BREASTFEEDING MEDICINE
Volume 12, Number 7, 2017
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DOI: 10.1089/bfm.2017.0038

Reviews

Breastfeeding: A Review of Its Physiology and Galactogogue Plants in View of Traditional Persian Medicine

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Abstract

Introduction: The beneficial effects of breastfeeding for the infant and mother are well recognized. Many natural products are reputed to be galactogogue agents in major Traditional Persian Medicine (TPM) textbooks. The aim of this study is to review those medicinal plants that are reported to be effective in increasing breast milk in TPM and to compare the data from TPM texts with the findings of modern pharmacological and clinical research.
Materials and Methods: Data on the medicinal plants used to increase breast milk were obtained from major TPM textbooks. A detailed search in PubMed, Science Direct, Scopus, Google Scholar, and Web of Science databases was performed to confirm the effects of medicinal plants mentioned in TPM on lactation in view of the identified pharmacological actions.
Results: *Foeniculum vulgare*, *Anethum graveolens*, *Pimpinella anisum*, *Nigella sativa*, and *Vitex agnus-castus* are among the most effective galactogogue TPM plants. Many pharmacologically relevant activities have been reported for these herbs.
Conclusion: The use of traditional knowledge can pave the way toward finding effective phytopharmaceuticals for increasing breast milk.

Keywords: milk production, breastfeeding, galactagogue plants, Traditional Persian Medicine

Introduction

Breastfeeding is considered the optimal infant feeding method. The World Health Organization (WHO) recommends that infants should be exclusively breastfed for 6 months, and breastfeeding should be continued in addition to complementary feeding up to 2 years.[1,2] The beneficial effects of breastfeeding for the infant and mother are well recognized.[2] Breastfeeding can be associated with better nutritional and non-nutritional outcomes in comparison with formula feeding.[3] The nutritional needs of infants aged 0–6 months can be acquired through breast milk.[4] Breast milk improves cognitive abilities, enhances neurological development, intelligence, and immunity, and reduces the incidence of allergic/hypersensitivity diseases, sudden infant death syndrome, obesity during adulthood, and development of type 1 and type 2 diabetes mellitus.[5–10]

The most common cause of breastfeeding failure is insufficient production of breast milk. Breast milk reduction can occur in many circumstances, such as illness of the mother or the child, mother–baby separation, preterm birth, anxiety, fatigue, and emotional stress. Although milk production can be increased by relaxation techniques and psychological support, many mothers tend to use medications or other products to increase their lactation. Galactagogue medicines, such as metoclopramide, oxytocin, domperidone, chlorpromazine, and sulpiride, are among the current therapeutic strategies in healthy mothers. However, these medications may cause adverse effects, such as extrapyramidal symptoms, arrhythmia, and iatrogenic hyperthyroidism in mother or infant.[3]

There is a long history of application of natural products to increase milk production.[3] Although many studies have been conducted to investigate the galactogogue effects of medicinal plants, no scientific study has focused specifically on the instructions in Traditional Persian Medicine (TPM) for increasing the production of breast milk. The aim of this study is to review medicinal plants recommended by TPM for increasing breast milk and to search for modern pharmacological evidence supporting the traditional use of these plants.

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Materials and Methods

In this review, we used a two-step search. The first search aimed at exploring major TPM textbooks to find physiology and etiology of insufficient lactation and medicinal plants recommended for enhancing milk production.

Among the most important TPM texts used in this review were *Al-Hawi fi al-tibb* (The Liber Continents) by Rhazes (865–925 A.D.), *Kamel-al-Sanaat al-Tibbiah* (The Perfect Art of Medicine) by Majusi Ahwazi (Haly Abbas; 930–994 A.D.), *Al-Qanun fi'l-Tibb* (The Canon of Medicine) by Avicenna (980–1037 A.D.), *Zakhireh Kharazmshahi* by Jorjani (1042–1136 A.D.), and *Makhzan-Al-Advie* by Aghili Khorasani (18th century).

The second search was conducted using electronic databases, including PubMed, Scopus, Google Scholar, Science Direct, and Web of Science (from 1960 to 2016) to find the relevant pharmacological activities supporting the effectiveness of TPM-recommended plants in increasing breast milk. The scientific names or common names of these plants and the keywords—milk production or breastfeeding or lactagogue plants or milk increasing or milk enhancing—were used in this search strategy.

Only studies in the Persian or English language were considered in this study.

Results

Physiology of lactation

Lactogenesis (milk production) is a complex neurophysiological process that involves the interaction of multiple physical and emotional factors along with the action of a number of hormones, mainly prolactin.[11] Prolactin is secreted by the anterior pituitary gland in response to nipple stimulation. It is under inhibitory control from the hypothalamus, which is mediated by dopamine.[12] Dopamine, therefore, has inhibitory effects on prolactin secretion.[13] Some experiments showed that chronic estrogen treatment similarly inhibited the dopamine receptor agonist.[14]

During midpregnancy, a rise in mRNA for milk proteins and enzymes involved in milk formation and secretion occurs. At this stage, estrogen, progesterone, prolactin, growth hormone, and human placental lactogen (HPL) synergize to stimulate mammogenesis.[15] This secretory differentiation stage is classified as lactogenesis I. At birth, the expulsion of the placenta results in a sudden decrease in progesterone, estrogen, and HPL levels, which consequently causes lactogenesis II in the presence of high prolactin levels. Glucocorticoids also support lactogenesis. Other hormones, such as insulin and thyroxin, are also involved in lactogenesis, but their roles are poorly understood. When the milk supply is securely established, autocrine (local) control begins. In this phase, which is termed ''galactopoiesis'' or ''lactogenesis III,'' milk removal is the primary control mechanism for milk production.[16] The lactation process can induce the release of prolactin, glucocorticoids, and oxytocin into the blood.[15] It is established that oxytocin, opioids, serotonin, substance P, histamine, and arginine-leucine, which modulate prolactin, are released through an autocrine/paracrine mechanism, whereas estrogen and progesterone are involved in hypothalamic and adenohypophysial levels. Follicle stimulating hormone (FSH), human chorionic gonadotropin, and luteinizing hormone (LH) are also involved in lactogenesis through the control of estrogen and progesterone, prolactin, and growth hormone production. Oxytocin mainly acts as a powerful galactokinetic hormone by inducing contractions in the smooth muscle layer surrounding the alveoli.[17]

TPM description and physiology of lactation

TPM is a comprehensive system of medicine, with a history of >2,000 years in the diagnosis and management of different illnesses. TPM is based on the concept of humors and temperament.[18,19] *Mezaj* (temperament)—which means the dominant quality of the composite object—results from the interactions between four elements, each of which have specific qualities: fire is hot and dry, air is hot and moist, water is cold and moist, and soil is cold and dry.[20]

According to TPM, distemperament (Su'e Mezaj) results from imbalances in a healthy temperament and may lead to organ dysfunction and disease. Humor is a fluid originating from the disposition of food in the stomach toward the liver and blood vessels. There are four natural humors in the body, and each of these is related to pairs of qualities: blood (*dam*) is hot and wet, yellow bile (*safra*) is hot and dry, phlegm (*balgham*) is cold and wet, and black bile (*sauda*) is cold and dry.[20]

In his book *Zakhireh Kharazmshahi*, Jorjani states that normal blood is the source of breast milk production. He believes that the blood, semen, and milk have the same source in the body, so medications with the ability to increase the quantity or quality of blood and semen can also increase milk production.[21]

Avicenna believes that breast milk insufficiency has three main etiologies. First, lack of proper nutrients may result in a decline in the quantity or quality of milk. Second, a decrease in the blood volume as a result of bleeding, for example, postpartum hemorrhage, can cause a decrease in milk volume. Lastly, any change in the breast or body temperament may lead to changes in milk quality or quantity.[22]

According to Rhazes, any food or plant that produces moderately hot and wet quality can be effective in the treatment of a decrease in breast milk. He assumes that the consumption of plants with dry and cold (e.g., *Rhus coriaria*) or excessive hot temperament (e.g., *Ruta graveolens*) can occasionally worsen the problem.[23]

Medicinal plants used to enhance lactation in TPM

Ten plants from six families have been recommended by TPM to enhance lactation.[21–25] Traditional information on these plants is given in Table 1.

Pharmacological activities of plants recommended in TPM

Lactation-enhancing effects of medicinal plants recommended in TPM have been studied by a large number of animal investigations as well as some clinical trials (Tables 2 and 3).

Foeniculum vulgare Mill. Fennel is a popular medicinal plant with various pharmacological activities mentioned in TPM and modern phytotherapy.[28] According to TPM scholars, all parts of this plant are used as a galactagogue and diuretic.[25,28] Pharmacological investigations support the galactagogue activity of fennel. Hydroalcoholic extract of fennel fruits could significantly increase the serum levels of prolactin,

TABLE 1. MEDICINAL PLANTS USED FOR THE ENHANCEMENT OF LACTATION

Scientific name[26]	*Common name*	*Arabic TPM name*	*Family*	*Parts used*	*Administration route*	*References*
Foeniculum vulgare Mill.	Fennel	Razianaj	Apiaceae	Seeds/leaves/root	Oral	21–25,27
Anethum graveolens L.	Dill	Shebet	Apiaceae	Seed/leaves	Oral	21–24
Pimpinella anisum L.	Anise	Razianaj roomi/Badian	Apiaceae	Seed	Oral	22,23,25
Nigella sativa L.	Blackcumin	Shoniz	Ranunculacea	Seed	Oral	23,25
Medicago sativa L.	Alfalfa	Ratbeh	Fabaceae	Seed	Oral	25
Vitex agnus-castus L.	Chaste tree	Aslagh	Verbenaceae	Fruit	Oral	22,23,25
Malva sylvestris L.	Marshmallow	Khobbazi	Malvaceae	Flowers/leaves	Oral	21,22,25
Trigonella foenum-graecum L.	Fenugreek	Holbeh	Fabaceae	Leaves/seed	Oral	21,23
Cicer arietinum L.	Chickpea	Hemmas	Fabaceae	Seed	Oral	21,23,27
Hordeum vulgare L.	Barley	Shaeer	Poaceae	Aqueous extract	Oral	21–23

TPN, Traditional Persian Medicine.

estrogen, and progesterone in mice.[29] In addition, fennel can increase the growth and development of mammary glands in virgin rats, increase the secretory substances in pregnant rats, and increase the secretion of milk in lactating rats.[30] Fennel extract was also found to increase nucleic acids and protein concentration as well as weights of oviductal and mammary glands.[31] In a randomized clinical trial (RCT) performed on 78 girl infants who were exclusively breastfed, nursing mothers received a herbal tea containing 3 g black tea in addition to 7.5 g fennel seed powder (intervention group) or only 3 g black tea (control group) three times a day for 4 weeks. Fennel significantly increased the signs of breast milk sufficiency in infants, including weight, head circumference, the number of wet diapers, the frequency of defecation times, and the number of breastfeeding times ($p < 0.001$).[32] Anethole, the main constituent of fennel, bears strong structural resemblance to dopamine. It has been established that the secretion of the milk-producing hormone prolactin could be inhibited by dopamine. Therefore, anethole may influence milk secretion by competing with dopamine at the receptor sites, thereby blocking the inhibitory effects of dopamine on prolactin secretion.[13] It has been reported that polymers of anethole, such as dianethole and photoanethole, are active agents responsible for the galactogenic activity of fennel.[33,34] However, the results of a case study revealed that premature thelarche (the onset of female breast development) was observed in four girls between 5 months and 5 years old given *F. vulgare* tea two to three times a day to alleviate abdominal pain and discomfort. The serum estradiol levels of all four patients were 15 to 20 times higher than the normal values for their age. Premature thelarche disappeared and hormone levels decreased to the normal range 3–6 months after stopping the intake of *F. vulgare* tea.[35]

Anethum graveolens L. Dill is a well-known vegetable and has been widely used as a galactogogue in TPM.[25] Pharmacological research investigating the galactogogue activity of dill is scarce. However, in an unpublished investigation, dill alcoholic extract could slightly increase the mammary gland weight in lactating rats. Moreover, it significantly increased litter weight gain and litter stomach weight.[36] Dill seed infusion could increase human uterus contractions in the active phase of labor, suggesting oxytocic-like activity.[37] Taking into consideration the important role of oxytocin in the lactation process, mimicking oxytocin activity would be a possible mechanism for the galactogogue effects of dill. It is noteworthy that linoleic acid, a polyunsaturated omega-6 fatty acid found abundantly in dill, and some of its metabolites such as gamma-linolenic acid and conjugated linoleic acid are important components of breast milk.[38–40]

Pimpinella anisum L. Anise is an annual plant with white flowers and small seeds, which is cultivated in Iraq, Turkey, Iran, India, and Egypt.[41] Some of its therapeutic activities, including digestive, anticonvulsant, antiasthma, diuretic, and galactogogue effects, have been considered in TPM texts.[25] Anise essential oil is known to enhance breast milk quantity, facilitating milk secretion and being a diuretic.[42] Hosseinzadeh et al. reported that aqueous (1 g/kg) and ethanolic (1 g/kg) extracts of anise could significantly increase milk production (68.1% and 81% more than the control group) in rats. They also reported that pups gained weight during the study period.[41] Anise seeds contain anethole, which is a weak estrogenic agent. It also acts as a dopamine receptor antagonist, thereby acting through increasing prolactin secretion.[43]

Nigella sativa L. This herb is commonly called "black cumin" in the West. Black cumin is an annual plant found in various countries bordering the Mediterranean Sea, Pakistan, India, and Iran.[44] Black cumin seeds have long been used in TPM to treat asthma, cough, bronchitis, headache, rheumatism, influenza, and as a diuretic and galactagogue.[25] In an animal study, aqueous (0.5 g/kg) and ethanolic (1 g/kg) extracts of black cumin significantly increased milk production, producing about 31.3% and 37.6%, respectively, more milk than control, in rats.[44]

Vitex agnus-castus L. *Vitex agnus-castus* is a medicinal plant that has been used in TPM to increase lactation and decrease libido in men.[25] Controversially, in some TPM textbooks, chaste-berry has also been recommended to increase sexual desire in women and suppress lactation.[23] Interestingly, evidence on the effects of chaste-berry on the levels of hormones involved in lactation is also controversial.[45] However, the results of a placebo-controlled clinical study of prolactin secretion in 20 healthy men during a period of 14 days suggest that effects of the chaste-berry extract on prolactin levels are dependent on the dose administered and the initial level of prolactin concentration. At low doses, as have been used in TPM and other traditional medicines,

Table 2. In Vitro and Animal Studies on Milk-Enhancing Plants Reported from Traditional Persian Medicine

Plant	Recommended dosage	Study design	Extract	Findings	References
Foeniculum vulgare Mill.	A total of 200 mg/g for 5 days, intraperitoneally	In vivo/mice	Seed/ethanol extract	Significant increase in serum prolactin levels 2.27 ± 0.85 ng/mL compared with control group 1.36 ± 0.51 ng/mL	29
	Fennel plant 5% and 10% of the daily food for a period of 10 and 20 days in rats	In vivo/mammary glands and oviducts in rats	Seed	Increase the growth of the mammary glands in virgin rats, the composition of milk in pregnant rats, and the secretion of milk in lactating rats	30
	Different dose levels (50, 150 and 250 μg/100 g body wt.)	In vivo/mammary glands and oviducts in rats	Acetone extracts of seed	Increase nucleic acids and protein concentration as well as the organ weights in both the tissues especially more effective with medium and high doses..	31
Anethum graveolens L.	0.017 mg of alcoholic extract of dill from 15th day of gestation till 11th day of lactation	In vivo/mammary glands in rats	Seed/alcoholic extract	Increase in mammary gland weight, litter weight gain, and litter stomach weight in lactating rats	36
Pimpinella anisum L.	One gram per kilogram of aqueous and ethanolic intraperitoneally	In vivo/rat pups	Seed/aqueous and ethanolic extracts	Increasing milk production in rats weight gain in rat pups	41
Nigella sativa L.	0.5 g/kg of aqueous and 1 g/kg of ethanolic extract intraperitoneally	In vivo/rat pups	Seed/aqueous and ethanolic extracts	Increasing milk production in rats weight gain in pups	44
Vitex agnus-castus L.	Extracting 100 g ground *V. agnus-castus* with ethanol 70%	In vitro	Seed/aqueous ethanol 70% (v/v) extract	A fractionation of chaste-berry extract resulted in the isolation of dopaminergic bicyclic diterpenes, which could inhibit cyclic adenosine monophosphate formation and prolactin release in rat pituitary cell cultures	45
Malva sylvestris L.	A total of 50 to 300 μg/mL of β-glucan for a time period of 24 or 48 hours.	In vitro	GH3/B6 cells	Twenty-four hours incubation of GH3/B6 cells in the presence of 50, 100, 200, and 300 μg/mL of β-glucan increase prolactin secretion in comparison with control. Forty-eight hours incubation of GH3/B6 cells in the presence of 100, 300, and 200 μg/mL of β-glucan increase prolactin secretion in comparison with the control.	51

(*continued*)

Table 2. (Continued)

Plant	*Recommended dosage*	*Study design*	*Extract*	*Findings*	*References*
Medicago sativa L.	A total of 60 mL of extract from *Carum carvi, Trigonella foenum-graecum and M. sativa* twice a day (morning and night) for 8 weeks	In vivo/cows	Extract from *C. carvi, T. foenum-graecum,* and *M. sativa*	Increase of daily milk, prolactin, and insulin levels of control cows had a 20–40%, 12–25.2%, and 3–17% increase, respectively, in comparison with those of placebo	71
T. foenum-graecum L.	A total of 20 to 320 μg/mL	In vitro/MCF-7 cells	Chloroform extracts of fenugreek seeds	Fenugreek seeds stimulated the proliferation of MCF-7 cells, and by binding to ER acted as an agonist for ER	53
	Two doses of genistein, 1 and 10 μg/100 μL/hour intracerebroventricularly from 12.00 to 16.00 hours	In vitro		Plasma prolactin concentrations during and after genistein infusion were also significantly higher than the control	54
Cicer arietinum L.	Intragastric gavage three different doses (20, 50, or 100 mg/kg/day) for 5 weeks.	In vivo/rats	Isoflavones extracted from chickpea sprouts	Estrogenic activities in ovariectomized rats	57
	Chickpeas in the concentrate mixture 100–0, 50–120, and 0–240 kg/ton for 12 weeks in three group	In vivo/Chios ewes	Chickpeas meal	No differences in average milk yield, or milk composition in Chios ewes/no affect in growing lambs	72
	Chickpeas at 0%, 50%, and 100% of concentrate dry matter from week 4 to week 16 postpartum for lactating Holstein cows	In vivo/cows	Dry chickpeas as a dietary supplement	Higher milk yield for cows fed 100% chickpeas than 0% chickpeas as dietary supplement	73
Hordeum vulgare L.	A total of 50 and 500 μg/mL of barley leaf extract	In vitro	Green barley leaf extract	An analogue of α-tocopherol or vitamin E namely α-tocopherol succinate in green barley leaf extract enhancing the release of growth hormone and/or prolactin from rat anterior pituitary cells	62

ER, estrogen receptor; MCF-7, human mammary cancer.

TABLE 3. CLINICAL STUDIES ON MILK-ENHANCING PLANTS REPORTED FROM TRADITIONAL PERSIAN MEDICINE

Plant	*Recommended dosage*	*Study design*	*Extract*	*Findings*	*References*
Foeniculum vulgare Mill.	Herbal tea containing 7.5 g fennel seed powder in addition to 3 g of black tea, three times a day	Double-blind randomized clinical trial with control group	Seed/herbal tea	Improving breast milk sufficiency signs	32
Anethum graveolens L.	One tablespoon whole dill seed seeped in a half or whole cup boiling water for 3–4 minutes	Historical cohort study	Seed/boiling	More contractions in the case group significantly than the control group	37
Vitex agnus-castus L.	Three doses (120, 240, and 480 mg/day) of a special *V. agnus-castus* extract (BP1095E1) during a period of 14 days	Placebo-controlled clinical	Ripe, dried fruits/alcohol, and water-free extract	A significant increase in the 24-hour prolactin secretion profile with 120 mg dose in comparison with placebo and a significant reduction with the 480 mg dose	46
Hordeum vulgare L.	One liter of commercial beer (6% alcohol)	Clinical trial	Beer	Increase in serum prolactin after beer consumption/not significant increase in serum prolactin after both sparkling water and alcohol solution consumption	59
	A total of 800 mL of beer (4.5% ethanol) and 800 mL of nonalcoholic beer	Clinical study	Beer	Increase in prolactin levels significantly in men and women/increase in prolactin level in subject receiving a nonalcoholic beer/salsolinol having no significant role in prolactin secretion	61
	A total of 660 mL of nonalcoholic beer	Prospective trial	Beer	Increase in antioxidant capacity and coenzyme Q_{10} content in the breast milk of the study group compared with the control group	65

chaste-berry inhibits activation of dopamine 2 receptor by competitive binding, causing a slight increase in the release of prolactin. Conversely, in higher concentrations, the binding activity is sufficient to reduce the release of prolactin.[46] In a randomized double-blind study, the daily dose of 20 mg *V. agnus-castus* did not cause any adverse effects in women with luteal phase defects.[47] In addition, no serious adverse event was observed after receiving two capsules per day containing 3.5–4.2 mg dried extract of *V. agnus-castus* fruit in women with premenstrual tension syndrome over a period of three treatment cycles.[48] However, nausea and headache were observed after receiving 20–40 mg/day *V. agnus-castus* for 2 months for the treatment of premenstrual dysphoric disorder.[49] In addition, case reports have documented ovarian hyperstimulation after the ingestion of *V. agnus-castus*.[50]

Malva sylvestris L. Marshmallow is a medicinal plant used orally as an expectorant and emollient in the treatment of common cold and topically to cure inflammation, abscesses, and breast engorgement. It is, moreover, prescribed to increase milk flow during breastfeeding.[25] Specific published data that support the use of this plant for the promotion of lactation are lacking. However, marshmallow mucilage contains high amounts of polysaccharides. A number of studies reported the ability of some polysaccharides to increase prolactin secretion.[51] Therefore, further studies may lead to a better understanding of the galactogogue effects of marshmallow polysaccharides and its other bioactive compounds.

Medicago sativa L. Alfalfa is a perennial flowering plant cultivated as an important forage crop in many countries around the world. It is used to increase sexual function and semen quantity, produce high-quality blood, and enhance lactation.[22,25]

Trigonella foenum-graecum L.. Fenugreek is an annual plant that is cultivated worldwide. Its seeds are used as a popular medication and a common ingredient in dishes in many cultures. In TPM, fenugreek is used to increase milk production, treat impotency, coughs, bronchitis and asthma, colitis, and inflammation.[21,23,25] In an RCT on 66 mother–infant pairs, the effects of maternal consumption of herbal tea containing fenugreek on breast milk production and infants' weight gain pattern were evaluated. The results showed that the loss of birth weight and the time of regain of birth weight were significantly lower in infants in the intervention group (fenugreek tea) than in placebo (apple tea) and control (without any recommendations except routine counseling) groups. Moreover, the amount of breast milk in mothers who received fenugreek tea was significantly higher than placebo and control groups ($p < 0.05$).[52] Chloroform extract of fenugreek seeds could stimulate the proliferation of human mammary cancer (MCF-7) cells, bind to estrogen receptor ($IC_{50} = 185.6 \pm 32.8$ μg/mL), and act as an agonist for estrogen receptor-mediated transcription through estrogen response elements. Fenugreek also induced the expression of estrogen responsive gene pS2 (a marker for assessing the estrogenicity of various compounds) in MCF-7 cells.[53] Moreover, as some phytoestrogens have been shown to modulate LH and prolactin secretion, fenugreek phytoestrogens may be involved in its galactagogue effects.[54] The average recommended daily dose of *Trigonella foenum-graecum* for internal use is 6 g of cut or crushed seeds, or equivalent of preparations, including consumption of several cups a day of

T. foenum-graecum infusion (0.5 g of cut seed macerated in 150 mL cold water for 3 hours); 6 mL of fluid extract (1:1 g/mL) and 30 mL of *T. foenum-graecum* tincture (1:5 g/mL).[55] But safety in adults does not guarantee safety in infants.

Cicer arietinum L.. Chickpea is one of the oldest consumed legumes, grown all over the world, particularly in the Afro-Asian countries.[56] In TPM, it is considered the best edible bean, inducing weight gain and appetite. It has been traditionally prescribed in cancer, liver, kidney, and lung diseases, and can boost libido and enhance milk production.[27]

Oral administration of isoflavones extracted from chickpea sprouts has significant estrogenic effects in ovariectomized rats, as evidenced by increasing uterine weight, restoring the uterine structure, and circulating 17β-estradiol, FSH, and LH levels.[57]

Hordeum vulgare L. Barley is the major cereal crop after wheat, maize, and rice in the world.[58] Barley is widely used as a source of beer production and as a component of various health foods. In TPM, a drink named maolshaeer (nonalcoholic beer) is prescribed to produce high-quality blood and to treat many diseases such as liver and respiratory problems, diarrhea, scurvy, nephritis, bladder inflammation, and gout. In a clinical study, consuming equal amounts of beer and ethanol in normal women showed significant increases in serum prolactin (from 11.6 to 27.1 ng/mL) within 30 minutes of drinking 1 L of 6% ethanol-containing beer. Interestingly, no significant change after drinking 6% ethanol solution or sparkling water was observed.[59] In another study, Carlson et al. gave 800 mL of beer that contained 4.5% ethanol to five men and seven women and an equal amount of nonalcoholic beer to one woman. The prolactin levels significantly increased in all men and women. The subject receiving nonalcoholic beer showed a similar response. Pretreatment of the studied women with naloxone had no effect on prolactin response. These results suggest that phytochemicals other than alcohol are responsible for the prolactin-increasing effects of beer.[60,61] Badamchian et al. reported that green barley leaf extract contains an analogue of α-tocopherol or vitamin E—namely, α-tocopherol succinate—which has the ability to enhance the release of growth hormone and/or prolactin from rat anterior pituitary cells in vitro.[62] Tocotrienols and tocopherols are also present in barley seeds and are possibly responsible for its galactogogue effects.[63] Sitosterol, a phytoestrogen isolated from barley seeds, has also been shown to increase spontaneous uterine contractions in rats, suggesting the presence of oxytocic activities.[64] β-glucan—a polysaccharide naturally occurring in the cell walls of barley—has been found to significantly increase prolactin secretion in GH3/B6 cells, which are known to secret prolactin and growth hormone.[51] In a prospective trial in mother–infant dyads, the effects of supplementing the diet of breastfeeding mothers with nonalcoholic beer (maolshaeer in TPM) on oxidative status and antioxidant content of their milk were evaluated. The results indicate an increase in antioxidant capacity and coenzyme Q_{10} content in the breast milk of the study group compared with the control group. Moreover, a positive effect of nonalcoholic beer supplementation on oxidative status of the mothers' plasma was also observed.[65]

Discussion

In this study, we explored the most useful galactagogue plants recommended by TPM. Some of these plants, such as anise, black cumin, dill, chaste-berry and marshmallow, are also traditionally used as diaphoretic agents.[23,66] Prolactin is a peptide hormone synthesized by the anterior pituitary gland. It is secreted into the blood after stimulus on the maternal nipple by sucking.

Galactagogues may act by increasing the production and release of prolactin by direct stimulation of the adenohypophysis. Some galactagogues act either by inhibiting dopamine-producing neurons or by blocking hypothalamic dopaminergic receptors.[3] Chemical components of some plants may act as a lactogenic in ingestion or oral administration. These components can be divided into two categories: pectins and β-glucans. Interestingly, these fragments of pectins and of β-glucans are well-known natural agents with hormonal activity in plants. So, like their role in carrying information for plants, they may be messengers in animal cells.[67]

Plants introduced in TPM contain many chemical compounds, such as phytoestrogens, polysaccharides, flavonoids, tannins, alkaloids, and saponins. Pharmacological studies have shown that phytoestrogens may play a role in increasing the amount of prolactin.[54]

According to TPM, the most significant factor in milk production is the ability to produce high-quality blood. Therefore, proper nutrition plays an essential role in the process of milk production. Using nutritious plants such as chickpea and barley might increase milk production in this way along with other hormonal mechanisms. The oxytocin hormone—which is secreted from the posterior pituitary after sucking—leads to the secretion and ejection of milk. According to TPM, mental stress and tension can quickly affect the amount of milk secretion. It is established that stress and anxiety contribute to decreased milk production by suppressing oxytocin release.[66] Therefore, it is important to avoid maternal stress and negative emotions. As mentioned in the previous sections, according to TPM instructions, the dry temperament of the body and breasts can lead to a decrease in breast milk. Therefore, any factor inducing dryness—such as excessive fatigue, consumption of foods with dry nature and diuretic medications, intense exercise, and heavy massage—may decrease milk production.[22]

Multiple case reports, case series, and pharmacokinetic trials have recently highlighted the possible interactions between herbal medicines and prescribed medicines. Although many of the herb–drug interactions are devoid of serious clinical consequences, some of them may require extreme vigilance.[50] However, only a limited number of animal studies and clinical trials have addressed the herb–drug interactions. *V. agnus-castus* has been found to interact with prolactin synergistically.[68] *T. foenum-graecum* has also synergistic effects with antidiabetic agents and laxatives. It can increase anticoagulant and antiplatelet effects.[69] *Medicago sativa* may interact with anticoagulant drugs.[70] Therefore, future studies on the herb–drug interactions seem to be required to a great extent.

Conclusion

In light of the long historical usage of the mentioned plants as galactagogue agents and their documented pharmacological activities and lack of serious adverse effects, some of these herbs (especially fenugreek) are widely used as galactogogues. Furthermore, additional pharmacological and clinical studies will open new avenues toward the understanding of the exact mechanisms through which these plants and their ingredients act.

Disclosure Statement

No competing financial interests exist.

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