unexpected reactions when used with other herbs or medications. Effects on the distribution, metabolism, or excretion of drugs may be pronounced and may lead to drug toxicity. For example, sassafras reportedly inhibits microsomal enzymes and can increase the half-life of drugs metabolized by the liver.³¹

Contaminants and adulterants of herbal products can be pharmacologically active and responsible for unexpected toxicity.³² Herbal plants may be harvested from contaminated soils or cleaned improperly such that they may contain illness-producing

microorganisms. Ayurvedic medications have been known to cause lead poisoning in children because of their contamination with this heavy metal and others, such as arsenic and mercury.^{33,34} Many Chinese patent medicines contain drugs such as phenylbutazone and barbiturates, warfarin-like chemicals, and contaminants such as lead or arsenic.³⁵⁻⁴⁰ An analysis of 260 imported traditional Chinese medicines by the California health department found high levels of contaminants in almost half.⁴¹

Finally, herbal products or folk remedies may be inherently unsafe. There is no required testing of safety before the marketing of such products, although plants often contain chemicals that are toxic to humans. For example, aconite, a widely used Asian remedy, can produce life-threatening cardiac and neurologic toxicity.⁴² Some toxic reactions in humans may be unforeseen until the remedy has been used widely. Table 1 lists some of the potent chemicals present in certain herbs used as remedies and provides references that discuss the toxic effects that these herbs can produce.

SUSCEPTIBILITY OF PATIENTS

Children differ from adults in their absorption, distribution, metabolism, and excretion of some substances. They have relatively larger livers and, thus, in some respects are more efficient at detoxification. However, they also have developing central nervous and immune systems that may make them more sensitive to the adverse effects of herbs. Infants and young children are physiologically more vulnerable to certain adverse effects of herbs than are adults. For example, some herbs such as buckthorn, senna, and aloe are known cathartics, and some herbal teas and juniper oil contain powerful diuretic compounds.^{31,43} These actions may cause clinically significant dehydration and electrolyte disturbances quickly in an infant or young child, whereas adults would more easily make up such fluid losses. The duration of use is another consideration, with longer courses of herbal therapy exposing the patient to a higher risk of acute and subacute, cumulative, or chronic adverse effects. For some herbs, such as those that contain pyrrolizidine alkaloids, there may be no safe dose or duration of use for children.

There may be subpopulations of children who are more susceptible than other children to the adverse effects of herbs. Individuals with allergies may be at increased risk, because the allergic potential of plants is well known. Infants and young children may be particularly sensitive to their first introduction to chemicals in herbs and dietary supplements. Some plants cause contact dermatitis, whereas others may produce wheezing, rhinitis, conjunctivitis, itchy throat, and other allergic manifestations. Chamomile, for example, can cause anaphylaxis in individuals who are allergic to members of the *Compositae* family of plants (eg, ragweed, chrysanthemum, chamomile).⁴⁴ Photosensitization can occur with herbs, such as angelica and rue, which contain psoralen-type furocoumarins; hypericin, the active ingredient in St John's wort, is also capable of photosensitization.⁴³

TABLE 1. Examples of Known Herbal Products and Their Associated Toxic Effects

Herbal Product	Toxic Chemicals	Effect or Target Organ	References
Monkshood <i>Aconitum</i> species	Aconite	Cardiac arrhythmias, shock, weakness, seizures, coma, paresthesias, nausea, emesis	53, 54
Wormwood <i>Artemisia absinthium</i>	Thujone	Seizures, dementia, tremors, headache, ataxia	55, 56
Chaparral <i>Larrea divaricata</i>	Nordihydro-guaiaretic acid	Nausea, emesis, hepatitis	57
Cinnamon oil <i>Cinnamomum</i> species	Cinnamaldehyde	Dermatitis, abuse syndrome	58–60
Comfrey (<i>Symphytum officinale</i>)	Pyrrrolizidines	Hepatic veno-occlusive disease	61–63
<i>Crotalaria</i> species	Pyrrrolizidines	Hepatic veno-occlusive disease	64–66
Eucalyptus <i>Eucalyptus globulus</i>	1,8 cineol	Drowsiness, ataxia, seizures, nausea, vomiting, coma	67–71
Garlic <i>Allium sativum</i>	Allicin	Nausea, emesis, anorexia, weight loss, bleeding, platelet dysfunction	52, 72
<i>Heliotropium</i> species	Pyrrrolizidines	Hepatic veno-occlusive disease	64–66
Jin bu huan	Tetrahydropalmatine	Hepatitis	73–75
Kava <i>Piper methysticum</i>	Kavapyrones	Hepatitis, cirrhosis	76
Laetrile	Cyanide	Coma, seizures, death, respiratory failure	77
Licorice <i>Glycyrrhiza glabra</i>	Glycyrrhetic acid	Hypertension, hypokalemia, Dysrhythmias	78
Ma Huang <i>Ephedra sinica</i>	Ephedrine	Hypertension, dysrhythmias, stroke, seizures	79, 80
Nutmeg <i>Myristica fragrans</i>	Myristacin, eugenol	Hallucinations, emesis, headache	81–84
<i>Strychnos nux-vomica</i>	Strychnine	Seizures, abdominal pain, respiratory failure	85
Pennyroyal <i>Mentha pulegium</i> or <i>Hedeoma</i> species	Pulegone	Centrilobular liver necrosis, fetotoxicity, abortion	86–90
<i>Senecio</i> species	Pyrrrolizidines	Hepatic veno-occlusive disease	64–66

Many herbal remedies are self-administered by adults without any guidance from knowledgeable sources as to their indications, efficacy, or safety. Herbal products can be misused—taken in excessive doses or in combinations without any known rationale. Some products are sold as mixtures of 10 or more different plants, vitamins, minerals, and so forth. The “stacking” of many different herbs increases the risk of toxicity from any 1 of them or from their interactions with each other. Parents may be tempted to give combinations of herbs to children on the basis of advertising for the products, information that they may glean from a magazine or web site, or advice from friends or relatives. Such experimentation is expensive and risks exposure of the child to unwanted adverse effects.

Some manufacturers even market herbs for inappropriate uses. Herbs that contain ephedra or caffeine are described as “safe” ecstasy alternatives, “safe” dietary aides, and a source of a “natural high” and euphoria. Adolescents and young adults are particularly easy targets for such promoting tactics.

OTHER CONSIDERATIONS

Significant uncertainty surrounds the long-term consequences of exposure to some herbal remedies for which the toxicity profiles are incompletely characterized. Classic concerns include carcinogenicity, mutagenicity, toxicity to the fetus, and the effects of herbs on the lactating woman and breastfeeding infant.

Although the chemicals in herbs may have carcinogenic effects, this concern has not been adequately investigated. Some chemicals found in plants are known carcinogens or tumor promoters in animals

(eg, pyrrrolizidines [comfrey, coltsfoot, senecio], safrole [sassafras], aristolochic acids [wild ginger], catechin tannins [betel nuts]).³¹ Whether such chemicals pose a threat for humans remains unknown; children, by virtue of their longer lives, may be particularly vulnerable to herbs that contain chemicals whose carcinogenic effects may not become manifest until a long latency period has passed.

Toxic effects of herbs on male or female reproductive systems are of concern but have not been investigated adequately. Some essential oils, for example, have cytotoxic properties or cause cellular transformation *in vitro*.^{45,46}

The effects of herbs on the embryo and fetus are not known in many cases. It is possible that herbal chemicals may be transported through the placenta to cause toxic effects on the sensitive growing fetus. For example, Roulet et al⁴⁷ in Switzerland reported the case of a newborn whose mother drank senecionine-containing herbal tea daily for the duration of her pregnancy. The infant was born with hepatic vaso-occlusive disease and died; senecionine is 1 of the pyrrrolizidine alkaloids associated with hepatic venous injury. Animal studies have confirmed the teratogenicity of some herbs; for example, the popular eastern European herb *Plectranthus fruticosus* was found to be teratogenic in mice.⁴⁸

How herbs may affect lactation in breastfeeding women has not been fully explored. The excretion of herbs into breast milk is a concern, as many herbs have lipophilic chemicals that are expected to concentrate in breast milk and be transferred to the infant. There has been little scientific study of this issue.

REGULATORY AND SAFETY SURVEILLANCE ISSUES

Unfortunately, gaps exist in the regulation of herbal products and dietary supplements. Congress has passed legislation, The Dietary Supplement Health and Education Act (DSHEA) of 1994, that does not include the usual consumer protections applied to medications used in the treatment of health problems.⁴⁹ The ability of the Food and Drug Administration (FDA) to require premarketing tests of safety and effectiveness is curtailed by this legislation, as is its ability to intercede in the marketing claims of an herbal product or dietary supplement unless the product has been shown to be overtly dangerous to health. DSHEA requires no testing of safety or efficacy for herbal products and dietary supplements, specifies few restrictions on product claims or controls on product purity or ingredients, and requires no postmarketing surveillance. DSHEA also makes no provision for the centralized reporting of adverse events.

Since this legislation was passed, however, initiatives to improve the data on the toxicity of herbs and dietary supplements have been implemented. A special segment of the MedWatch program administered by the FDA tracks adverse events involving such products. To report adverse reactions to the FDA, the MedWatch telephone number is 800-FDA-1088 and the fax number is 800-FDA-0178. Local poison control centers are additional sources for clinicians who wish to report adverse events associated with herbal products; the new nationwide toll-free number for poison control is 800-222-1222. Poison control centers aggregate their data for surveillance purposes under the Toxic Exposure Surveillance System maintained by the American Association of Poison Control Centers.⁵⁰

ADVICE TO PARENTS

The assessment of children whose parents are seeking CAM options requires strategies to promote the therapeutic interaction among clinician, parent, and child for the benefit of the patient. Eisenberg⁵¹ suggested guidelines for clinicians that have been modified slightly in this report to make them more specific to the needs of pediatricians.

It is important for clinicians to ask the unasked question—to find out about the beliefs of the parents and alternative therapies, herbs, or other remedies used by the family and given to children. In the study by Spigelblatt et al,⁶ up to 50% of families that used CAM did not reveal this to their primary care clinician.

As always, clinicians are urged to carry out a thorough medical evaluation and to obtain consultations as needed. For example, if the child has frequent unresolved ear infections and medical treatment has failed, then an early referral to an otolaryngologist may allay parental concerns and provide a solution before they try untested alternative therapies.

Conventional therapeutic options should be explored by establishing a dialogue with the parents about what in the clinician's opinion is the best treatment for the condition as well as established or un-

tested alternatives. When parents are considering herbal therapies, it is prudent to research what is known about the efficacy and safety of the therapy in question. The medical record should contain documentation of the parent's CAM requests, therapeutic refusals, or the exhaustion of medical treatment. If there are disagreements with the parent's plan, then these should be noted in the medical record.

It is important to remember that acknowledging a practice does not necessarily mean endorsing it. The following practical points may be useful when clinicians counsel parents about the use of herbal remedies:

- Parents should not equate "natural" with "safe."
- Parents should seek expert guidance when considering the use of CAM practices, including herbal remedies, and avoid self-medication.
- Herbs and plants (just like drugs) may have beneficial effects as well as expected and sometimes unanticipated toxicity.
- Unlike drugs, herbal products have not been scrutinized by the FDA, so it is truly a case of "buyer beware." Variable and unpredictable concentrations, ingredients, and contaminants are of concern, especially when such products are used in children.
- Parents should inform clinicians of any herb or dietary supplement that they are giving their children.

Lack of information about alternative remedies being used by a child can prolong a hospital stay or hamper the clinician's approach to diagnosis and management. For example, a recent review of adverse effects of herbal products and the surgical care of patients concluded that there is a considerable risk of intraoperative and postoperative complications when patients do not inform physicians of their use of the products before surgery.⁵²

Parents may seek help from the clinician in identifying practitioners of CAM. Such requests may pose a problem for the clinician who does not have confidence in CAM as a therapeutic modality. Some key questions need to be asked and answered when counseling the family through the decision-making process:⁵¹

1. Is the therapy likely to confer a benefit for this child's condition?
2. Will the therapy subject the child to unreasonable risk?
3. Is the CAM practitioner licensed in this state?
4. Does the CAM practitioner carry malpractice insurance?
5. Do I know of the competence of this particular CAM practitioner?
6. Should this be an "arm's length" referral?
7. How will I follow-up with the family and keep their trust?

Eisenberg⁵¹ suggested that the clinician answer the key question, "Would I let a family member follow this course of action?" In every case, the best interests of the child are paramount; when the clinician disagrees with the family's intended actions, such dis-

agreement should be voiced along with the reasons behind it. In other circumstances, the clinician can and should support the parents' decision to pursue CAM when the risk of harm is low, the possibility of benefit is backed by scientific evidence, and the parents can be engaged in an integrative approach to the child's care.

INTERNET RESOURCES

National Center for Complementary and Alternative Medicine
 nccam.nih.gov
 Longwood Herbal Task Force
 www.mcp.edu/herbal
 Center for Holistic Pediatric Education and Research (CHPER)
 www.childrenshospital.org/holistic
 Dr Duke's Phytochemical and Ethnobotanical Databases, Agricultural Research Service
 www.ars-grin.gov/duke
 American Botanical Council
 www.herbalgram.org
 Consumer Federation of America
 www.quackwatch.com
 Herb Research Foundation
 www.herbs.org
 National Council Against Health Fraud
 www.ncahf.org
 US Department of Agriculture, Food and Nutrition Information Center
 www.nal.usda.gov/fnic
 Center for Food Safety and Applied Nutrition
 vm.cfsan.fda.gov
 National Certification Commission for Acupuncture and Oriental Medicine
 www.nccaom.org

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