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Herbs and Lactation

By Tieraona Low Dog, MD, and Adriane Fugh-Berman, MD

LACTATING WOMEN HAVE USED PLANTS TO INCREASE MILK PRODUCtion, treat complications of lactation (sore nipples, mastitis), and decrease breast engorgement for centuries. Herbs used to increase milk flow are called galactagogues or lactagogues. Commonly used lactagogues include blessed thistle (*Cnicus benedictus*), borage leaves (*Borago officinalis*), goat's rue (*Galega officinalis*), fennel (*Foeniculum vulgare*), fenugreek (*Trigonella foenum-graecum*), chaste-tree berry (*Vitex agnus-castus*), vervain (*Verbena officinalis*), nettles (*Urtica dioica*), and raspberry leaves (*Rubus strigosus*).[1,2] Mixtures of these herbs are common.

Lactation-Inducing Herbs

No clinical trials of herbs for inducing lactation were identified. Fennel is commonly used in foods and is benign; nettles and raspberry leaves also are harmless. Fenugreek is used extensively as a lactagogue and there are no reports of adverse effects found in the literature.[3] The taste and odor of fenugreek are similar to maple syrup and this odor can be imparted to the urine. In children, this may mistakenly lead a practitioner to consider the diagnosis of maple syrup urine disease, or branched-chain hyperaminoaciduria, a rare, inherited metabolic disorder. This should be kept in mind, as fenugreek commonly is used as a lactagogue in the United States.

Chaste-tree berry (*Vitex agnus-castus*) is used as a lactagogue, although it decreases prolactin levels in humans[4,5] (it seems as though it should have the opposite effect). One animal study demonstrated a reduction of milk production and increased mortality in suckling rats when chaste-tree berry was administered to the mothers;[6] another study demonstrated a lactogenic action with no change in chemical composition of breastmilk.[7] Lactogenic activity may be related to dose. An open placebo-controlled study of 20 healthy males found that thyrotropin-releasing hormone-stimulated prolactin secretion increased with the 120 mg dose and decreased with the 480 mg dose.[8] Interestingly, the manufacturers of Agnolyt®, the

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most extensively studied German chaste-tree product, contraindicate its use during lactation.[9]

No serious adverse effects have been associated with chaste-tree berry, although symptoms reported in clinical trials include gastrointestinal symptoms, dermatological reactions (acne, skin rashes, urticaria), and menstrual cycle changes.[10]

Goat's rue is a traditional lactagogue and hypoglycemic herb used in Europe and South America. Gillet-Damitte presented the herb to the French Academy in 1873 with the observation that goat's rue increased milk production in cows by 35-50%. Remington later confirmed its lactogenic activity in 1913.[11] There have been no controlled human trials to establish its lactogenic activity in nursing women.

Adverse Effects

The use of borage leaves should be discouraged; borage leaves contain unsaturated pyrrolizidine alkaloids, which have been associated with hepatotoxicity.

Maternal ingestion of a lactation tea containing extracts of licorice (*Glycyrrhiza glabra*), fennel, anise, and goat's rue was linked to drowsiness, hypotonia, lethargy, emesis, and poor suckling in two breast-fed neonates; an infection work-up was negative and symptoms and signs resolved upon discontinuation of the tea (and a two-day break from breastfeeding).[12] Non-specific symptoms (drowsiness and weakness) also were reported by one of the mothers. Anise is widely used in both children and adults and is considered safe, and the other herbs in this tea would not be expected to cause these effects. It is possible that this tea contained a contaminant, an adulterant, or a misidentified herb. Interestingly, goat's rue is known to be toxic to sheep at doses as low as 0.8 g/kg; however, the animals quickly adapt to the plant and can subsequently consume doses up to 10 times this amount after repeated exposure.[13]

Herbs to Decrease Breast Milk Production

Herbs purported to decrease milk production include sage (*Salvia officinalis*), peppermint (*Mentha piperita*), and bugleweed (*Lycopus europaeus*). Peppermint is benign. Sage contains thujone, the neurotoxic component of absinthe; although thujone is inactivated by heat, it is unknown what levels of thujone are in sage tea. Sage tincture would not be recommended if a woman is still nursing. On rare occasions, extended therapy with high doses of bugleweed has resulted in enlargement of the thyroid. Sudden withdrawal of the herb can precipitate an increase in thyroid function.[14] Oral administration of *L. europaeus* extract caused T3 levels to decrease for more than 24 hours, presumably as a consequence of reduced peripheral T4 deiodination. Luteinizing hormone and thyroid-stimulating hormone were significantly decreased in spite of reduced T4 and T3 levels, indicating activity at the hypothalamic or pituitary level.[15] Due to hormonal effects, bugleweed is probably best avoided by lactating mothers.

Sore Nipples

Although prevention is key for avoiding the development of sore nipples, several herbs commonly are recommended by herbalists and naturopathic physicians. Calendula (*Calendula officinalis*) ointment is one of the most popular for chafed nipples. In vitro data demonstrate that the polysaccharides in calendula stimulate phagocytosis; aqueous and alcoholic extracts have been shown to stimulate epithelialization in surgical wounds in vivo. The herb is bactericidal to *Staphylococcus aureus*.[16] There are no clinical trials evaluating the effectiveness of calendula ointment for chafed nipples, but there are no reports of adverse effects when topically used by lactating women.

Persistently cracked, sore nipples may indicate the presence of a *Candida* infection. Tea tree oil (*Melaleuca*

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alternifolia) often is recommended in the lay literature. Tea tree oil has been used for centuries in Australia for the treatment of wounds. There are no clinical trials in nursing women to determine its use for candidal mastitis, but in vitro research indicates that the essential oil has excellent coverage against *Candida* spp.[17,18] One clinical trial found it to be effective for fluconazole-resistant oral thrush.[19] Essential oils can be toxic when taken in large doses internally, so breastfeeding mothers should rinse the breast prior to nursing.

Herbs for Breast Engorgement

Topical application of cabbage leaves was tested in a randomized, controlled, open trial conducted in Johannesburg, South Africa.[20] One hundred twenty breastfeeding women, 72 hours postpartum, were randomized to application of cabbage leaves to their breasts or routine care. Of the 132 women who were approached, 12 chose not to participate because they believed that cabbage leaves relieve engorgement and did not want to be assigned to a control group. Holes were cut in the cabbage leaves so that the nipples would not be covered. The leaves were kept in the refrigerator and applied cold after four feeds; the leaves were kept in place until they reached body temperature (approximately 20 minutes). Mothers assessed their own level of breast engorgement by completing questionnaires prior to the next four feeds (after treatment), and also completed a questionnaire six weeks postpartum. Perception of breast engorgement and frequency of feeding did not differ significantly between the treated and control groups. The only statistically significant difference between the groups was in duration of breastfeeding, which was longer in the treated group than in the control group (36 vs. 30 days, $P = 0.04$).

A Cochrane review of three other trials using cabbage leaves and/or cabbage leaf extracts concluded that the treatment failed to demonstrate superiority over placebo.[21]

Topical applications of jasmine flowers (*Jasminum sambac*) are traditionally used in South India to suppress lactation. Sixty women in Vellore, India, whose babies were stillborn or died within 24 hours of birth, were randomized to bromocriptine 2.5 mg every eight hours for five days or jasmine flowers (strung on a 50 cm string), apparently taped to each breast.[22] Flowers were replaced daily for five days. Paracetamol (acetaminophen) was allowed for breast pain. Prolactin levels were taken 24 hours after delivery and after 72 hours of treatment. Breast engorgement was assessed on a 4-point scale, and milk production was evaluated by manual pressure. Prolactin levels fell in both groups but were significantly lower in the bromocriptine group compared to the jasmine group. Lactation scores were similar between groups after 72 hours of treatment. Bromocriptine failed to suppress lactation in one woman and jasmine flowers failed in two. Two women receiving bromocriptine had rebound lactation at two-week follow-up. Consumption of analgesics was similar between groups. This study would have been improved by use of a placebo group.

In lactating mice, topical contact with jasmine flowers inhibited milk production and caused regressive changes in breast parenchyma.[23]

Conclusion

Most herbs used for inducing lactation are benign; internal use of borage leaves, bugleweed, or uncooked sage should be discouraged. Clinical trials do not support topical application of cabbage leaves for breast engorgement in lactating women, but one clinical trial does support the use of topical jasmine for treating engorgement in women who want to suppress lactation. Calendula preparations are a benign treatment for sore nipples, and tea tree oil is a benign treatment for a candidal infection, but care should be taken to avoid ingestion of tea tree oil by an infant. ❖

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Echinacea for Colds

By Dennis Awang, PhD, FCIC, and Adriane Fugh-Berman, MD

DOES ECHINACEA WORK TO PREVENT OR TREAT UPPER respiratory infections (URIs)? This is not a simple question. Although numerous trials of echinacea-containing products exist, many trials tested echinacea combined with other herbs. This article will review echinacea-only trials, but this limitation narrows the range of products only slightly: Products tested are made from different species and different parts of plants.

The taxonomy of echinacea has recently been revised. Until now, *Echinacea purpurea*, *E. angustifolia*, and *E. pallida*, all of which are used commercially, were considered three different species. *E. angustifolia* is now considered a variety of *E. pallida*, respectively designated *E. pallida* var *angustifolia* and *E. pallida* var *pallida*.[1] We are adopting the new taxonomy, but all literature to date refers to the old taxonomy.

Single-herb products tested in clinical trials that are available in the United States include two *E. purpurea* products: Echinaforce® (Bioforce), a hydroalcoholic extract (65% ethanol, extract ratio 5.9:1) of fresh herb (95%) and root (5%), and Echinaguard® (United States) or Echinacin® (Madaus AG, Germany), the freshly expressed juice from aerial parts of flowering *E. purpurea*, stabilized with 22% ethanol.[2]

Prevention of URIs

None of the three placebo-controlled RCTs of echinacea-only products for the prevention of URIs found a benefit. A three-armed trial in 302 subjects (289 were analyzed) compared *E. pallida* var *angustifolia* root extract to *E. purpurea* root extract and placebo (2 x 50 drops daily 5 x/wk × 12 weeks); there was no difference among groups in the time to occurrence of the first URI, nor in the proportion of groups that developed URIs.[3]

Another trial, published in two publications, tested pressed juice of *E. purpurea* herb (4 mL twice daily for 8 weeks) in 109 subjects and found no benefit on the incidence, duration, or severity of colds or URIs.[4,5]

The only trial using a rhinovirus challenge found no effect of echinacea (an uncharacterized preparation containing 0.16% cichoric acid, but devoid of echinacoside and alkamides, consistent with an aqueous extract of *E. purpurea*) on the incidence of experimentally induced infection, or incidence of colds.[6]

Treatment of URIs

Six randomized, placebo-controlled trials, with a total of 881 subjects, found echinacea beneficial for URI treatment in at least one treated group. Tested extracts included: *E. pallida* root (two publications of the same trial);[7,8] pressed juice;[9,10] *E. purpurea* root;[11,12] two doses of Echinaforce;[11] and Echinacea Plus® tea, containing *E. purpurea* herb, *E. angustifolia* herb, and a dry extract of *E. purpurea* root in a 6:1 ratio.[13]

Except for two extracts of *E. purpurea* root, most formulations were significantly better than placebo in the primary outcome measures. Most trials examined duration of symptoms; the Hoheisel study (sometimes classified as a prevention trial) administered echinacea at first onset of symptoms and found a significant reduction in proportion of subjects who developed a "real cold," as well as shorter duration of symptoms.[10]

Extracts of *E. purpurea* root may be inferior to *E. pallida* var *pallida* root or *E. purpurea* herb. The Brinkeborn study, a four-armed study in 559 subjects that compared placebo to two potencies of Echinaforce and *E. purpurea* root extract, found that Echinaforce, but not the *E. purpurea* root extract, was superior to placebo.[12] The Braunig 1992 trial compared two doses, 450 mg (90 drops) vs. 900 mg (180 drops) daily of *E. purpurea* root extract to placebo and found a significant ($P < 0.0001$) benefit only in the latter group;[11] however, this trial has been criticized as not truly blinded.[14]

It is interesting to note that these trials seem to bear out the conclusions of the German Commission E, the organization that until 1995 evaluated herbal products for the German government. Before most of these trials were published, Commission E had issued positive monographs on *E. pallida* var *pallida* root and *E. purpurea* herb, and had concluded that evidence of efficacy for other extracts, notably *E. purpurea* root and *E. pallida* var *angustifolia*, was not sufficient. *E. pallida* var *angustifolia* was thought to be active because of promising pharmacological studies, but the Commission E, based on research by Bauer and Wagner,[15] concluded that earlier pharmacological studies of *E. pallida* var *angustifolia* actually involved *E. pallida* var *pallida*.

Active Compounds/Mechanisms

Active constituents of echinacea are believed to be alkylamides (alkamides), caffeic acid derivatives (e.g., cichoric acid, caftaric acid), ketoalkenes/ketoalkynes, glycoproteins, and polysaccharides. Compounds vary in type and ratio among plant parts and species, and the most effective constituents remain to be determined. "Standardized" extracts of echinacea are widely available, but cannot be compared to each other, as preparations are standardized to different compounds. Echinacoside, a caffeic acid derivative, which often has been used to "standardize" commercial echinacea preparations, and occurs in *E. pallida* var *angustifolia* and *E. pallida* var *pallida*, is virtually absent from *E. purpurea*, and lacks immunostimulatory effect.[16] Cichoric acid, also used to "standardize" extracts, is regarded as a significant active constituent of freshly squeezed juice preparations, but is unsuitable for standardizing extracts of *E. pallida* var *angustifolia*, because only traces exist in that species. Cichoric acid is very susceptible to enzymatic degradation and is rapidly degraded unless echinacea expressed juice is treated thermally or with alcohol.

A recent HPLC analysis of alcoholic extracts of the roots of the three *Echinacea* species reports that cichoric acid and verbascoside, two caffeic acid derivatives, are dominant in *E. purpurea*; cynarin and dodeca-2E, 4E, 8Z, 10Z/E-tetraenoic acid isobutylamide are the major constituents of *E. pallida* var *angustifolia*; and echinacoside and 6-O-caffeoylechinacoside predominate in *E. pallida* var *pallida*.[17]

Although the predominant mechanism of action of echinacea extracts has been thought to be through stimulation of phagocytosis, a recent double-blind, placebo-controlled crossover study in 40 healthy men found no effect of freshly expressed juice of *E. purpurea* herb, compared to placebo juice (each phase lasted 14 days, with a four-week washout between phases) on phagocytic activity of mononuclear leucocytes and monocytes.[18] This study also found no benefit of echinacea on production of tumor necrosis factor (TNF-α) or interleukin-1β by LPS-stimulated blood monocytes. The authors of this study note that the three small studies done previously were all by the same group and found inconclusive results. The Schwartz study noted significantly decreased serum ferritin ($P = 0.0005$) during the echinacea phase, compared to the placebo phase. Noting that serum ferritin is closely associated with the concentration of acute phase proteins, Schwartz et al suggest that the effect of echinacea on pro-inflammatory reactions should be explored. Although many in vitro assays and in vivo experiments using parenteral administration have shown enhanced phagocytosis, it has been noted that polysaccharides credited with stimulating macrophage cytotoxicity would be unlikely to survive oral administration.[19]

Quality

A survey of 25 commercial echinacea-containing products evaluating alkamide and cichoric acid content revealed extreme variation among different formula-

tions, among different species, and among plant parts.[20] Large differences also were found in comparable drugs from different manufacturers, as well as among different lots of the same preparation.

Adverse Reactions

Four cases of anaphylaxis, 12 cases of acute asthma, and 10 cases of urticaria/angioedema attributed to echinacea were reported to the Australian Adverse Drug Reactions Advisory Committee; three of five cases evaluated by the reviewers had positive skin prick tests.[21]

Four episodes of erythema nodosum temporally associated with use of an unidentified preparation of purported echinacea occurred over 18 months in a 41-year-old healthy man (who also was taking St. John's wort and occasional loratidine).[22] He remained free of episodes for one year after discontinuing the purported echinacea product.

With oral products, unpleasant taste is the most common side effect, but allergic skin reactions may also occur. Parenteral administration of *E. purpurea* squeezed sap (Echinacin) may cause shivering, fever, or muscle weakness.[23]

A 49-year-old woman treated with intramuscular injections of a homeopathic product (containing *E. pallida* var *angustifolia* D2 1.1 mL, lachesis D8 [snake venom] 0.3 mL, and "echinacea comp Hevert inject" 0.3 mL), administered with her own blood, developed numbness and weakness in her arm and was diagnosed with acute disseminated encephalomyelitis.[24] Given confounding factors, it is difficult to attribute these effects to echinacea.

Theoretical concerns that echinacea may worsen symptoms of autoimmune disease have been raised, but no such cases have been reported.

Pregnancy

A controlled study compared 206 women who reported gestational use of echinacea to the Motherisk program (112 reported first trimester use) with 206 controls; there were no significant differences between groups for major or minor malformations.[25]

Summary

Echinacea extracts may reduce the duration of symptoms associated with URIs, but atopic individuals may experience adverse reactions, including anaphylaxis. There is no evidence that echinacea is beneficial in preventing URIs, and this use should be discouraged. Preparations made from pressed juice of *E. purpurea* herb (Echinacin and others) or *E. pallida* var *pallida* root appear to be superior to those made from *E. purpurea* root. The most active constituents have not been identified, so "standardized" products of echinacea are no guarantor of effectiveness. Additionally, products on the market vary widely. ❖

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CME Questions

25. Which of the following herbs contains unsaturated pyrrolizidine alkaloids?
a. Goat's rue
b. Chaste-tree berry
c. Borage leaves
d. Nettles

26. Cabbage leaves have been shown to decrease breast engorgement in clinical trials.
a. True
b. False

27. Echinacea extracts appear to be effective for:
a. preventing upper respiratory infections.
b. decreasing duration of upper respiratory infections.
c. Both a and b
d. None of the above

28. Adverse reactions associated with echinacea include:
a. asthma.
b. hepatotoxicity.
c. increased bleeding risk.

Clinical Abstracts

With Comments by Adriane Fugh-Berman, MD

Wheat Grass Juice for Ulcerative Colitis

Source: Ben-Arye E, et al. Wheat grass juice in the treatment of active distal alternative colitis. *Scand J Gastroenterol* 2002; 4:444-449.

Design/Setting/Subjects: A randomized, double-blind, placebo-controlled multi-site study of 238 subjects with active distal alternative colitis (diagnosed via sigmoidoscope) in three major cities in Israel.

Intervention: Wheat grass (*Triticum aestivum*) juice (100 cc) or placebo juice, daily for one month. Sigmoidoscopy was performed within a week of starting treatment and within three days after treatment ended.

Main Outcome Measures: Disease activity was assessed via symptom diary (including rectal bleeding, stool frequency, urgency, pain, distension, mucus, general well-being, and appetite), sigmoidoscopy, and subjective improvement. Physicians also performed a global assessment.

Results: Twenty-one subjects completed the study; full information was available on 19. Three patients withdrew early; two in the treatment group (one could not tolerate the taste of the juice and the other was convinced she was receiving placebo); one in the placebo group withdrew after 14 days because of deterioration of her illness. Wheat grass use was associated with a significant reduction in the overall disease activity index ($P = 0.031$) and in the severity of rectal bleeding ($P = 0.025$), abdominal pain ($P = 0.019$), the physician global assessment ($P = 0.031$), and

patients retrospective evaluation (P = 0.00533). Blinding was adequately maintained. The most common side effect reported by wheat grass juice users was increased vitality, reported by five subjects (41.6%), and nausea, reported by four subjects (33.3%); two subjects reported decreased morning appetite and one subject reported constipation. No serious adverse effects were noted.

Funding: Not stated.

Comments: If you've noticed what looks like patches of turf in the produce section of your grocery store, it's probably wheat grass: wheat seedlings that proponents mow (oh, all right, clip) and blend into fresh juice purported to benefit a variety of conditions, including cancer. It's sold in shot-sized portions at health food stores. Out of curiosity, I purchased a jiggerful. It tasted exactly as one might imagine juiced lawn would taste—revolting. At any rate, this is the first randomized controlled trial of wheat grass juice, and it appears to have found a benefit in ulcerative colitis. It is unknown what the active ingredients of wheat grass juice are; the researchers suggest that flavonoids, particularly apigenin, may be implicated. No serious adverse effects of wheat grass have been reported, and this seems a harmless adjuvant treatment, for those with no functional taste buds. ❖

Oxalate Content of Soy Products

Source: Massey LK, et al. Oxalate content of soybean seeds (*Glycine max*: Leguminosae), soy foods, and other edible legumes. *J Agric Food Chem* 2001;49:4262-4266.

Funding: Virginia Schafer Fund and Agricultural Research Center Project 3057-0246, Washington State University, and Project 3352 of the Iowa Agriculture and Home Economics Experiment Station, Ames, IA, Project 3352, Hatch Act and State of Iowa funds, and U.S. Department of Agriculture.

Comments: Eleven cultivars of soybean and 13 commercial soy foods were examined for oxalate content. Among soybean seeds, total oxalate levels ranged from 0.67-3.5 g/100 g dry weight. Commercial soy foods contained 16-638 mg total oxalate per serving *(see Table)*. Soy foods contain substantial amounts of oxalates. High urinary oxalate is associated with increased risk of nephrolithiasis, and patients with calcium oxalate kidney stones are advised to limit total intake of oxalates to 50-60 mg/d. Should stone-formers avoid soy products? The answer is not that simple, because some soy products contain substantial amounts of calcium, which binds oxalates.

Dietary calcium binds oxalates in the gastrointestinal tract and is actually associated with decreased risk of kidney stones.[1,2] Supplemental calcium, however, was associated with increased incidence of renal stones (relative risk 1.20) in the Nurse's Health Study, possibly because supplements were not consumed with meals; two thirds of those who took calcium took the supplements between meals or with low-oxalate meals.[1]

The primary form of oxalate found in soybeans is calcium oxalate, an insoluble form. However, up to 10 % of calcium oxalate is absorbed by healthy volunteers. Additionally, soy contains lesser amounts of soluble oxalates (bound to potassium or sodium in the range of 14.7-29.9 mg/100 g).

The current analysis found a wide range of oxalate content even among similar products. The best test would be a trial designed to examine actual absorption of oxalates from soy foods in humans. No such trial has been performed, although an absorption study found that 3.8% of total oxalates were absorbed from peanuts. Until an adequate clinical trial is performed, the most cautious course of action would be to inform recurrent calcium oxalate stone-formers that soy products are high in oxalates and should be consumed in moderation. ❖

References

1. Curhan GC, et al. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. *Ann Intern Med* 1997;126:497-504.
2. Curhan GC, et al. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. *N Engl J Med* 1993; 328:833-838.

Table

Oxalates and calcium content of soy foods*

Breakfast links	69 mg/14 mg
Lentils, cooked	100 mg/16 mg
Peanut butter	225 mg/10 mg
Refried beans	193 mg/27 mg
Soy beverage	336 mg/122 mg
Soy burger	58 mg/48 mg
Soy cheese	16 mg/nondetectable
Soy nuts	392 mg/56 mg
Soy yogurt	113 mg/nondetectable
Tempeh	23 mg/77 mg
Textured vegetable protein	496-638 mg/nondetectable-204 mg
Tofu prepared with calcium	116-235 mg/nondetectable-247 mg
Tofu prepared with magnesium	43-94 mg/nondetectable-60 mg

*Amount presented per serving of oxalates and calcium, respectively

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