## Systematic Review of the Efficacy of Herbal Galactogogues


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# Systematic Review of the Efficacy of Herbal Galactogogues

**Mylove Mortel[1] and Supriya D. Mehta, MHS, PhD[1]**


## Abstract

Exclusive breastfeeding has been linked to many positive health outcomes, yet its widespread adoption as the primary mode of providing nutrition to infants remains challenging. The most common reported reason for early breastfeeding cessation is perception of inadequate milk production. To augment breast milk production, a substantial number of women turn to herbal galactogogues despite the limited scientific evidence of their efficacy and safety. We conducted a systematic review of published literature to evaluate the efficacy of herbal galactogogues. PubMed was searched from inception to October 2012 using an iterative search process that proceeded from broad categories to specific herbs. Manuscript references were also reviewed. Only experimental studies with objective outcome measures were included. Six trials met our search criteria. Using an adapted version of the CONSORT checklist, each trial was evaluated for potential sources of bias in design and reporting. Shatavari, torbangun, fenugreek, milk thistle, and a Japanese herbal medication were the 5 herbal preparations studied. Five trials found an increase in breast milk production. Several limitations exist that affect the validity of the trial results, including small sample size, insufficient randomization methods, poorly defined eligibility criteria, use of poly-herbal interventions, and variable breastfeeding practices among enrolled subjects. Given the insufficiency of evidence from these trials, no recommendation is made for the use of herbs as galactogogues. Well-designed and well-conducted clinical trials that address the above limitations are necessary to generate a body of evidence as a basis for recommendations regarding herbal galactogogues.



## Keywords

breastfeeding, galactogogues, herbs, lactation


## Background

Breast milk has long been accepted as the gold standard of infant nutrition.[1] Although breast milk has been linked to many positive health outcomes, widespread adoption of exclusive breastfeeding as the primary mode of providing nutrition to young infants has been challenging. According to the Centers for Disease Control and Prevention's most recent Maternity Practices in Infant Nutrition and Care, in the United States, the exclusive breastfeeding rate for infants under 6 months is 16.3%, and 24.6% of breastfed infants received formula before 2 days of age.[2] Worldwide, maternal perception of insufficient milk production is the most common reason reported by mothers for early cessation of breastfeeding; reported prevalence is between 30% and 80%.[3] For those mothers in whom milk production has declined and is not responding to nonpharmacologic measures, the use of galactogogues is often considered.[4]

Galactogogues are substances thought to assist in the initiation, continuation, or augmentation of breast milk production.[5] They include pharmaceutical agents and herbal supplements. Recently, the Cochrane Collaboration published a review of pharmaceutical galactogogues given to mothers of preterm hospitalized infants. Two trials of domperidone met the review criteria, and meta-analysis showed a modest increase in expressed breast milk volume of 99.49 mL/day (95% confidence interval [CI], –1.94-201) in mothers of preterm infants given domperidone.[6] As an alternative to pharmaceutical agents, many clinicians recommend the use of herbs to improve milk output.[7] In the United States, it is estimated that 15% of breastfeeding women use herbal galactogogues,[8] whereas in a Norwegian study, this estimate is 43%.[9] Although some evidence exists regarding pharmaceutical drug–herb interactions, there is limited evidence explaining

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the mechanism of action of herbs as galactogogues. Given the recency and depth of the Cochrane review and the common practice of using herbal galactogogues as an alternative to pharmaceutical agents, we sought to evaluate available evidence regarding the efficacy of herbal interventions in increasing breast milk production.

## Methods

### Search Methodology

Because our goal was to assess *efficacy*, we limited our review to published manuscripts with an experimental design that had an objective outcome measure of breast milk production. The search procedure to identify eligible manuscripts was conducted in 3 steps. First, PubMed was searched from inception to October 2012 using the keywords "galactogogues" or "galactagogues" or "lactogogues" or "lactagogues" (no field restriction), limited to humans and the English language. The search returned 28 articles, 2 of which were randomized controlled trials (RCT) of pharmacologic galactogogues, 15 were reviews, 1 was a practice guideline, 2 were case reports, and the rest were articles that were either observational, survey, or commentary in nature. From these 28 articles, 16 different herbal galactogogues were identified: shatavari, torbangun, fenugreek, fennel, milk thistle, chasteberry, goat's rue, anise, blackseed, caraway, coriander, dill, alfalfa, blessed thistle, nettle, and red clover.

Next, we searched PubMed using each of the herbal galactogogues (no field restriction), limited to humans and the English language, and following the search criteria: [common name of the herb] OR [Latin name of the herb] AND (lactation OR breast OR milk OR breastfeed). Appendix A shows a summary of the search results on each herbal galactogogue.

Of the 16 different herbs initially identified, only 7 herbs had articles directly related to the topic of lactation or breastfeeding. As a final search procedure, we reviewed references of these manuscripts. Combining the 3 searches conducted on these 7 herbal galactogogues and the manual search of associated references resulted in a total of 63 articles. Of the 63 articles, only 6 were RCTs. Further review of the references cited by the 6 RCTs did not yield additional experimental studies. The RCTs were reviewed for study design characteristics as well as proposed mechanism of lactogenesis. The proposed mechanism and primary study outcomes for each trial are summarized in Table 1. Each trial was also evaluated for potential sources of bias in design and reporting, using an adapted version of the CONSORT checklist as a guide.[10] The results are summarized in Table 2.

## Results

Five of the 6 RCTs were designed to assess the galactogogue activity of shatavari, torbangun, fenugreek, or milk thistle as primary compounds, and 1 was designed to assess the efficacy of a multicompound regimen consisting of 13 different herbs. All trials were conducted outside the United States.

### Results of Trials

None of the trials reported sample size calculations. Only 3 of the 6 trials[1,19,27] had reproducible recruitment and screening methods. One trial[15] reported its sequence generation, and 2 trials[15,28] reported their mechanism of allocation concealment to ensure that treatment allocation was unbiased. Only 1 trial described how randomization was actually implemented,[15] and only 2 trials reported blinding of those assessing outcome.[15,19] Three trials reported adherence,[15,19,25] and 5 trials reported absence of side effects.[15,19,25,27,28] There is insufficient information to verify whether side effects were systematically assessed. These potential sources of bias are summarized in Table 2.

*Sharma S, et al. Randomized controlled trial of* Asparagus racemosus *(Shatavari) as a lactogogue in lactational inadequacy.*[27] Women with uncomplicated term delivery and who reported lactational inadequacy during 14-90 days postpartum were recruited for this multicenter, randomized, double-blind, placebo-controlled, parallel-arm study of shatavari. Lactation inadequacy was defined either as inability to regain infant's birth weight at 15 days of life, or infant weight gain less than 15 g per day, or mother supplementing greater than 250 mL per day of milk 4 weeks after birth. All mothers diagnosed with lactation inadequacy were advised to exclusively breastfeed and were instructed on proper position and frequency of feeds, as well as maintenance of adequate rest and nutrition. Sixty-four mothers were enrolled and randomized 1:1 into treatment and placebo arms, and 11 mothers failed to complete the trial. The mothers were randomized to receive either 2 teaspoons twice daily of a 100-g mixture containing 15% shatavari by weight for 4 weeks (n = 32), or a physically indistinguishable placebo mixture (n = 32). Adherence was not explicitly reported, although the authors reported that 26 mothers in the treatment arm and 23 mothers in the placebo arm offered supplementary feeding during the study.

The primary outcome was change in serum prolactin level. Additional outcomes were infant weight gain and change in volume and frequency of supplementary feedings. Maternal characteristics at baseline were comparable. Median prolactin level after treatment was 25 ng/mL for the treatment arm and 38 ng/mL for the placebo arm. Although no results of statistical significance testing are reported, these levels were deemed comparable by the researchers. Infant weight gain after therapy for the treatment arm was 30 g/d versus 26 g/d for the placebo arm. These levels were reported as comparable. The researchers concluded that shatavari did not have any effect on milk production.

*Damanik R, et al. Lactagogue effects of Torbangun, a Bataknese traditional cuisine.*[1] Women in North Sumatra, Indonesia aged 20-40 years in their last trimester of pregnancy, who were

**Table 1.** Summary of Experimental Trials of Herbal Galactogogues

| Reference, Location | Herb Common Name (Latin Name) | Proposed Mechanism | Intervention | Outcomes Measured | Primary Outcome Comparing Treatment vs Placebo (vs Control, if Used)[a] |
|---|---|---|---|---|---|
| Sharma et al,[27] 1996, India | Shatavari (*A. racemosus*) | Estrogenic effect on mammary glands | 2 tsp twice daily for 4 wk of a 100-g galactogogue mixture (15% shatavari by weight) or placebo | Primary outcome: change in serum prolactin level. Other outcomes: infant weight gain, change in volume and frequency of supplementary feedings | Median prolactin level (range): 25 (8-210) ng/mL vs. 38 (7-156) ng/mL<br>Median infant weight gain (range): 30 (14-52) g/d vs 26 (10-75) g/d<br>No statistical significance testing provided |
| Damanik et al,[1] 2006, Indonesia | Torbangun (*C. amboinicus Lour*) | Proliferation of secretory mammary cells | 150 g of torbangun leaves served as a soup 6 d/wk for 1 mo; or 1 fenugreek capsule 3x/d for 1 month; or 1 tablet of Moloco+B12 3x/d for 1 month. Amount of fenugreek per capsule not reported | Primary outcome: breast milk volume. Other outcomes: nutritional quality of breast milk | Day 28 mean breast milk volume (SD): I, 479 (157) mL; F, 400 (215) mL; M, 385 (202) mL ($P < .05$) |
| Ushiroyama et al,[28] 2007, Japan | Xiong-gui-tiao-xue-yin Drug X contains: 2 g each of Japanese angelica root, cnidium rhizome, rehmannia root, atractylodes rhizome, hoelen, citrus unshiu peel, cyperus rhizome, moutan bark, and lindera root, 1.5 g each of jujube fruit, Siberian motherwort, ginger rhizome, and glycyrrhiza root | Regulation of prolactin and oxytocin secretion | 6.0 g/d of commercial compound Xiong-gui-tiao-xue-yin or 0.375 mg/d of ergometrine | Outcomes: mean breast milk volume, plasma prolactin and oxytocin levels | Day 4 breast milk volume (SD): 277 (21) g vs 155 (61) g ($P < .05$)<br>Day 6 breast milk volume (SD): 414 (68) g vs 293 (98.5) g ($P < .05$)<br>Day 1 plasma prolactin level (SD): 158 (78) ng/mL vs 129 (65) ng/mL ($P < .05$)<br>Day 6 plasma prolactin level (SD): 168 (95) ng/mL vs 117 (54) ng/mL ($P < .01$) |
| Di Pierro et al,[25] 2008, Peru | Milk thistle (*S. marianum*) | Unknown, possibly estrogenic | 420 mg/d of BIO-C (micronized Silymarin) or placebo | Primary outcome: breast milk quantity. Other outcome: macronutrient analysis of breast milk | Day 30 mean breast milk quantity (SD): 990 (102) g vs 650 (78) g ($P < .01$) |
| Gupta and Shaw,[15] 2011, India | Shatavari (*A. racemosus*) | Steroidal action of saponins in plant | 1 capsule 3x/d containing shatavari root powder for 30 d, based on dosing formula: 60 mg/kg of body weight or placebo | Primary outcome: change in serum prolactin level. Other outcomes: change in infant's weight and mother's weight, subjective satisfaction of mother, and overall well-being and happiness of the infant | Mean percent increase in prolactin level (SD): 32.9% (6.5) vs 9.6% (4.6) ($P < .05$)<br>Mean percent increase in infant weight (SD): 16.1% (3.7) vs 5.7% (2.6) ($P < .05$) |
| Turkyilmaz et al,[19] 2011, Turkey | Fenugreek (*T. foenumgraecum*) | Possibly estrogenic; stimulate sweat production | At least 3 cups daily of commercial herbal tea (Still tea, Humana) containing fenugreek; or apple tea (placebo); or no intervention (control). Humana Still tea contains 100 mg fenugreek and other ingredients | Outcomes: breast milk volume, maximum weight loss (% of birth weight), and time to regain birth weight (d) | Mean breast milk volume (SD): I, 73.2 (53.5) mL; P, 38.8 (16.3) mL; C, 31.1 (12.9) mL ($P < .05$) |

Abbreviation: SD, standard deviation.
[a]For comparison purposes, only serum prolactin level or breast milk volume outcomes are shown.

**Table 2.** Potential Sources of Bias in Study Design and Reporting

| Study Measure | Sharma et al[27] | Damanik et al[1] | Ushiroyama et al[28] | Di Pierro et al[25] | Gupta et al[15] | Turkyilmaz et al[19] |
|---|---|---|---|---|---|---|
| Reproducible recruitment and screening methods | Yes | Yes | No | No | No | Yes |
| Reproducible eligibility criteria | Yes | Yes | Yes | Yes | No | Yes |
| Reproducible intervention administration | Yes | No | Yes | Yes | Yes | Yes |
| Sample size calculation | NR | NR | NR | NR | NR | NR |
| Adequate sequence generation | NR | NR | NR | NR | Yes | NR |
| Allocation concealment mechanism | NR | NR | Yes | NR | Yes | NR |
| Randomization implementation (enrollment and assignment of subjects) | NR | NR | NR | NR | Yes | NR |
| Blinding of subjects | Yes | No | Unclear | Yes | Yes | No |
| Blinding of care providers/ those assessing outcome | Unclear | No | NR | NR | Yes | Yes |
| Methods of maintaining blinding of researchers reported | NR | Unclear | NR | NR | Yes | Yes |
| Intention to treat analysis | Yes | Yes | Yes | Yes | Yes | Yes |
| Groups balanced at baseline | Yes | NR | Yes | Yes | Yes | Yes |
| Number lost to follow-up reported by arm | Yes[a] | Yes | Yes | Yes | Yes[a] | Yes |
| Exclusions after randomization reported by arm with reasons | No | No | No | Yes | Yes | Yes |
| Adherence reported | Unclear | Unclear | No | Yes | Yes | Yes |
| Harms of treatment (ie, side effects) reported | Yes | No | Yes | Yes | Yes | Yes |

Abbreviations: No, sufficient information was reported, and the measure was not appropriately addressed; NR, not reported or no information is reported to assess the measure; Yes, sufficient information was reported, and the measure was appropriately addressed; Unclear, insufficient information was reported to fully assess whether the measure was appropriately addressed.
[a]Total number of subjects lost to follow-up was reported, but no information was provided for the distribution between treatment and placebo arms.

generally healthy and planned to exclusively breastfeed their infants for a minimum of 4 months, were recruited to this parallel randomized trial of torbangun leaves (*Coleus amboinicus Lour*). Women were eligible if they delivered a healthy term infant weighing at least 2.5 kg. Starting on the second postpartum day, 75 subjects were enrolled and randomized 1:1:1 into 3 arms: 150 g per day of torbangun leaves served as soup 6 days a week (n = 25); 1 capsule containing fenugreek seeds 3 times per day (n = 25); or 1 sugar-coated Moloco+B12 tablet 3 times per day (n = 25) for 30 days. The amount of fenugreek in each capsule was not reported. The women were followed for an additional 30 days after the initial 30-day supplementation period. Twenty-three subjects from the torbangun group, 22 subjects from the fenugreek group, and 22 subjects from the Moloco+B12 group completed the 2-month study period. Medication count was used to measure adherence for those randomized to the fenugreek capsule group and the Moloco+B12 tablet group; delivery staff checked daily whether mothers in the torbangun group consumed the soup. Blinding of subjects was not achieved, and insufficient information was reported to assess blinding of researchers.

The primary outcome was change in the volume and nutritional quality of breast milk. The difference between pre- and postfeeding weight of the infant in grams was used to calculate milk volume, which was then converted into milliliters using the conversion factor 0.983 mL/g to adjust for breast milk density. There were no significant differences among the 3 groups at baseline. On day 28, the mean breast milk volume for the torbangun group, the fenugreek group, and the Moloco+B12 group was 479 mL (65% increase from baseline), 400 mL (20% increase), and 385 mL (10% increase), respectively. The percent increase for the torbangun group was statistically significant ($P < .05$). Data collected on days 42 and 56 showed that the percent increase in milk volume for the torbangun group remained higher than that of the other 2 groups. The researchers concluded that torbangun leaves enhanced milk production, and the galactogogue effect was sustained even after the supplementation period.

*Ushiroyama T, et al. Xiong-gui-tiao-xue-yin (Kyuki-chouketsu-in), a traditional herbal medicine, stimulates lactation with increase in secretion of prolactin but not oxytocin in the postpartum period.*[28] Eighty-two women who had uncomplicated delivery in Osaka, Japan were enrolled in this parallel-arm, randomized trial of Xiong-gui-tiao-xue-yin (herein referred to as drug X), a traditional herbal preparation consisting of 13 different herbs. The women were randomized 1:1 to either 6.0 g per day of commercially prepared drug X (n = 41) or 0.375 mg per day of ergometrine (n = 41). No information was reported to assess how blinding of researchers was achieved and whether subjects were blinded. Outcomes were mean milk volume and mean plasma prolactin and oxytocin levels. Breast milk volume was measured daily until postpartum day 6 by weighing the infant before and after feeding, and plasma prolactin and oxytocin levels were measured on days 1 and 6. Maternal and infant characteristics at baseline did not differ between the groups. On day 4, the mean milk volume for the treatment group and the ergometrine group was 276.5 g and 155.3 g, respectively ($P < .05$). On day 6, the treatment group continued to have higher mean milk volume of 413.7 g versus 293.3 g for the ergometrine group ($P < .05$). On day 6, plasma prolactin level for the treatment group and the ergometrine group was 167.5 ng/mL and 117.1 ng/mL, respectively ($P < .05$). No statistical difference was observed between the 2 groups regarding their oxytocin level on day 6. No adverse reactions were noted. The researchers concluded that drug X enhances breast milk production among postpartum women.

*Di Pierro F, et al. Clinical efficacy, safety and tolerability of BIO-C (micronized Silymarin) as a galactagogue.*[25] Fifty healthy lactating women in a hospital in Lima, Peru were enrolled in this placebo-controlled trial of micronized silymarin. The mothers were instructed to maintain a diet of about 2600 Kcal per day and were randomized 1:1 into treatment or placebo arms: 420 mg per day of micronized silymarin (BIO-C; n = 25) or placebo (n = 25) for 63 days. Treatment and placebo forms were indistinguishable. No information was reported to assess how blinding of researchers was achieved. All mothers completed the study. The women were comparable at baseline. The outcomes were mean quantity of milk in grams and a qualitative assessment of the chemical composition of milk reported as percent water, fats, carbohydrates, and protein. Milk was quantified by weighing the infant before and after feeding and adding the quantity taken from manual breast expression. On day 30, the mean quantity of milk for the treatment group and the placebo group was 990 g and 650 g, respectively ($P < .01$), representing a 64.4% increase in the treatment group and a 22.5% increase in the placebo group over baseline values. On day 63, the percent increase in the quantity of milk remained significantly higher in the treatment group compared to the placebo group (85.9% and 32.1%, respectively). No difference was noted in the chemical composition of milk between the 2 groups on day 30 or day 63. No adverse reactions were noted. The researchers concluded that BIO-C has effective galactogogue activity.

*Gupta M, Shaw B. A double-blind randomized clinical trial for evaluation of galactogogue activity of* Asparagus racemosus *wild.*[15] Lactating mothers aged 20-40 years, with an infant younger than 6 months, were enrolled at a single hospital in Kolkata, India in this double-blind, placebo-controlled, parallel arm trial of shatavari. At least 1 of the following symptoms was present: deficient lactation, pain in breasts during feeding, poor appetite, any anxiety disorder, or an infant that cries just after feeding. Deficient lactation was not defined. Sixty subjects were randomized 1:1 into treatment and placebo arms: 1 capsule 3 times daily containing shatavari root powder for 30 days (60 mg/kg of body weight; n = 30), or 1 capsule 3 times daily containing rice powder as placebo (n = 30) for 30 days (same dosing formula as the treatment group). Those assessing outcomes were blinded to treatment assignments. Subjects were examined weekly and advised during the study period to avoid contraceptives and steroid-containing drugs and to follow normal feeding technique and schedule.

The primary outcome was percent change in serum prolactin level from baseline to after treatment (actual prolactin levels not reported). Additional outcomes included change in mother's and infant's weight, maternal satisfaction with lactation, and maternal satisfaction with the infant's well-being and happiness. Baseline characteristics were not significantly different between the 2 groups. Mean prolactin level increased by 32.9% for the treatment group compared to 9.6% for the placebo group ($P < .05$). Similarly, mean infant weight increased by 16.1% for the treatment group compared to 5.7% for the placebo group ($P < .05$). The treatment group had higher mean percent increases in the secondary outcomes compared to the placebo group ($P < .05$). No adverse reactions were noted. The researchers concluded that shatavari has significant galactogogue activity.

*Turkyilmaz C, et al. The effect of galactagogue herbal tea on breast milk production and short-term catch-up of birth weight in the first week of life.*[19] Healthy mothers from a maternity unit in Ankara, Turkey were enrolled in this placebo-controlled, randomized, double-blind study. To be eligible, the women had healthy term infants, were willing to exclusively breastfeed, and agreed to use a specific breast pump on postpartum day 3. One lactation consultant nurse educated the women on proper positioning, latch-on, and breastfeeding techniques. Sixty-six subjects were enrolled and randomized 1:1:1 into treatment, placebo, and control arms. Mothers in the treatment group (n = 22) were instructed to consume daily a minimum of 3 cups of a commercially available herbal tea (Still tea, Humana) containing 100 mg of fenugreek and other ingredients. The placebo group (n = 22) was prescribed an apple tea daily in the same amount as the treatment group. The fenugreek tea and apple tea were the same color and form. The duration of the intervention was not reported. The control group (n = 22) received routine advice without any specific recommendation. One person randomized the mothers to treatment arms and assessed adherence with tea intake, and 2 other persons blinded to the study collected outcome data. All mothers completed the study.

The outcomes were mean breast milk volume, maximum weight loss as a percentage of birth weight, and days until birth weight was regained. Each breast was pumped consecutively for 15 minutes using the same model of an electric breast pump to measure breast milk volume. Baseline maternal characteristics were comparable in the 3 groups. The mean breast milk volume for the treatment group, the placebo group, and the control group was 73.2 mL, 38.8 mL, and 31.1 mL, respectively ($P < .05$). Maximum weight loss was lowest in the treatment group ($P < .05$). Infants in the treatment group also regained their birth weights faster than the placebo and control groups ($P < .05$). The researchers concluded that the commercially prepared herbal tea containing fenugreek enhanced breast milk production and might be used to support exclusive breastfeeding in the first week of life.

## Biologic Plausibility

Little is known about how herbs function as galactogogues. Our review indicates several potential pathways, but for the most part, the studies were done on animal models and untested on humans, limiting their generalizability. In contrast, the biologic pathway for pharmaceutical galactogogues has been extensively researched. Multiple trials of domperidone and metoclopramide have shown that they stimulate the release of prolactin by blocking dopamine receptors in the anterior pituitary gland.[6,11,12] We present a brief review of the pathways cited by the 5 RCTs (excluding the trial of the 13-compound regimen) to shed light on the possible mechanism of action of these herbs in enhancing breast milk production.

*Shatavari*. In a study by Sabins et al,[13] among rats, an alcohol extract of shatavari increased milk production concurrent with increased growth of the mammary glands, alveolar tissues, and acini. Three other studies have demonstrated the estrogenic effects of shatavari in the mammary glands and genital organs of rats.[14] Chemical analysis of shatavari roots reveals the presence of saponins and steroidal saponins,[15] and 1 hypothesis states that the estrogenic activity results from the hormone-like actions of these steroidal saponins.[14] Another hypothesis states that the growth of mammary tissue is caused by the action of released corticoids or prolactin.[14] Although estrogens have a stimulating effect on the ductal epithelial cells, causing them to lengthen, their primary role seems to be the potentiation of the prolactin production.[16]

*Torbangun*. For centuries, torbangun has been used as a galactogogue by Bataknese people in Indonesia.[1] It has been hypothesized, based on mouse models, that torbangun has an effect on the proliferation of secretory mammary cells.[1] Increases in DNA and RNA were observed in mice receiving torbangun extract, and this effect was dose dependent.[1] The number of epithelial cells and their secretory activity are thought to determine the shape of the lactation curve, and increases in either number of cells or their secretory activity result in increased milk production.[17] Two related studies support this finding. One study involving goats showed that an increase in the number of mammary cells followed by an increase in the secretory activity of each cell was associated with an increase in milk production in the early lactation period.[17] Another study using bovine models showed an increased milk yield as a result of an increase in the secretory activity of cells alone.[17] In the latter study, there was no increase in mammary cell number. Despite the use of torbangun in many medical conditions such as malarial fever, hepatopathy, renal calculi, and chronic asthma,[18] little is known about its specific properties. Phytochemical screening of the plant reveals the presence of alkaloids, flavonoids, tannins, and saponins in its extracts.[18]

*Fenugreek*. Fenugreek (*Trigonella foenumgraecum*) is the most commonly used herbal galactogogue in published literature,[5,19] although there is conflicting evidence of its efficacy. It is thought that fenugreek stimulates sweat production, and since the breast is a modified sweat gland, fenugreek may affect breast milk production in this manner.[20] It has also been suggested that fenugreek may have estrogenic activity. One study using in vitro assays found that fenugreek seeds contain estrogen-like compounds, and that they stimulate pS2 expression in MCF-7 cell lines.[21] pS2 is frequently used as a marker for assessing the estrogenicity of a compound.[21] The phytoestrogens and diosgenin content (a type of steroidal sapogenin) of fenugreek appear to account for the increase in milk flow observed from its use,[19] but the exact mechanism of action is as yet undefined. Phytoestrogens are similar in chemical structure to endogenous estrogen and can bind to both α and β estrogen receptors. Thus they have the potential to act as estrogen agonists or antagonists, which could alter the structure or functioning of the endocrine system.[22,23]

*Milk thistle*. The lactogenic activity of milk thistle (*Silybum marianum*) remains largely anecdotal, although its use as a galactogogue is increasing.[24] Animal studies suggest milk thistle has promising lactogenic properties. In 1 study, cows given silymarin (an extract of *Silybum marianum*) were observed to have increased milk production of 5-6 L per day per cow.[25] It is thought that the administration of silymarin after calf delivery improves the physiological status of the cow, which leads to faster recovery of the cow and increased food intake, and thus increased milk production. This finding was supported by the observation of reduction of blood β-hydroxybutyric acid and decreased outcomes of ketonuria in cows treated with silymarin.[25] Other experimental studies show a weak anti-estrogenic property arising from the flavonolignan component of silymarin[25]; flavonolignan is the major biologically active component of milk thistle.[26] It is rapidly metabolized and measurable in plasma, mainly in the form of glucuronides.[26]

## Discussion

Despite their prevalent use among lactating women, our review finds that herbal galactogogues have limited reported safety and efficacy data. In our extensive review, we found 6 trials of herbal galactogogues with outcomes addressing the effect on breast milk production. These outcomes included effect on serum prolactin and oxytocin levels, breast milk volume, infant weight, weight loss as a percentage of birth weight, time to regain birth weight, and the chemical composition of breast milk. Four of the 6 trials showed positive galactogogue activity of 4 herbs based upon different outcome measurements.[1,15,19,25] Gupta and Shaw[15] observed shatavari to increase serum prolactin level by 3.5 times that of placebo and mean infant weight by almost 3 times that of placebo. The increase in serum prolactin level, however, contradicts the results by Sharma et al,[27] who found no galactogogue effect of shatavari. Damanik et al[1] reported an increase in breast milk volume using torbangun, but not fenugreek, which is in direct contrast with the result of the study by Turkyilmaz et al.[19] Turkyilmaz et al found that the fenugreek group had almost twice the expressed breast milk volume as placebo.[19] The differing results may stem from different dosages and formulations of fenugreek used; the Turkyilmaz et al study used 100 mg of fenugreek,[19] but it is unclear how much was used in the Damanik et al[1] study; there were different study populations; and there were different measures of breast milk volume:infant weight in the study by Damanik et al[1] versus expressed milk from pumping the breasts in the study by Turkyilmaz et al.[19] Di Pierro et al reported an increase in breast milk volume from the administration of silymarin.[25] There are no other studies evaluating silymarin with which to compare these results. Ushiroyama et al reported increases in breast milk volume and serum prolactin level in their study of Xiong-gui-tiao-xue-yin,[28] but polyformulation, duration of the treatment, and dates of sample collection make it difficult to draw conclusions about the galactogogue efficacy of this herbal preparation.

Although we reviewed randomized trials, the gold standard for assessing efficacy, the trials had significant flaws: variable recruitment and screening methods, poorly defined eligibility criteria, failure to report sample size calculation, insufficient methods of randomization and blinding, and poor reporting of adherence and assessment of side effects. These design flaws limit reproducibility and generalizability and introduce significant bias and confounding, such that effects are imprecise and cannot be validly attributed to the treatment tested.

Although 5 of the trials aimed to assess the efficacy of 1 primary herb, only 2 of the 6 trials used a purified version of the herb.[15,25] The Sharma et al study used a mixture that is 15% shatavari by weight; there were 6 other herbs added to the intervention product.[27] There is insufficient information to determine whether other ingredients were added to the torbangun soup in the Damanik et al study.[1] The Turkyilmaz et al study used a commercially prepared herbal tea containing fenugreek[19]; however, the herbal tea also included fennel, raspberry leaf, and goat's rue, substances that are traditionally used to enhance lactation.[24] It is not possible to assess which herb or combination of herbs used in the Ushiroyama et al study is responsible for the reported positive galactogogue activity.[28] Because the intervention products contained other substances the concurrent actions of which are unknown, there is potential for erroneously attributing the effect to the main herb. It is recommended that purified individual compounds or derivatives be used, as was done in the trials conducted by Di Pierro et al[25] and Gupta and Shaw.[15] It is also important to note that although the studies mentioned here used known preparations of herbs, at least in the United States, herbal preparations are not regulated and standardized, posing a safety concern. Under the 1994 Dietary Supplement Health and Education Act, which covers any product taken by mouth that contains a "dietary ingredient" intended to supplement the diet, manufacturers are responsible for ensuring safety of the supplement, but there are no rules that limit the amount of nutrient(s) in any form of these supplements.[29]

The studies varied in terms of eligibility criteria and outcomes. Three trials required inadequate lactation as main eligibility criteria,[15,25,27] and of those 3 trials, only 2 trials explicitly defined lactation inadequacy.[15,27] Inconsistencies in eligibility criteria may attenuate any possible differences observed between treatment and placebo arms,[11] particularly if the outcome is change in breast milk volume from baseline. It is also important to consider infant eligibility criteria, such as whether babies were born at term or preterm, given that milk production is affected by local feedback mechanisms. Three of the trials explicitly stated including only term infants as subjects,[1,19,27] whereas the Ushiroyama et al study stated including women who had spontaneous labor pain followed by normal delivery.[28] This information was not reported in the Gupta and Shaw[15] and Di Pierro et al[25] studies. For those assessing serum prolactin levels, the timing of intervention initiation varied, which is an important consideration given that the role and level of prolactin depend upon the stage of lactation.[11]

Three trials used serum prolactin level as primary outcome.[15,27,28] Multiple studies have shown that there is poor correlation between serum prolactin level and milk production[11,30]; thus, studies that rely on this measure alone do not provide usable evidence of galactogogue activity. Four trials measured breast milk volume or change in infant weight as primary outcome.[1,19,25,28] However, only 2 trials explicitly described how breast milk volume was measured, and whether it included milk from breast expression.[19,25]

The trials also used different units of measurement, making comparison of the magnitude of effects difficult. Given the paucity and lack of standardization of experimental studies on herbal galactogogues, it is recommended that future studies include lactation inadequacy as an explicitly defined eligibility criteria and that the timing and duration of intervention be considered to yield clinically significant findings.[6] Additionally, future studies should use the same, multiple outcome measures and units of measurement to enable comparison and extension into a generalizable finding.

Outside the review of the trials and biologic plausibility of herbs as galactogogues, there are other limitations to the study of herbal galactogogues. We found variable terminology regarding substances thought to enhance milk production. The use of multiple terminologies makes it difficult to synthesize and pool information necessary to make a consensus on the safety and efficacy of herbal products in increasing breast milk production.

Difficulty in interpreting studies on herbal galactogogues also arises from the lack of attention given to ensuring that enrolled subjects adhere to the same practices throughout lactation. It is requisite in studies of galactogogues that the subjects be comparable, not only on their baseline demographic data but also in their breastfeeding practices, such as whether they are exclusively breastfeeding or supplementing, whether they are feeding or expressing at similar frequencies, and whether they received the same advice on supportive measures.[6,11] If mothers in the study have different breastfeeding practices, these differences may confound or modify the association observed. The intervention product may not be the only contributing factor to the presence or absence of galactogogue activity of the product.

Three other reviews were published recently on the topic of galactogogues. Zapantis et al reviewed the prevalence and types of herbs used as galactogogues without systematic assessment of validity.[24] Budzynska et al conducted a systematic review to determine the safety and efficacy of herb use during lactation,[31] but studies reviewed included surveys and nonexperimental designs and did not include a critical review of validity. Forinash et al reviewed the efficacy of galactogogues (pharmaceutical and nonpharmaceutical) in the breastfeeding mother,[32] and although the review included studies with experimental designs, a systematic assessment of validity was not performed. Our review differs from these manuscripts in that we focused on evaluating the efficacy of herbal galactogogues; thus, we included only published manuscripts with an experimental design that had an objective outcome measure of breast milk production. Given that the available published data on the use of herbs as galactogogues are predominantly based on case reports or anecdotal evidence, we deemed it more important to highlight the areas of concern regarding the design and reporting of the presently limited experimental studies on herbal galactogogues and make recommendations to guide future studies.

## Conclusion

Currently, the Academy of Breastfeeding Medicine does not have recommendations for the use of herbs as galactogogues. Four herbs (shatavari, torbangun, fenugreek, and milk thistle) with potential as galactogogues were reviewed in this article. However, the trials assessing these potential galactogogues had several limitations that decreased the validity of their results. Given the insufficiency of evidence from these trials, no recommendation is made for the use of herbs as galactogogues. Well-designed and well-conducted clinical trials that address the limitations are needed to generate evidence for recommendations regarding the use of herbs as galactogogues. More importantly, before the assessment of clinical efficacy, studies must first provide evidence for the mechanism of action of herbs as galactogogues and their safety through phytochemical and pharmacokinetic assays. This information will lead to a greater understanding of the herbs' composition, breakdown into active and inactive forms, and bioavailability after ingestion. Any attempt at conducting trials without this a priori information is futile and will add little value to the expansion of our current knowledge. Given the widespread use of herbs among lactating women today, establishing a strong evidence base for herbal galactogogues to guide recommendations is a public health concern.

## Appendix A

### *Common Herbal Galactogogues and Proposed Mechanism of Action*

| Herb Common Name (Latin Name) | Proposed Mechanism | Total Search Results | Type of Study (Specific to Topic)[a] |
|---|---|---|---|
| Shatavari (*Asparagus racemosus*) | Estrogenic effect on mammary glands; steroidal action of saponins in plant | 2 | 1 RCT<br>1 review |
| Torbangun (*Coleus amboinicus Lour*) | Proliferation of secretory mammary cells | 3 | 1 review<br>1 RCT<br>1 focus group discussion |
| Fenugreek (*Trigonella foenumgraecum*) | Possibly estrogenic; stimulate sweat production | 24 | 2 RCTs<br>7 reviews<br>1 case study<br>1 phytochemical assay<br>1 commentary |
| Fennel (*Foeniculum vulgare*) | Possibly estrogenic | 12 | 1 case report<br>2 reviews |
| Milk thistle (*Silybum marianum*) | Unknown, possibly estrogenic | 255 | 4 reviews<br>1 RCT |
| Chasteberry (*Vitex agnus castus*) | Estrogenic (hormone modulator) | 16 | 3 reviews<br>2 phytochemical assay<br>1 monograph |
| Goat's rue (*Galega officinalis*) | Unknown | 3 | 1 review |

Abbreviation: RCT, randomized controlled trial.
[a]Additional filters were applied to initial search methods to limit results to those related to the topic of lactation and breastfeeding or to the bioavailability and pharmacokinetics of the herbs.

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