ISSN: 2347-467X, Vol. 11, No. (2) 2023, Pg. 589-604

Current Research in Nutrition and Food Science

www.foodandnutritionjournal.org

Ethnopharmacology of Botanical Galactagogues and Comprehensive Analysis of Gaps Between Traditional and Scientific Evidence

MONIKA THAKUR[1]*, RENU KHEDKAR[1], KARUNA SINGH[2] and VATSALA SHARMA[1]

[1]Amity Institute of Food Technology, Amity University Uttar Pradesh, Noida, Uttar Pradesh– 201303, India.
[2]Sharda University, Department of Allied Health Sciences, Greater Noida.

Abstract

The functional potential of plants and plant-based components have been used in different cultures since time immemorial to promote milk production in women. Conditions like agalactia or insufficient production of breast milk due to various barriers intended to be a greater risk of weight loss for neonates and prompting for supplementation of infant formula. Multiple plants are traditionally used worldwide as galactagogues during the lactation period. This study aims to extract information on traditionally used galactagogue plants and compare their ethnopharmacological evidence with scientific evidence. This will help to understand the gaps in the ethnopharmacological and scientific data and thus provide future research information. Information on traditional and scientific studies was collected and analyzed on galactagogues. The ethnopharmacological data of the focused plant species were analyzed for part used, formulations, and region of its uses. All cultures traditionally used natural products as galactagogue from times immemorial, and due to scientific advances, these have also been seen as commercial products. However, because of the limited studies, it is of interest to standardize the doses, and composition of bioactive components and study the mechanism of action, its side effects, and interaction with food. This is a forward-looking research area that could be projected for manufacturing herbal formulations for lactating mothers.

Article History
Received: 23 November 2022
Accepted: 31 March 2023

Keywords
Bioactive Components; Ethnopharmacology; Galactagogues; Herbal Formulation; Lactation.

Introduction

Breast milk provides optimum nutrition and immunity with lifelong health benefits to mother and child. However, lactating women face significant barriers during lactation, especially in low-economic settings, impacting social, psychological, and physiological

CONTACT Monika Thakur mthakur1@amity.edu Amity Institute of Food Technology, Amity University Uttar Pradesh, Noida, Uttar Pradesh– 201303, India.

Doi: http://dx.doi.org/10.12944/CRNFSJ.11.2.11

health. Remitting childbearing practice, higher caesarean section delivery rates, stressful labor lasting more than an hour, and excess body fat and other complications can exaggerate physiological barriers to setting up lactation. In addition to the causes of agalactia or hypokalaemia, mammary hypoplasia and excess intake of analgesics during labor are also responsible for low lactation. Furthermore, a history of alcohol consumption and obesity can also inhibit the response of prolactin necessary for the production of milk immediately after postpartum. Delayed onset of milk production leads to early discontinuation of breastfeeding, and thereby newborn is at greater risk of excess neonatal weight loss and prompting for supplementation of infant formula.[1]

Galactagogues are generally derived from plants or are synthetic, which stimulates, maintains, and increases breast milk production. Galactagogues interact with lactation-stimulating hormones, such as Prolactin (PRL) and activate them, increasing milk production. However, medroxyprogesterone, somatotropin, progesterone, cortisol, leptin and insulin, oxytocin, thyrotropin-releasing hormone (TRH), and recombinant bovine somatotropin (rBST) also play a significant role as a galactagogue. Galactagogues are taken into account to produce sufficient milk by typically increasing prolactin levels in the female body, thereby initiating the let-down reflex and aiding the ejection of breast milk. These may act by one or more mechanisms, including dopamine antagonists (domperidone and metoclopramide), antipsychotics (chlorpromazine, reserpine, sulpiride, trifluoperazine, and thioridazine), increasing the level of hormones - oxytocin, prolactin, and others. The most commonly used synthetic galactagogues available in the market are sulpiride, metoclopramide, domperidone, and chlorpromazine, which exerted prolonged adverse effects on the health of the lactating women.[2] Traditionally, plants have been used as natural galactogogues worldwide and reported in the literature as well. Few have been listed as - asparagus, barley, basil leaves & seeds, beets, borage, caraway, vegetables like carrots, cherries, chickpeas, coconut, coriander seeds, cumin, dandelion, dill, fennel, fenugreek, flax seeds, garlic, ginger, alfalfa, almonds, star-anise, green beans, hibiscus, hops, lemon balm, lentils, lettuce, malunggay (Moringa), marshmallow root, millets, molasses (black strap), mushrooms, nettle, oat straw (oats), papaya, peas, pumpkin, quinoa seeds, red raspberry, rice, sage, seaweed soup, sesame seeds, spinach, sunflower seeds, sweet potatoes, thistles, turmeric, and vervain and many more.[3]

Ethnomedicinally, these plants have been used to provide a natural ability to support lactation. Various tribes, cultural practices, and regions are known to use these plants. Also, many of them are scientifically investigated for determining the active constituent, pharmacological activity, and mechanism for supplying lactation. Moreover, toxicity studies have been conducted to provide safety and better guidance for its use. Some reviews are available on galactagogue plants on their traditional and scientific evidence; however, these are primarily region-specific or are comprehensively not discussed.

Thus, the present review will provide comprehensive research on ethnomedicinally and scientific investigations on galactagogue plants and the role and mechanism of bioactive compounds in lactating mothers. Moreover, the review will highlight the gaps in traditional and scientific research/evidence, thus laying the stone for further research possibilities.

Methodology

The present systematic review complied with the recommendations specified in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[4] Online research databases platforms like PubMed and Google Scholar have been sued for searching various papers on keywords. The search was restricted to the studies published from 2006 to 2021 (i.e., the past 15 years) in the language English only.

The search strategy devised following the PRISMA guidelines involved a thorough review of the titles and abstracts, then review of the entire document articles. The screening of papers was grounded on the PICOS inclusion and exclusion criteria decided at the start of the study. The papers were screened from the online research database platforms by using the main keywords - "galactogogues" related to "lactation", "interaction", "agalactia", "botanical galactagogues", "supplementation reduced fractures", "supplementation for lactating women", and "breastfeeding".

The initial database search returned 558 articles (Figure 1), including 486 articles from PubMed and 72 articles from Google Scholar. Out of the total of 558 articles, we removed 82 articles that were found to be duplicated. The remaining 476 studies were further screened by reading titles and abstracts, and it yielded 16 articles for full-text review. Out of these 16, we further excluded 4 studies due to various reasons: insufficient data, editorial, and intervention not matching the inclusion criteria. Therefore, finally, 12 studies were selected for the qualitative analysis.

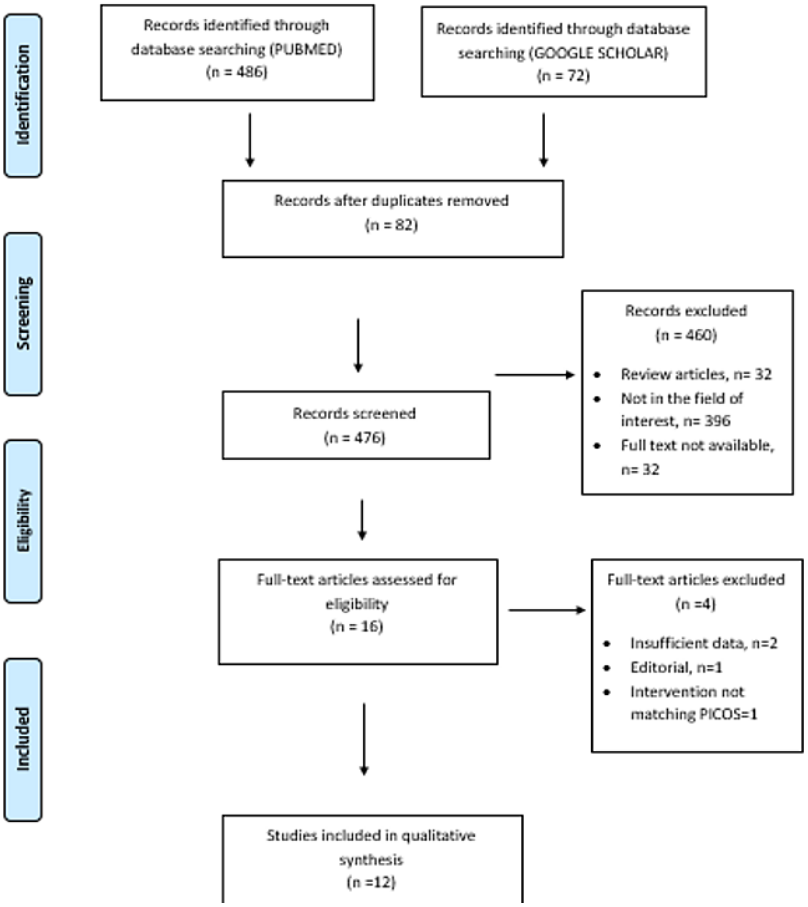


Fig. 1: Flowchart of selection the process for eligible studies

Plant-Based Galactogour: Traditional & Scientific Evidence

Galactagogues are the substances considered to support the commencement, continuance, or accretion of the rate of synthesis of human milk. It is a natural component of food or herb that has the quality to increase breast milk supply. Medicinal plants or herbs have always been advantageous during postpartum or during breastfeeding in conditions like IMS. Therefore, the usage of several ethnic-gynecological plants is significant in the primary maternity healthcare system. According to WHO, 3.5 billion people in developing countries, accounting for 80 % of the populace, depend on plant-based conventional medicines. In addition, for lactation, ethno-gynaecological uses of plants have been documented for various ethnic groups in India or other countries.

Most of the plants collected for the galactagogue recipes are fresh and from natural habitats as they have a more significant amount of bioactivity. Therefore, the most commonly used preparations are decoction or juice extract with a simple mode

of administration. Evaluating such galactagogue preparations for verifying the phytoconstituents and mechanism of action is crucial for the discovery and development of new products that are standardized and more productive. Also, incorporating traditional medicines or formulations into healthcare will facilitate culturally appropriate healthcare implementation, respecting indigenous knowledge.[5] The commonly used plants (Fig. 2 a & b) as galactagogues are discussed with both traditional and scientific evidence.

Amaranth

It belongs to the Amaranthaceae family, mainly grown in Russia, Kenya, China, India, Mexico, and Guatemala. *Amaranthus hypochondriacus* L., *A. cruentus*, and *A. caudatus* are commonly available varieties for safe human consumption. It is said to be drought resistant, high temperatures, and saline soils, and therefore it is also known as an "unfading flower".[6] Amaranthus is exceptionally nutritious, and both the grain and leaves of this plant are put to use for human and animal food. All the species are nutritious but slightly vary in chemical composition. It is manifested that the leaves of amaranth are a significant source of protein, providing approximately 17–32 % of protein from dry weight for diverse samples.[7] Another species of the Amaranth family is *A. spinosus* L., which exerts a non-synthesis galactagogic effect which increases the production of milk as it has a significant impact on prolactin levels. It contains alkaloids, amino acids, b-sitosterol, carotenoids, catechuic tannins, flavonoids, glycosides, linoleic acid, phenolic acids, saponins, steroids, stigmasterol and terpenoids. Steroids and polyphenols found in amaranth increase prolactin levels and stimulate milk from the alveoli of the mother's breast. Leaf extract of *A. pinosus* administered to the lactating mother for 14 days stimulates the amount of prolactin and elevates milk secretion. It could be said that the leaf concentrate exerted a potential galactagogues effect and thereby, postpartum women with the problem of agalactia can include amaranthus in their diet.[8]

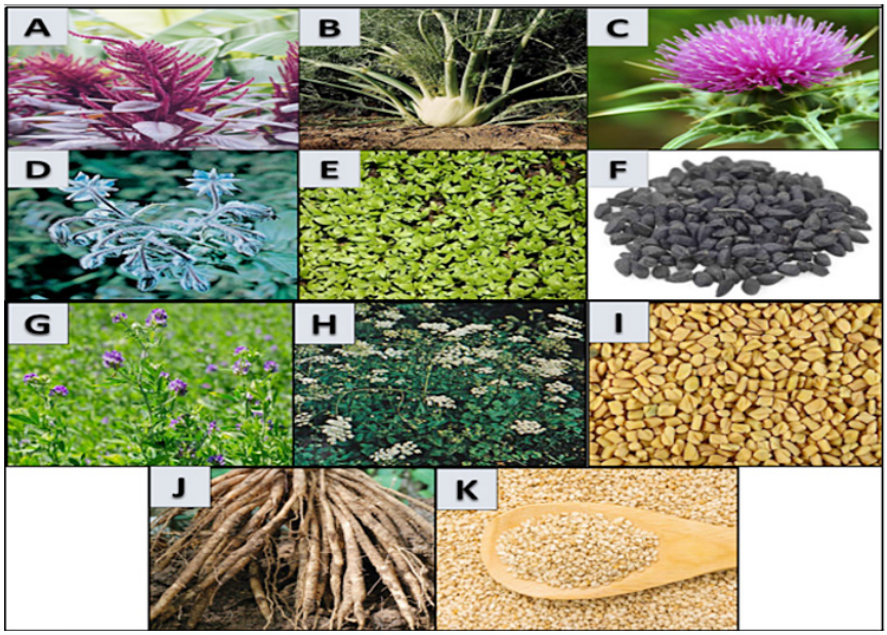
Fennel

Botanically known as *Foeniculum vulgare* Mill., belongs to the family of Apiaceae. There are three types of varieties available, namely, annual, biennial, and perennial. Fennel is grown on a macro scale in Argentina, France, Germany, India, Italy, Romania, Russia, and the USA. The main bioactive components of the essential oil extracted from fennel seeds are anethole (50-60 %) and fenchone (15-20 %). The extracted oil is chiefly comprised of (E)-anethole, (Z)-anethole, and α-thujone with proteins (14-22 %) and fat content (12-18 %). Different fatty acids are also present, i.e., linoleic, linolenic, oleic, palmitic, palmitoleic, stearic acid with flavonoids, iodine, barium, kaempferols, lithium, copper, manganese, umbelliferone, silicon, titanium, stigmasterol, and ascorbic acid. Indian fennel is rich in dietary fiber (28.7%), which showed beneficial properties for the digestive system.[9] It has other therapeutic properties such as anti-flatulent, anti-microbial, anti-spasmodic, anti-carcinogenic, muscle relaxant, stress relaxer, hepatoprotective, anti-dysmenorrheal, and anti-parasitic. Various studies showed that the consumption of 10 % of fennel seeds for 20 days helps stimulate the prolactin hormone to increase the secretion of breast milk. Prolactin plays a significant role in milk production during lactation, whereas oxytocin simultaneously causes contraction in the mammary glands to push milk toward milk ducts. The consumption of fennel seeds also acts as a dopamine antagonist, which stimulates prolactin secretion, thereby acting as a galactagogue.[10] In an animal study, two herbal products, namely P-I (fenugreek oil 400 mg, fennel oil 15 mg, and caraway oil 15 mg) and P-II (fenugreek seed powder 250 mg, caraway fruit powder 150 mg, fennel fruit powder 50 mg, and dill fruit powder 50 mg) were tested for its galactagogues effect in albino female rats with regular estrous cycle. It was found that both the herbal formulation increased the lactating hormonal levels (prolactin, estradiol, and progesterone), and P-II exerted significantly higher levels as compared to P-I.[11]

Milk Thistle

Botanically recognized as Silybum marianum Gaertn., is a part of the Asteraceae family and native to the Mediterranean, Europe, also commonly cultivated in Jammu & Kashmir, India. The plant is erect and stout with 1-3 m and a large purple flower, and distinct milky veins characterize its leaves. The bioactive components include flavonolignans-silybin, silydianin, and silychristin, together known as silymarin, similar to steroid hormones responsible for its protein synthesis facilitatory actions. The primary constituent of Silymarin is 60% of silybinin, primarily found in fruits and seeds. Milk thistle has

various medicinal properties like anti-oxidative, hepato-protective, positive effects on liver cirrhosis, anti-inflammatory, immune-modulatory, anti-virus activity, glycemic and lipidemic controller, anti-fibrotic, and anti-carcinogenic activity.[13] Milk thistle is traditionally used by lactating mothers to increase the secretion of breast milk. Various studies showed that the bioactive component, silymarin present in Silybum, increases the activity of the mammary gland and, therefore, the production of milk. Therefore, Silymarin increases prolactin levels on consumption during pregnancy and lactation. Studies suggested that silymarin does not have adverse allergic reactions and reported no toxicity and is considered safe; however, dosage as a galactagogue is unclear.[13] In an animal study, the milk thistle seed extract containing 70 % silymarin was tested for its galactagogues effect in rabbits during pregnancy and lactation. Different dosage of the extract as 3, 6, and 9 mL/Kg diet was tested and was found to increased prolactin level with increasing dose. It was found that the seed extract helps in milk production through increased hormonal levels.[14]



A- *Amaranthus spinosus* L. B- *Foeniculum vulagare* Mill. C- *Silybum marianum* Gaertn.
D- *Borago officinalis* L. E- *Lepidium sativum* L. F- *Nigella sativa* L.
G- *Medicago sativa* L. H- *Illicium verum* Hook f. I- *Trigonella foenum-graecum* L.
J- *Asparagus racemosus* Willd. K- *Sesamum indicum* L.

Fig. 2 a: Plant based galactagogues

Borage

Botanically known as *Borago officinalis* L. belongs to the plant family *Boraginaceae*, is a bushy herb that is cultivated once a year and is also recognized as 'Gaozaban' or 'Lisan al-Thawr' commonly in Pakistan. It consists of various phytochemicals such as tannins, flavonoids, resins, scopoletin, ascorbic acid, rosmarinic acid, beta carotene, caffeic acid, niacin, gentisic acid, riboflavin, p- hydroxybenzoic acid, thiamin, p- coumaric acid, silicic acid, vanillic acid, phenolic acid, choline arabinose, and unsaturated pyrrolizidines alkaloids.[15] Borage contains 30% of gum and parts green in color and consists of nitrate potassium, phosphoric acid, malate, resin, manganese, a small amount of essence, and allantoin. Stearidonic Acid (SDA), a precursor for prostaglandin synthesis, is also present in the leaves of Borage. Although animals

cannot synthesize SDA, it is essential to include it in the daily diet because it bears therapeutic properties and increases the quality of individuals' life.[16] In addition, it has other medicinal properties such as anti-inflammatory, anti-spasmodic, anti-oxidative, seborrheic dermatological properties, anti-nociceptive, galactagogic and anxiolytic. *B. officinalis* is also used as a galactagogue, mainly in rural areas, to ensure an abundant milk supply during agalactia. In addition, Borage may stimulate several cells of mammary glands. The action of this herb is similar to the stimulators which release the prolactin, corresponding to the mechanism of chlorpromazine, metoclopramide, and theophylline. In an animal study, 100mg/ kg body weight/ ml is considered effective and safe for its consumption as a galactagogue for female albino rats,[17] however human clinical trials need to be conducted for accurate information.

Garden-Cress Seeds

Botanically known as *Lepidium sativum* L., is a rapidly growing annual crop, mainly cultivated in Egypt and worldwide. It is locally known as 'Chandrashoor' and 'Halim'. The plant has an erect stature, with a height of about 15-45 cm. It can be pitted and reaped around the year; however, months like January, February, and November are the ideal months to sow. The seeds hold 22.5% protein, 27.5% fat, and 30% dietary fiber. It also consists of primary fatty acids like oleic, linolenic, palmitic, linoleic, erucic, stearic, and arachidic acids. The oil is rich in α and y- tocopherols and accommodates antioxidants like Vitamin A and D and eugenol, which prevents the oil's oxidation. This property also makes it a functional food. It has several bio-activities like anti-anemic properties, anti-oxidative, anti-histaminic, aphrodisiac, and tonic in various diseases like diarrhea, dysentery, asthma, and coughs. It is added to the diets of lactating women to augment breast milk production. 18 It contains generous amount of iron and protein and therefore induces milk secretion in lactating mothers. In addition, it interacts with dopamine receptors and results in increased levels of prolactin and thus augmenting the production of milk.[19] In an animal study, the result of the Garden-cress seeds on the maturing and growth of the mammary glands in female Rats during virgins, pregnancy, and lactating periods were investigated. In virgins, female rats, the treatment was found to increase the magnitude of lobules and alveoli, while in the pregnant female, it increases the furcating of vesicles. In lactating female rats, an increase in the magnitude of the alveoli and more furcated alveoli were recorded after treatment. Moreover, notable improvements in the levels of estrogen, progesterone and prolactin levels were recorded in all tested groups.[20]

Black Cumin

Botanically known as Nigella sativa L. and commonly known as Black cumin in English, Black caraway seeds in the USA, Shonaiz in Persian, and Kala Zeera in Bengal, is a yearly flowering plant that shoots up to 20–30 cm (7.9–11.8 inch) in height and has slender, narrow oval-shaped leaves with delicate flowers having 5-10 petals typically in various colors, like., pale purple, yellow, pink, pale blue, and white. Its fruit is large and looks like a swollen capsule constituting 3-7 united follicles, having several black-colored seeds of height 0.2 cm and width 0.1 cm, and a flat, oblong, angular, and funnel shape. Substantial studies on N. Sativa suggested that it comprises 32-40 % of fixed oil, which includes unsaturated fatty acids (i.e., arachidonic, sterol glucosides, sterol esters, eicosadienoic, oleic, linoleic, cycloeucalenol, beta-sitosterol, linolenic, palmitoleic, cycloartenol, palmitic acid) and 0.4-0.45 % volatile oil carries saturated fatty acids (i.e., nigellone, thymoquinone (TQ), thymoquinone, thymol, thymohydroquinone (THQ), carvacrol, α and β- pinene, d-limonene, d- citronellol, p cymene volatile oil). The seeds of black cumin also hold two distinct forms of alkaloids, namely, isoquinoline and pyrazole. N. sativa seeds nutritionally comprise proteins (which include 8-9 essential amino acids), vitamins, carbohydrates, mineral elements, and fats. The beneficial effects of black cumin seeds are because of the presence of TQ in abundance, which possesses anticonvulsant, anti-oxidative, anti-inflammatory, anti-cancerous, anti-bacterial, and anti-fungal properties.[21] It is one of the widely used galactagogue herbs which contains lipid elements with hormonal structures in which TQ participates effectively in the production of milk as it activates the prolactin. N. sativa is devoid of histological, hematological, and biochemical side effects, many previous studies record s and the safe consumption of the herb. However, there were cases of hypoglycemia and hypouricemic effects on black cumin consumption. 9 In an animal study, aqueous and ethanolic extract of N. sativa was provided to lactating rodents, significantly increasing milk

production and pup weight.[22] In another study, the Holland lactating cows were fed with black cumin and Curcuma species for three months. It was found that milk production significantly increased in the black cumin and Curcuma aeruginosa groups.[23]

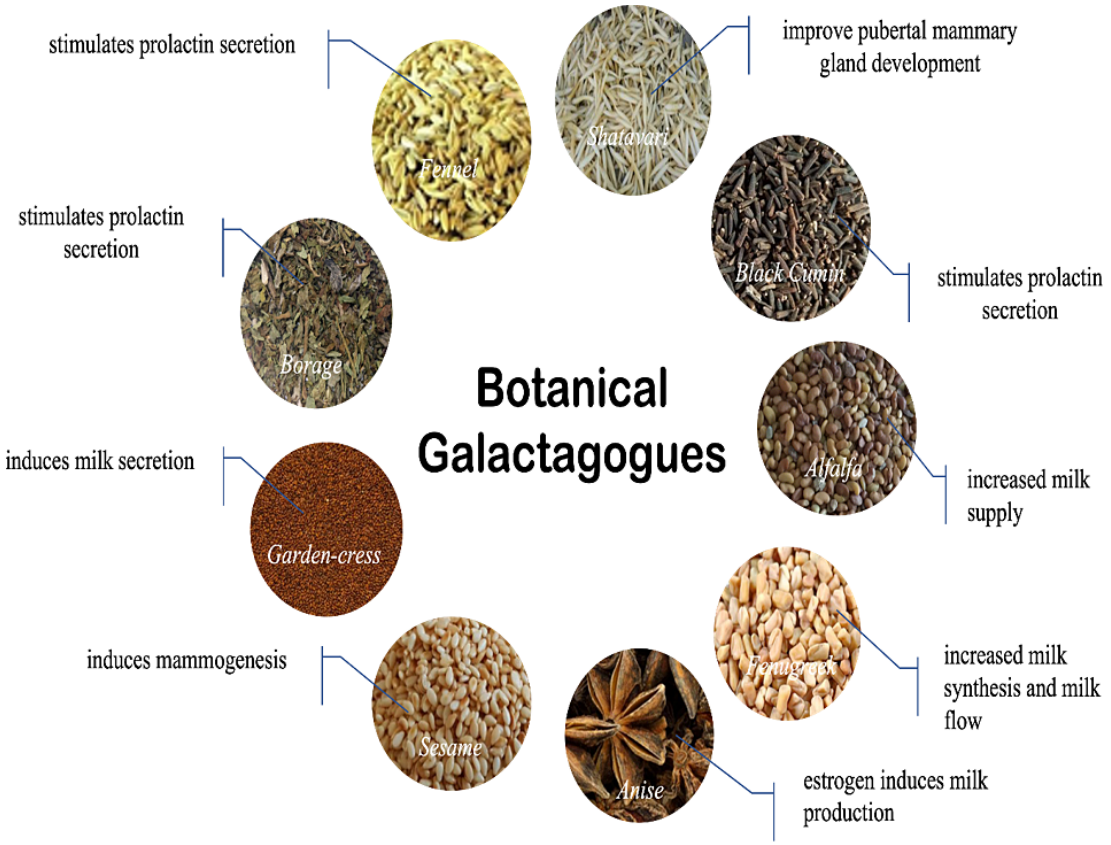


Fig. 2 b: Botanical Galactagogues with their functions

Alfalfa

Botanically known as *Medicago sativa* L., it is often known as 'Lucerne' or Alfalfa' belonging to the family Fabaceae which is largely found in the European region and the mountainous zone of Iran, Afghanistan, and neighboring localities. It is also known as "the queen of forages" since it is an inexpensive source of protein and contains a high amount of bioactive compounds in both aerial parts and roots of the plant. Alfalfa is also viewed as a functional food because of the limited amount of saturated fat, cholesterol, and sodium and the huge amount of different nutrients like folate. Bioactive components present in this plant are saponins (soyasapogenol, hederagenin) and phenolic components (gallic acid, caffeic acid, pyrogallol, and salicylic acid). The main flavonoids and isoflavonoids present in the leaves of Alfalfa are naringenin, daidzin, apigenin, myricetin, and querceitin. The leaves also contain β-carotene, vitamin K, and various other trace minerals, chromium, tin, molybdenum, selenium, manganese, and nickel. It provides multiple health benefits like improving arthritic conditions, and being helpful with asthma, hay fever, and many more.[24] As per the National Library of Medicine, US (2006), Alfalfa is a galactagogue, although no scientific clinical trial supports this. Some galactopoietic mixtures including alfalfa, are known to increase milk supply. Studies have shown saponins, estrogenic isoflavanoids (daidzein, genistein), vitamin K, and amino acid (L- canavanine) in the leaves and sprouts of Alfalfa where Daidzein and genistein are excreted in small amounts in breast milk. It is also certified as "Generally recognized as Safe" (GRAS) by, USFDA.

Anise

Botanically known as Illicium verum Hook. f. is an enduring average-sized tree that belongs to the plant family Illiciaceae. More than 42 species and 166 varieties belonging to the genus of Illicium are vegetated in the East and Southeast Asian tropical areas and mainly in China, Jamaica, Japan, Vietnam, Laos, Indonesia, and the Philippines. The most prevalent species of Illicium are Star aniseed (I. anisatum), star anise (I. verum), Japanese anise (I. anisatum), and Mexican anise (I. mexicanum), among which the most popularly known species is Star anise (I. verum) which can grow in different types of climatic and environmental conditions. It provides 359 kcal energy per 100g, proteins (2-4 g), carbohydrates (65-75 g), ascorbic acid, and vitamin A, also contains 4-6 g of fats with a good amount of dietary fiber and minerals like sodium, copper, magnesium, calcium, zinc, potassium, and iron. In addition, it contains 2.5-3.5 % and 8-9 % of essential oil present in fresh fruit and dried anise, respectively, resulting in the aromatic odor of Illicium verum. The volatile essential oil present in star anise comprises trans-anethole and shikimic acid (3,4,5- trihydroxy-1-cyclohexene-1-carboxylic acid), whereas other chemical compounds include palmitic acid, phenylpropanoids, lignans, sesquiterpenes, and flavonoids. Trans-anethole in I. verum has various health-beneficial properties like anticancer, anti-viral, antimicrobial, anti-inflammatory, antidiarrhoeal, anti-fungal, analgesic, sedative, and convulsive properties.[25] Star anise has significant estrogenic activity in rats study agrees with anti-estrogenic, progestational, and anti-progestational activities. Estrogen present in star anise stimulates the milk duct system to grow and increases breast milk production and the prolactin hormone level.[26]

Further studies are required to study the palatability and adequate level of anise as galactagogues.

Fenugreek

Botanically known as Trigonella foenum-graecum L., is a yearly plant that is associated with the Leguminosae family originating in India, Western Asia, Canada, and North Africa. It is commonly used for seasoning in Indian food. Traditionally, the pit and foliole of fenugreek have medicinal properties. The leaves of the fenugreek plant contain approximately 86% of moisture, 4 % protein, 1 % fat, and 1.5 % minerals like calcium, iron, zinc, phosphorus, and 6% of carbohydrates. Fenugreek seeds, popularly known for their bitter taste, contain 44 % of protein with 2 % of a chemical component named diosgenin. It also consists of several coumarin compounds and a few alkaloids like trigonelline, gentianine, and carpaine. Fenugreek also contains rhaponticin and isovitexin. It has various health-benefiting activities like lactonic, immunological, hypoglycemic, hypercholesterolemic, anti-bacterial, and anti-fungal. 27 It has been found that fenugreek stimulates the production of sweat and modifies sweat glands like the breast.

To test the efficacy of fenugreek as a galactagogue, animal studies have shown 16 % higher milk production and increased lactose concentration in breast milk.[28] In an animal study, pregnant Sprague-Dawley rats were fed with a fenugreek-supplemented (FEN) diet during lactation. It was found that the supplemented diet increases the gene expression of macronutrient synthesis, energy metabolism, and IGF-1 receptor in the Mammalia. In addition, pituitary oxytocin expression and plasma insulin concentration were also remarkably elevated. These results demonstrated that fenugreek stimulates the expression of genes involved in the production and milk flow.[28] In another study, fenugreek was tested in rodent models of lactation test to determine its influence on milk yield and to verify unfavorable results on dams and offspring metabolism. It was found that fenugreek augments milk synthesis by 16%, and an 11% growth in pup without deleterious effect on dam-litter metabolism was observed.[29] A polyherbal formulation containing a concentration of Sauropus androgynous (L.) Merr., Trigonella foenum-graceum L., and Moringa oleifera Lam were tested for their galactagogues effect on lactating Wistar rats. It was found that the polyherbal formulation significantly increased milk production of lactating rats by increasing the alveoli diameter and by upregulating the expression of α-lactalbumin (LALBA) and aquaporin (AQPs), thereby increasing milk production.[30] Various studies confirmed the galactopoietic effect of fenugreek on mammals which is helpful in human clinical trials. However, research on the safe dosage and toxicity of fenugreek during lactation is insufficient.

Shatavari

It is reviewed as both a general tonic and for female reproductive health. It is botanically known

as Asparagus racemosus Willd. belonging to the Liliaceae family is a woody climber having a height of 1-2 m with leaves like pine neeles, and small and uniform flowers. It is grown mainly in Srilanka and India. Shatavari is known to have a varied range of bioactive components like steroidal saponins such as shatavarins, oligospirostanoside, pyrrolizidine alkaloid, isoflavones, racemofuran, quercetin, kaempferol, and trace minerals like zinc, manganese, copper, cobalt, calcium, potassium, selenium, and magnesium. In addition, Shatavari possesses various medicinal benefits like anti-ulcer, anti-tussive, adaptogenic, anti-bacterial, anti-protozoal, molluscicidal, anti-hepatotoxic, anti-neoplastic, anti-oxidative, immunomodulatory, and anti-lithia-tic activity in addition to galactagogue effect. 31 In an animal study, Galega officinalis and Asparagus racemosus extract was found to improve pubertal mammary gland development, increase milk yield, and enhance rabbits' productivity. However, it was suggested to avoid supplementation with A. racemosus in pregnant rabbits.[32]

Clinical studies have shown the positive effect of Shatavari on the milk yield of lactating mothers. Oral administration of the herb increased the levels of prolactin three times due to the steroidal saponins as shatavarins I- IV. An oral dosage of up to 64g/kg of Shatavari is considered safe for consumption.[33]

Sesame Seeds

Botanically known as Sesamum indicum L., are associated with the Pedaliaceae family and are native to India, China, and Burma. It contains 18-25 % of protein, 13 % of carbohydrates, and 5 % of ash. Sesame is an annual shrub having white bell-shaped flowers with a touch of blue, yellow, or red branches. It is 1-2 m tall and has an unpleasant smell, and it matures in 80-180 days. Sesame seeds contain 44- 58 % of oil and 14% saturated, 39% monounsaturated, and 46% polyunsaturated fatty acids. It is also rich in sulfur-containing amino acids and has 2.5 % oxalic acid and 5 % phytic acid. It is a superior source of calcium, copper, phosphorus, iron, magnesium, manganese, vitamin B1, and Zinc. Sesame seeds contain lignan compounds, namely sesamin and sesamolin, converted to sesamol and sesamolin on processing.[34] Its seeds have various medicinal properties like liver-protecting from oxidative stress, healing properties, anti-bacterial, anti-fungal, anti-inflammatory, anti-viral, anti-diabetic effects, analgesic activity, inhibiting effects on the growth of malignant tumors, and maintenance of good cholesterol.[35]

Various animal studies showed the galactopoietic properties of Sesame seeds. On administering sesame seeds to female albino rats, an improvement in the size of lobules that branched with alveoli was recorded, mainly during pregnancy and lactation. Also, it induces mammogenesis in the mammary glands, in addition to an increase in estrogen, progesterone, and prolactin hormones. With the combined effect of progesterone and prolactin, growth of the tubuloalveolar system was reported in the Mammalia. Moreover, the existence of different vitamins and minerals in the sesame seeds leads to an improvement in milk production.[36] Further studies are required to recognize the safe dosage of sesame seeds.

Results & Discussion

Clinical Studies of Plant-Based Galactagogues

Since the galactogogue have been basically consumed as traditionally validated products, therefore, there have been shortage of clinical trials on the same products. A few clinical trials have also been conducted on using plant-based galactagogues as natural agents promoting lactation. Table 1 enlists the plant based galactogogues with the evidence of Clinical trials conducted so far.

Mothers of premature babies were administered herbal tea containing fenugreek and found that the weight loss was significantly lower in the treated mother than in the placebo. Also, the breast milk volume of the mother taking herbal tea was significantly higher than placebo-treated mothers.[37] In a clinical study, the efficacy of a commercial dietary supplement Femaltiker in the augmentation of initiation and stimulation of lactation among mothers of preterm infants was determined. A total of 109 mothers of preterm infants were selected, and 7.7 g of Femaltiker two times a day for 14 days was administered. The volume of expressed milk and prolactin level was estimated. It was found that the dietary supplement 'Fermaltiker' significantly improve volume and prolactin levels as compared to the placebo.[38]

The standard galactagogues, including banana flower, lemon basil, Thai basil, bottle gourd, and

pumpkin, were tested in Thai breastfeeding mothers. It was found that these traditional galactagogues increased milk volume significantly as compared to the control. In addition, the eternal energy and carbohydrate intake was significantly correlated to the milk volume.[39] In another clinical study, 50 healthy women during lactation were provided micronized Silymarin (420 mg/day) for 63 days and were found to increase daily milk production by 85.94 % as compared to the placebo.[40]

Also, few clinical trials are currently conducted on testing plant-based galactagogues. As such, in a clinical study, silicides, a standardized eextract of Milk thistle, was tested for postpartum milk production in mothers of very premature newborns.[41] A total of 92 participants were involved in a randomized and quadruple masking clinical trial for 21 days. The study is still in process, and the effect of silicides will be scrutinized by observing milk production before, during, and one week after cessation of the intervention on daily basis. Additional parameters were monitored in newborn infants with hormone level, weight gain, the volume of enteral feeding, and the ratio of human milk feeding to total enteral feeding volumes. Also, the breast milk composition (in terms of fatty acids, protein, and carbohydrate content) was investigated and compared between study groups. In another clinical study, a combination of Silybum marianum (400 mg) and Galega officinalis (150 mg) at a dose of once a day for six weeks was administered in pregnant mothers for determining its effect on breastfeeding and milk production.[42] Weight gain experienced by the newborn babies and prolactin level will be recorded. Galactagogues plants such as Moringa oleifera[43] and Fenugreek seed meal[44] are also under clinical study.

The overall clinical trials are very limited with plant galactagogues, which further require a more detailed study on its effectiveness in increasing milk production and thus could be commercially used for wider populations.

Table 1: List of plant based galactogogues with the evidence of Clinical trials conducted

S. No.	Plant Name	Local Name	Part Used	Clinical studies on the plant based Galactogogues (References)
1.	*Amaranthus spinosus* L.	Amaranth	Leaves	[8]
2.	*Foeniculum vulgare* Mill.	Fennel	Seeds	[10, 11]
3.	*Silybum marianum* Gaertn.	Milk thistle	Leaves	[13, 14]
4.	*Borago officinalis* L.	Borage	Leaves	[16, 17]
5.	*Lepidium sativum* L.	Garden Cress seeds	Seeds	[18, 19, 20]
6.	*Nigella sativa* L.	Black cumin	Seeds	[9, 22, 23]
7.	*Medicago Sativa* L.	Alfalfa	Leaves	[24]
8.	*Illicium verum* Hook f.	Anise	Dried fruit	[25, 26]
9.	*Trigonella foenum graecum* L.	Fenugreek	Leaves, seeds	28, 29, 30]
10.	*Asparagus racemosus* Willd.	Shatavari	Leaves	[32, 33]
11.	*Sesamum indicum* L.	Sesame seeds	Seeds	[35, 36]

Plant-Based Commercial Galactagogue Products and Their Safety and Efficacy

Commercially plant-based galactagogues are available; however, due to insufficient data regarding dosage safety and efficacy, and clinical trials for testing galactagogues in pregnant women, the market still lacks in several of products. Furthermore, to maximize the effect of galactagogues, several traditional herbs have also been blended into commercially available products and care must be taken for the right dosage and safety. It also concerns variability in the potential, standardization, and unregistered ingredients, which remains a factor in the herbal marketplace. Table 2 represents some products claimed as a plant-based galactagogues in the market.

Bazzano *et al*. (2016b)[45] conducted a systematic review and reported that healthcare providers recommended herbal galactagogues as effective

and useful, and more than this, 86.4 % of healthcare providers have expressed to use them again. In 60.5 % of cases, the healthcare providers have asserted that galactagogues increased the supply of breast milk, whereas 31.6 % were not sure about the change in the volume of the milk secreted, and 7.9 % have claimed that there was no change in the volume of breast milk secretion. Sources (35 %) reported that their subjects faced aftereffects on using an approved galactagogue. Health care providers (7.5 %) have also disclosed that their patients have faced side effects like depression and fatigue on the use of metoclopramide and reported changes in body odor with the smell of maple syrup in urine on the consumption of Fenugreek.[45]

Table 2: List of some of the plant-based Galactagogue products available in the market

Product Name	Galactagogue Ingredient	Administration of Dosage
Gaia Lactate Support (USDA certified)	Fenugreek, Fennel Seed, Raspberry leaf, marshmallow root	1 capsule thrice every day between meals
MotherLove-More milk (USDA certified)	Blessed thistle, nettle, fennel	< 80kg: 1ml orally 4 times daily, Above 80 kg: 2ml orally thrice daily
MotherLove - More milk Two (USDA certified)	Raspberry leaf+nettle+alfalfa	< 80kg: 1ml orally 4 times daily, Above 80 kg: 2ml orally thrice daily
MotherLove - More Milk + (USDA certified)	Fenugreek seed+ blessed thistle +nettle+ fennel seed	< 80kg: 1ml or 1 capsule orally 4 times daily, Above 80 kg: 2ml or 2 capsules orally thrice daily
MotherLove - More milk (special blend) (USDA certified)	Goats' rue+ Fenugreek seeds+ blessed thistle+ nettle+ fennel seed	For extract: Under 80kg: 1ml or 1 capsule orally 4 times daily, Above 80 kg: 2ml or 2 capsules orally (thrice daily)
Vitanica Lactation Blend (USDA certified)	Fennel, nettles leaf, borage flower, hops, vervain, oat straw, raspberry leaf, goats rue, chaste tree, fenugreek, milk thistle, blessed thistle,	1-2 capsules twice daily (orally)
Traditional Medicinals Organic Mothers Milk Tea (USDA certified)	Fennel, Aniseed, coriander fruit, fenugreek, blessed thistle, proprietary blend of spearmint, West Indian lemon grass, lemon verbena leaf, marshmallow root	Oral consumption of Tea (3-5 cups regularly)
Nature's Milk Drops (USDA certified)	Goats' rue, Borage, Fenugreek, milk thistle	Addition of 15 droplets of tonic to 1/4 cup of boiled water, consumption at room temperature (thrice daily)
Solaray Baby Me Now Lactation Ease (USDA certified)	Fenugreek, Fennel, Nettle	2 capsules with a meal /glass of water
Yogi Woman's Nursing Support Tea (USDA certified)	Proprietary blend of Chamomile, Stinging nettle, Anise, Fenugreek, Fennel, English lavender flower	2-3 cups of tea (daily)
nuMom Breast Milk Enhancer (USDA certified)	Fenugreek seed powder, blessed thistle powder	2 capsules (daily)
Fairhaven Health Nursing Blend Breastfeeding Supplement (USDA certified)	Proprietary Blend of Fenugreek, Fennel, Coriander, Anise, Chamomile, Vervain	2 capsules (daily)

Fairhaven Health Nursing Time Tea (USDA certified)	Fennel Seed, Goats' rue, Blessed thistle, alfalfa, anise seed, lemon verbena	2-3 cups of tea (daily)
Herb Pharm Mother's Lactation Tonic (USDA certified)	Chaste tree berry, fenugreek seed, caraway seed, fennel seed, anise seed	Dropperful of the tonic with little water thrice daily between meals
Reme- Lac (USDA certified)	Asparagus racemosus, Gossypium indicum, Cuminum cyminum, cyperus rotundus, Leptadenia reticulata, Piper longum, Centella asiatica	2-3 capsules twice daily with milk
Lactation booster (USDA certified)	Malt powder, Anise seeds, Shatavari, Fennel seeds, Jaggery powder, Black cumin	add 1 spoon of powder to a 120ml milk or water
HealthKart Milk Thistle (USDA certified)	Milk Thistle,	1 capsule /day
Lactosone (USDA certified)	*Asparagus racemosus, Withania somnifera, Hemidesmus indicus*	1 Capsule twice / per day

There are numerous ways for evaluating herbal galactagogue efficacy, which is generally known as "breastfeeding adequacy indicators". The frequently used measure is the fullness of the breasts. Other indicators reported by lactating women were alterations in the course of feeding sessions or improvement in the value of the infant's contentedness and feeding behavior, increase in the infant's growth rate, or alterations in body weight, with an improvement in the measured amount of milk fed to the child. In addition, positive expressions in lactating women, i.e., confidence and self-empowerment, are also linked with breastfeeding adequacy indicators. These psychological benefits to the mothers increase the milk supply.

Most studies have identified fenugreek as a widely used galactagogue, however, the dosage form varied as crude seeds, encapsulated dried seed powder, extract tincture, and in the form of nursing tea. However, the strength and dosage of these herbal tinctures differ among the distinct companies as it is not regulated.

The galactogogue plays as very significant role in the life span of every women life, but there have been no full fleged toxicity studies available on the subject. People consume them in traditional preparation methods and their consumption varies region to region. There is also no scientific evidence available for effectiveness of herbs on human milk secretion, but the ethnomycological data reveals some of the traditional methods. A lot of efforts are required from the scientific community of these parameters.

Limitation

This study has compiled and analyzed plant galactagogues which support clinical investigation results, and can be considered as a restricted scope as (i) recent publications on plants and lactation studies are scanty in contrast to that of general topics (ii) The time frame was not defined for the publications gathered in this research, therefore there is a prospect of ignorance of several reports which are published in preceding years (iii) journals that were not available in English were excluded.[46] Moreover, some drawbacks surrounds the drug-induced surveillance of herbal medicines in the common people, and most importantly among lactating women. There is minimal evidence briefing the workings of herbs as a galactagogue, likewise the studies on the effectiveness of herbs on human milk secretion are also lacking. Various other limitations lies of the herbal galactagogues which affect the (a) sustainability of the trial outcomes; (b) undersized sample; (c) scanty randomization methods; (d) abysmally defined eligibility criteria; (e) effect of poly-herbal formulations; (f) inconsistent breastfeeding practices among the subjects.[47]

It is necessary to discern that herbal preparations are commonly not monitored and graded which is a huge safety concern for the lactating mothers.[48] Sim *et al*., (2013)[49] stated that there is very little

understanding of adverse effects and medicinal information to certain women which that leads to the exclusion of usual recommendations for treatment of limited human milk supply, for example commonly prescribed medicine domperidone.

Conclusion & Future Aspects

Lactation failure or agalactia, also known as hypokalaemia, is a critical physiological limitation in lactating women. It should be cured at the earliest as it affects the delivery of basal nutrients to an infant post-birth. Furthermore, World Health Organization (WHO) has advised the first six months of exclusive breastfeeding for the newly born. Nevertheless, both synthetic and herbal products having galactopoietic effects have been used. The herbal galactagogues have advantages like lower cost and fewer adverse effects that are more tolerable to lactating mothers as and their children. However, their use is mostly based on traditions with little or, in some cases, limited scientific data. Moreover, indigenous knowledge of plant-based galactagogue is continuously diminishing as the newer generation is restrained from inheriting the legacy of ethnomedicine due to their lifestyle, industrialization, urban lives, allopathic medications, and deforestation may be the reasons for this changed behavior in the generations. Hence, there is a need for the collection of systematic documents to validate traditional knowledge and provide scientific data to prove the benefits of such plants and their formulations for the interest of humanity before they are lost forever. Noticeably there's an increase in the difficulty of breastfeeding due to under-nutrition caused by the unaffordability of food, and lack of protein consumption. Consequently plants with good source of protein maintain not only the stability of the environment, ethics, food affordability, but also food safety, fulfill higher demands of consumers, and fight protein-energy malnutrition, and therefore it is essential to scientifically study these plants based galactagogues with higher protein content.[50] In addition, standardization of formulation is required with the investigation of their bioactivity and nutritional data. Although the commercial products are available in the market, however, more trials should be conducted on these herbal galactagogues to examine the safety and efficacy of these herbs as a basis for commercial production and their usage. Limited pharmacological knowledge is present on the uses of botanical galactagogues in comparison to synthetic drugs. Because of the limited studies, it is of interest to standardize the doses, and composition of bioactive components and to study the mechanism of action, its side effects, and interaction with food. This is a forward-looking research area that could be projected for manufacturing herbal formulations for the optimization of to optimize lactating mothers. These plants could be administered in distilled extracts like essential oils, alcohol extracts, or lyophilized extract/powder in the form of supplements safety measures should be of utmost importance in the utilization of plants as galactagogues.

Acknowledgements

This study was supported by the Department of Science and Technology- Science for Equity, Empowerment and Development (SEED) Division for the research grant.

Funding

The authors received financial support from the Department of Science and Technology- Science for Equity, Empowerment and Development (SEED) Division (Grant Number: SEED/TIASN/038/2018 (G&C).

Conflict of Interest

The author(s) declares no conflict of interest.

References

1. Bazzano A.N., Hofer R., Thibeau S., Gillispie V., Jacobs M., Theall K.P. A Review of Herbal and Pharmaceutical Galactagogues for Breast-Feeding. *Ochsner Journal.* (2016a); 16(4): 511–24.
2. Penagos F.P., Jaramillo J.V.B., Ruiz-Cortés Z.T. Pharmacological overview of galactogogues. *Veterinary Medicine International*. (2014); 1-20. doi:10.1155/2014/602894.
3. Nice F.J. Selection and Use of Galactogogues. ICAN:Infant, Child, and Adolescent Nutrition. (2015); 7(4): 192–94.
4. Singh V., Jain S., Prakash S., Thakur, M. Studies on the Synergistic Interplay of

Vitamin D and K for Improving Bone and Cardiovascular Health. *Current Research in Nutrition and Food Science Journal*. (2022); 10(3): 840-857.

5. Sonowal R., Sonowal S. 2017. In: Anthropological Aurora of North East India, Delhi, India
6. Rastogi A., Shukla S. Amaranth: a new millennium crop of nutraceutical values. *Critical Review in Food Science and Nutrition.* (2013); 53(2): 109-25.
7. Kumar MN, Arya P. Amaranthus grain nutritional benefits: A review. *Journal of Pharmacognosy and Phytochemistry.* (2018); 7(2): 2258–62.
8. Kuswaningrum O., Suwandono A., Ariyanti I., Hadisaputro S. The Impact of consuming Amaranthus spinosus L extract on prolactin level and breast milk production in postpartum mothers. *Belitung Nursing Journal*. (2017); 3: 541-47.
9. Al-Snafi A.E., Majid W.J., Talab A. Galactagogue action of Nigella sativa seeds. *IOSR Journal of Pharmacy.* (2014); 4(6): 58–61.
10. Rifqiyati N., Wahyuni A. Fennel (Foeniculum vulgare) leaf infusion effect on mammary gland activity and kidney function of lactating rats. *Nusantara Bioscience.* (2019); 11(1): 101–5.
11. Taha K.F., El-hawary S.S., El-hefnawy H.M., Ali Z.Y., Abd El-khalek M.R. Assessment of Two Herbal Galactagogue Products and a New Suggested Formula. *International Journal of Bioassays*. (2015); 4(10): 4382-93.
12. Das S., Mukherjee S., Vasudevan D. Medicinal properties of milk thistle with special reference to silymarin – An overview. *Natural Product Radiance.* (2008); 7 (2): 182-92.
13. Mohammad B.I, Alzamely H., Gharrawi A.L., Al-Aubaidy H.A.M. Milk Thistle Seed Extract Favourably Affects Lactation and Development of Mammary Gland in Female Rats. *Egyptian Journal of Vetenarian Sciences.* (2019); 50(1): 27–36.
14. Refaie A.M., Ghazal M.N., Abo El-Azayem E.H., El-Maged A., Marwa H. Impact of dietary supplementation of milk thistle (Silybum marianum) seed extract on doe rabbits' performance. *Egyptian Journal of Nutrition and Feeds*. (2019); 22(2): 375-82.
15. Gilani A.H., Bashir S., Khan A. Pharmacological basis for the use of Borago officinalis in gastrointestinal, respiratory and cardiovascular disorders. *Journal of Ethnopharmacology.* (2007); 114(3): 393-300. doi:10.1016/j.jep.2007.08.032.
16. Bin Nayeem M.A., Haque M.S., Hoque M.A., Islam M.M., Islam S. Phytoconstituents and Pharmacological Activity of Gauzaban (Borago officinalis Linn): A review. *International Journal of Food Sciences and Nutrition.* 2017; 2(1): 148–52.
17. Saidi W.A., Yawer M.A., Mangalo H., Hammoudi S.R. Elucidation of a Role for the Aqueous Extract of Borage in Mammary Gland Growth and Development. *Iraqi Postgraduate Medical Journal.* (2006); 5(1): 54-61.
18. Sharma S., Agarwal N. Nourishing and healing process of garden cress (Lepidium sativum Linn.) - A review. *Indian Journal of Natural Products and Resources*. (2011); 2(3), 292–97.
19. Singh C.S., Paswan V.K., Naik B. Exploring potential of fortification by garden cress (Lepidium sativum L.) seeds for development of functional developing. *Indian Journal of Natural Products and Resources*. (2015); 6(3): 167–75.
20. Obeid A.K., Al-Bazii S.J., Al-masoudi F.J. Mammmagensis effect of Lepidium sativum seeds (garden cress) in mammary gland growth and development during three physiological stages in female rats. *EurAsian Journal of BioSciences.* (2022); 14(1): 2273-78.
21. Forouzanfar F., Bazzaz B.S.F., Hosseinzadeh H. Black cumin (Nigella sativa) and its constituent (thymoquinone): A review on anti-microbial effects. *Iranian Journal of Basic Medical Sciences.* (2014); 17(12): 929-38.
22. Hosseinzadeh H., Tafaghodi M., Mosavi M.J., Taghiabadi E. Effect of aqueous and ethanolic extracts of Nigella sativa seeds on milk production in rats. *Journal of Acupuncture and Meridian Studies*. (2013); 6(1): 18-23.
23. Nurdin E., Amelia T., Makin M. The effects of herbs on milk yield and milk quality of mastitis dairy cow. *Journal of the Indonesian Tropical Animal Agriculture.* (2011); 36(2): 104-8.

24. Rafińska K., Pomastowski P., Wrona O., Górecki R., Buszewski B. Medicago sativa as a source of secondary metabolites for agriculture and pharmaceutical industry. *Phytochemistry Letters.* (2017); 20: 520–39.
25. Boota T., Rehman R., Mushtaq A., Kazerooni E.G. Star Anise: A review on benefits, biological activities and potential uses. *International Journal of Chemical and Biological Sciences.* (2018); 14: 110-14.
26. Tavakkolifar B., Massoudi M., Zarringhalam J. Review on pharmacological activities of Gum olibanum. *Journal of Medicinal Plants.* (2009); 8(32): 1–13.
27. Wani S.A., Kumar P. Fenugreek: A review on its nutraceutical properties and utilization in various food products. *Journal of the Saudi Society of Agricultural Sciences.* (2018); 17(2): 97–106.
28. Sevrin T., Boquien C.Y., Gandon A., Grit I., de Coppet P., Darmaun D., Alexandre-Gouabau, M.C. Fenugreek stimulates the expression of genes involved in milk synthesis and milk flow through modulation of insulin/GH/IGF-1 axis and oxytocin secretion. *Genes.* (2020); 11(10): 1-28.
29. Sevrin T., Alexandre-Gouabau M.C., Castellano B., Aguesse A., Ouguerram K., Ngyuen P., Darmaun D., Boquien C.Y. Impact of fenugreek on milk production in rodent models of lactation challenge. *Nutrients.* (2019); 11(11): 1–21.
30. Yuliani F.S., Purwono S., Sadewa A.H., Damayanti E., Heriyanto D.S. Polyherbal formula (ASILACT®) induces Milk production in lactating rats through Upregulation of α-Lactalbumin and aquaporin expression. *BMC Complementary Medicine and Therapies.* (2020); 20(1): 368.
31. Alok S., Jain S.K., Verma A., Kumar M., Mahor A., Sabharwal M. Plant profile, phytochemistry (Shatavari): A review and pharmacology of Asparagus racemosus. *Asian Pacific Journal of Tropical Disease.* (2013); 3(3): 242–51.
32. Hamed R.S. Effect of aqueous extracts of Galega officinalis and Asparagus racemosus supplementation on development of mammary gland, milk yield and its impact on the productivity of rabbit does. *Egyptian Poultry Science Journal.* (2016); 36(4): 985-1004.
33. Gupta M., Shaw B. A double-blind randomized clinical trial for evaluation of galactogogue activity of Asparagus racemosus willd. *Iranian Journal of Pharmaceutical Sciences.* (2011); 10(1): 167-72.
34. Thakur M., Modi V.K. Emerging technologies in Food Science- focus on the developing world. *Springer Nature.* (2020).
35. Elleuch M., Besbes S., Roiseux O., Blecker C., Attia H. Quality characteristics of sesame seeds and by-products. *Food Chemistry.* (2006); 103(2): 641-650. doi:10.1016/j.foodchem.2006.09.008.
36. Al-Bazii S.J., Al-Masoudi F.J., Obeid A.K. Histological effects of sesamum indicum seeds on mammary gland tissue in female white rats. IOP Conference Series: *Materials Science and Engineering*. (2019); 571: 1-10.
37. Turkyılmaz C., Onal E., Hirfanoglu I.M., Turan O., Koç E., Ergenekon E., Atalay Y. The effect of galactagogue herbal tea on breast milk production and short-term catch-up of birth weight in the first week of life. *Journal of Alternative and Complementary Medicine.* (2011); 17(2): 139-42.
38. Kornacka M.K. Effectiveness of Femaltiker in Stimulation Lactation among Mothers of Preterm Infants (FEMA). In: ClinalTrials.gov. [US National Library of Medicine]. Kenya: NIH; 2022. https://clinicaltrials.gov/ct2/show/NCT03341481.28th June 2019. 21st August 2022.
39. Buntuchai G., Pavadhgul P., Kittipichai W., Satheannoppakao W. Traditional galactagogue foods and their connection to human milk volume in Thai breastfeeding mothers. *Journal of Human Lactation.* (2017); 33(3): 552-59.
40. Di Pierro F., Callegari A., Carotenuto D., Tapia M.M. Clinical efficacy, safety and tolerability of BIO-C (micronized Silymarin) as a galactagogue. *Acta Biomed.* (2008); 79 (3): 205-10.
41. Petersen H. Efficacy of Herbal Galactagogue Silitidil after Preterm Birth. In: ClinalTrials.gov. [US National Library of Medicine]. Kenya: NIH; 2022. https://clinicaltrials.gov/ct2/show/NCT03577587. 3rd May 2022. 21st August 2022
42. Cromi A. Double-blind, Placebo controlled A

Randomized Trial on the Efficacy of Herbal Galactogogues. In: ClinalTrials.gov. [US National Library of Medicine]. Kenya: NIH; 2022. https://clinicaltrials.gov/ct2/show/NCT02233439. 8th September 2014. 21st August 2022.

43. Attia S.L. Nutritional Impact of Moringa Oleifera Leaf Supplementation in Mothers and Children. In: ClinalTrials.gov [US National Library of Medicine]. Kenya: NIH; 2022. https://clinicaltrials.gov/ct2/show/NCT04587271. 17th October 2022. 21st October 2022.
44. Marom R. Effect of Fenugreek Use in Mothers of Preterm on Breast Milk Production and Macronutrient Content. In: ClinalTrials.gov. [US National Library of Medicine]. Kenya: NIH; 2022. https://clinicaltrials.gov/ct2/show/NCT02384655. 17th June 2020. 21st August 2022.
45. Bazzano A.N., Littrell L., Brandt A., Thibeau S., Thriemer K., Theall K.P. Health provider experiences with galactagogues to support breastfeeding: a cross-sectional survey. *Journal of Multidisciplinary Healthcare*. (2016b); 623–30.
46. Kwan S.H., Abdul-Rahman P.S. Clinical Study on Plant Galactagogue Worldwide in Promoting Women's Lactation: a Scoping Review. *Plant Foods for Human Nutrition*. (2021); 76: 257–269. https://doi.org/10.1007/s11130-021-00901-y
47. Mortel M., Mehta S.D. Systematic Review of the Efficacy of Herbal Galactogogues. *Journal of Human Lactation*. (2013); 29(2): 154- 162. doi:10.1177/0890334413477243.
48. US Food and Drug Administration. Dietary supplements. In: ClinalTrials.gov. [US National Library of Medicine]. Kenya: NIH; 2022. http://www.fda.gov/Food/DietarySupplements/default.htm. 6th February 2022. 21st August 2022.
49. Sim T.F., Sherriff J., Hattingh H.L., Parsons R., Tee L.B. The use of herbal medicines during breastfeeding: a population-based survey in Western Australia. *BMC Complementary Medicine and Therapies*. (2013); 13(1): 2-10. doi: 10.1186/1472-6882-13-317.
50. Sharma V., Thakur, M. Horsegram (Macrotyloma uniflorum): an underutilized pulse crop as a sustainable plant based protein. *Future of food: Journal on Food, Agriculture & Society*. (2022); 10(3): 1-12. Doi: 10.17170/kobra-202204136009

Abbreviations

PRL- Prolactin; TRH- Thyrotropin- releasing hormone; rBST- Recombinant Bovine Somatotropin; IMS- Insufficient Milk Supply; WHO- World Health Organization; SDA- Stearidonic Acid; TQ- Thymoquinone; THQ- Thymohydroquinone; GRAS- Generally recognized as Safe; USFDA- US Food and Drug Administration; FEN- Fenugreek Supplemented; IGF 1- Insulin Growth Factor 1; LALBA- α- Lactalbumin; AQPs- Aquaporin.