Ethnoveterinary importance of herbal galactogogues - a review

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Abstract
Galactogogues elicit pharmacological effects, resulting in increased prolactin concentration through interactions with dopamine receptors and thereby augmenting milk supply. Commercially available synthetic drugs induce adverse effect on the neuro-endocrine axis of lactation physiology. Their prolonged uses have caused toxicity which opens a detrimental platform to normal health status of both human and animals. So the researchers have developed a keen interest in traditional herbs, because these are easily available, cheap and with a hope that they may not leave any toxic residues in milk. Phyto-pharmacological research on natural products can contribute for the discovery of new active compounds with novel structures which may serve as a lead for the development of new galactogogues. Although majority of these herbal preparations have not been evaluated their traditional use suggests that they are safe and effective. The purpose of this review paper was to succinctly review recent progress made in the field of commercially available and traditional galactogogues.

Keywords: agalactia, galactogogues, hypogalactia, phytonutrients, prolactin.

Introduction
Galactogogues are medications that aid in initiating, maintaining, and augmenting of adequate milk production. The term galactogogue refers to substances that augment established lactation, whereas the term galactopoietic is used independently to describe the hormone preparations which enhance milk production in an animal already in lactation [1].

Galactogogues may be synthetic, plant-derived or endogenous products. They act through exerting an influence on adreno-hypothalamo-hypophysal-gonadal axis by blocking hypothalamic dopaminergic receptors or by inhibiting dopamine producing neurons. These medications increase prolactin secretion by antagonizing dopamine receptors [2]. Most of the information about herbal medication comes from Indian Traditional Knowledge (ITK) because more than 80% of world population depends on it for primary health care and the information is passed through generations [3]. Herbs and their preparations have multiple diverse useful actions on the human and animal health. The advantages of herbal medicines are due to constituent chemicals developed as a result of co-evolution between flora and fauna and their enzyme driven synthesis leading to development of optically pure chiral molecules with specific reactions in the mammalian body [3].

So, phyto-pharmacological research on natural products can show a ray of hope for the discovery of new active compounds with novel structure which have potential to serve as a natural lead compound for development of new galactogogues. Majority of these herbal preparations have however not been scientifically, systematically and thoroughly evaluated, but their traditional use suggests some safety and efficacy.

Lactogenesis and role of galactogogues
Milk production (lactogenesis), which is a consequence of neuro-endocrine event, is a complex neuro-physiological process that involves interaction of a number of physical and emotional factors along with action of multiple hormones, mainly prolactin. During parturition and expulsion of the placenta, progesterone concentration reduced resulting in initiation of full milk supply [4]. Dopamine agonists and antagonists regulate prolactin synthesis and secretion through interaction with the hypothalamus and anterior pituitary and thereby control milk production [3]. Thereafter, prolactin levels gradually decrease but milk supply is maintained or increased by local feedback mechanisms [5]. Therefore, an increase in prolactin levels is mandatory to increase milk production but not to maintain its supply. The anterior pituitary plays a significant role for the development of the mammary gland, initiation of lactogenesis and lactation that has been described following the administration of pituitary extracts. So the term ‘prolactin’ has been described for pituitary substance. It is assumed that, pituitary extract is rich in growth hormone responsible for milk production in lactating cattle. Lactogenesis and ejection both are stress for lactating cows and in turn are affected by stress of any other reason. As because hormone action is completely dependent on emotion and stress, so control of stress is the primary factor on the way of lactogenesis.

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### Table-1: Herbs reported to have galactopoietic properties [7-23].

<table>
<thead>
<tr>
<th>Common name</th>
<th>Botanical name</th>
<th>Family</th>
<th>Parts used</th>
<th>Chemical constituents</th>
<th>Effects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfalfa</td>
<td>Medicago sativa</td>
<td>Fabaceae</td>
<td>Leaves</td>
<td>Alkaloids (stachydrine, 1-homostachydrine), coumarester, flavonoids, iso-flavonoids, carotenoids, phenolic acids and minerals (Fe, Ca, K, P and Zn)</td>
<td>Estrogenic and lactogenic stimulant, presence of “TRH-like material” in turn stimulates prolactin release.</td>
<td>[7]</td>
</tr>
<tr>
<td>Black seed/Black cumin</td>
<td>Nigella sativa</td>
<td>Umbelliferae</td>
<td>Seeds</td>
<td>Triterpene glycosides (actein, cimicidine, cimifugine, macrotin, racemoside), isoflavonoids (formononetin) and isoflavonoids.</td>
<td>Analgesic, anti-inflammatory, galactopoetic, improves FCR in buffalo and lambs.</td>
<td>[11]</td>
</tr>
<tr>
<td>Borage</td>
<td>Borago officinalis</td>
<td>Boraginaceae</td>
<td>Leaf and flower</td>
<td>Pyrrolizidine alkaloids (amabiline, leptidin-1 and -2), flavonoids, flavonoids (quercetin), limonene, germacrene D and trans-dihydrocarvone.</td>
<td>Effective galactagogue with red raspberry and fenugreek acts as ruminotonic and increases blood flow to the mammary gland improves post partum hemorrhage. Effective galactagogue, restorative effect on adrenal cortex.</td>
<td>[7]</td>
</tr>
<tr>
<td>Caraway</td>
<td>Carum carvi</td>
<td>Umbelliferae</td>
<td>Seeds</td>
<td>Anethole, thujone, pinen, carvone, dihydrocarvone, carveol, dihydrocarveol, flavonoids (quercetin), limonene, germacrene D and stearyl-glucoside, tannins, essential fatty acids, essential amino acids, ascorbic acid and minerals (Fe and Ca).</td>
<td>Post-partum galactagogue and lactational herbs.</td>
<td>[13]</td>
</tr>
<tr>
<td>Chaste berry</td>
<td>Vitex agnuscastus</td>
<td>Verbenaceae</td>
<td>Fruit</td>
<td>Iridoid glycosides (agnoside, aucubin) flavonoids (casticin, kaempferol, quercetin, vitexin), progestosterone, hydroxy-progestosterone, testosterone, epi-testosterone, androstenedione, alkaloids (vitexin), volatile oil (1,8-cineole, limes, linalool, terpinyl acetate, alpha pinenes, beta pinenes), palmilic acid, oleic acid, linoleic acid and stearic acid.</td>
<td>Normalizing effect on progesterone function of the pituitary gland stimulates prolactin production, uterine tonic, and hyper-prolactinemia.</td>
<td>[8]</td>
</tr>
<tr>
<td>Dill</td>
<td>Anethum graveolens</td>
<td>Umbelliferae</td>
<td>Seed</td>
<td>Carvone, dihydro-carvone, Eugenol, limonene, phellandrene, anethole, carvole, myrictin, x-pinen, flavonoids (kaempferol, vicenin blucuronide), coumarins (esculetin, scopoletin, bergapten, umbeliferone) and xanthone (dillanose).</td>
<td>Anti-spasmodic, anti-inflammatory, galactagogue. Contraindicated for low sodium diets.</td>
<td>[14]</td>
</tr>
<tr>
<td>Fenugreek</td>
<td>Trigonella foenumgraecum</td>
<td>Fabaceae</td>
<td>Seed</td>
<td>Elemene, selinene, furanone, dihydro-benzofuran, muurolone, dihydro-actinidolide, Alkaloids (trigonelline, gentianine, carpaine), saponins (diosgenin, magnogenin, gilogenin, tigogenin), flavonoids (vitexin, isovitexin, orientin, vicenin, quercetin, luteolin) and galactomannan.</td>
<td>Carminative, anti-spasmodic, anti-inflammatorv, promote milk ejection, stimulates milk flow, and increases udder milk production. Contraindicated due to its allergic and estrogenic effects. Anti-inflammatorv, anti-spasmodic,[8,7,15] emmenagogue, galactagogue, hypotensive, oxytocic, stimulate milk ducts of mammary gland tissue, promotes milk ejection. Contraindicated in pregnancy due to its uterotonotic effect.</td>
<td>[8]</td>
</tr>
<tr>
<td>Levant cotton</td>
<td>Gossypium herbaceum</td>
<td>Malvaceae</td>
<td>Root</td>
<td>Alkaloids, flavones, β-sitosterol, α-amyrin, terpenes and naphthalene derivative gossypol.</td>
<td>Abortifacient, uterotonic, ecbolic, galactagogue.</td>
<td>[7]</td>
</tr>
<tr>
<td>Goat’s Rue</td>
<td>Galega officinalis</td>
<td>Papilionaceae</td>
<td>Dried aerial parts</td>
<td>Galegin, peganie, flavonoids and saponins.</td>
<td>Stimulate breast growth, improve milk yield, moderately regulate estrogen levels, toxic to sheep. Ancient Mayan galactagogue, double the volume of milk, no effect on mammary gland, milk composition.</td>
<td>[7,8]</td>
</tr>
<tr>
<td>Ixbut</td>
<td>Euphorbia lacinifolia</td>
<td>Euphorbiaceae</td>
<td>Dried aerial parts</td>
<td>Sesquiterpenes, oleinol, ingenol, 3-angelate, kaempferol, scopoletin, kaempferol 3-O-glucopyranoside, quercetin, vanillin acid, p-hydroxyximic acid, protocatechatic acid, dihydroxycoumarin, β-sitosterol, brevifolin, daucosterol, piceatannol, jokkinolide β, D-glucopyranoside, octacosyl cis-ferulate, ethylbrevifolin carboxylate, octacosyl trans-ferulate and chrysophanol.</td>
<td>Double the volume of milk, no effect on mammary gland, milk composition.</td>
<td>[16]</td>
</tr>
<tr>
<td>Jivanti</td>
<td>Leptadenia reticulata</td>
<td>Asparagaceae</td>
<td>Root</td>
<td>Leptadeno, triacantane, cetyl alcohol, lepidin-1 and sitosterol.</td>
<td>Increase milk yield and correct milk irriquality.</td>
<td>[3,17]</td>
</tr>
<tr>
<td>Marshmallow</td>
<td>Althea officinalis</td>
<td>Malvaceae</td>
<td>Root and leaf</td>
<td>D-glucon, diosmetin glucosides, flavonoids (kaempferol, quercetin), polyphenolic acids (syringic, caffeic, salicyclic, vanillic), pectin, asparagine and tannins.</td>
<td>Synergistic galactagogue effect with alfalfa, blessed thistle and fenugreek.</td>
<td>[18]</td>
</tr>
</tbody>
</table>

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of numerous active principle including α-linolenic acid, with organic or aqueous solvents has revealed the presence compiled in Table-1 [7-23].

Important herbs and their effect over galactopoiesis are status, subclinical mastitis and agalactia [3]. Some herbs are also helpful in improving reproductive health performance and health as well. These indigenous efficiency of feed utilization to alleviate adverse effects stomachic and carminatives by improving the are the herbal supplements those act as galactagogues,

marshmallow, lemon balm, pot marigold, chamomile are the herbal supplements those act as galactagogues, stomachic and carminatives by improving the efficiency of feed utilization to alleviate adverse effects of environmental stress and enhance the overall animal performance and health as well. These indigenous herbs are also helpful in improving reproductive health status, subclinical mastitis and agalactia [3]. Some important herbs and their effect over galactopoiesis are compiled in Table-1 [7-23].

**Natural lead compounds**

Phytochemical screening of plants extracts either with organic or aqueous solvents has revealed the presence of numerous active principle including α-linolenic acid, steardionic acid, ascorbic acid, domperidone, metoclopramide, risperdal, sulphiride (egonyl) and chlorpromazine (thorazine), amentoflavone, curcumin, vanillic acid, ferulic acid, saponins, glycosides (shatavarin, sarasapogenin, diosgenin), essential oils (thymol, eugenol, vanillin, guaiacol, limonene), isoflavones, racemosol, α-pinene, asparagamine, α-thujene, sabinene, myrcene, limonene, α-phellandrene, γ-terpinene, p-cymene, carvone, α-pinene, piperitone, cadinene, eudesmol, bisabolol, zingiberene, bisabolene, cadina-4,8-diene, isopulegol, anfaferine, andrographolide, pregnane derivatives etc which contribute to galactopoietic effect [24]. The active component of many medicinal herbs and their preparations is polyphenol which is the largest and most ubiquitous group of phytochemicals having anti-oxidative, anti-microbial, anti-allergic, hypo-lipidaemic, anti-cancer, anti-mutagenic, hepato-protective, immune-modulatory, and cardio-protective effect [25]. Although, phytochemicals are established as frontline antioxidants to combat oxidative stress by scavenging free radicals in lactating cows, they also play a vital role in milk augmentation process. Phytochemical groups with effect on galactopoiesis have been summarized in the Table-2 [26-33].

**Table-1:** Continue from page no.

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</tr>
</thead>
<tbody>
<tr>
<td>Milk thistle</td>
<td>Silybum marianum</td>
<td>Asteraceae</td>
<td>Leaves and seeds</td>
<td>Flavonoids/ flavonolignans, silymarin (silybin, silychristin, apigenin, isosilybin, dehydrodiol, deoxyxylcyristin, deoxyxylsilydianin, silydianin, silybromine, silybonol, silyhermin, neosilyhermin), myristic, oleic, palmitic and stearic acids.</td>
<td>Galactagogue, cholagogue. Increase milk supply, side effects include allergy and diarrhoea.</td>
<td>[7,8]</td>
</tr>
<tr>
<td>Stinging Nettle</td>
<td>Urtica dioica</td>
<td>Urticaceae</td>
<td>Aerial parts</td>
<td>Vitamin (A, B complexes, C, D), minerals(Fe, P, K, S, Mg), fiber, acetylcholine, histamine and serotonin.</td>
<td>Stimulate milk production, increase the flow of milk.</td>
<td>[7]</td>
</tr>
<tr>
<td>Raspberry/ Red raspberry</td>
<td>Rubus idaeus</td>
<td>Rosaceae</td>
<td>Leaves and fruits</td>
<td>Polypeptides, flavonoids, glycosides of kaempferol and quercetin, tannins, pectin, fructose, volatile oil, citric acid, malic acid, vitamin (A, B complexes, C, E), and minerals (Fe, Ca, K, P).</td>
<td>Galactagogue effect uncertain, help the uterus to recover and regain its shape and size quickly following parturition.</td>
<td>[19]</td>
</tr>
</tbody>
</table>
| Red Clover | Trifolium pratense | Papilionaceae | Flower | Isoflavones (biochanin A, daidzein, formononetin, genistein, pratensein, trifoside) flavonoids (pectolinarin, trifolin) contracted in pregnancy. Aneseel, flavones (thorazine), amentoflavone, curcumin, vanillic acid, steardonic acid, ascorbic acid, domperidone, metoclopramide, risperdal, sulphiride (egonyl) and chlorpromazine (thorazine), amentoflavone, curcumin, vanillic acid, ferulic acid, saponins, glycosides (shatavarin, sarasapogenin, diosgenin), essential oils (thymol, eugenol, vanillin, guaiacol, limonene), isoflavones, racemosol, α-pinene, asparagamine, α-thujene, sabinene, myrcene, limonene, α-phellandrene, γ-terpinene, p-cymene, carvone, α-pinene, piperitone, cadinene, eudesmol, bisabolol, zingiberene, bisabolene, cadina-1,4-diene, isopulegol, anfaferine, andrographolide, pregnane derivatives etc which contribute to galactopoietic effect [24]. The active component of many medicinal herbs and their preparations is polyphenol which is the largest and most ubiquitous group of phytochemicals having anti-oxidative, anti-microbial, anti-allergic, hypo-lipidaemic, anti-cancer, anti-mutagenic, hepato-protective, immune-modulatory, and cardio-protective effect [25]. Although, phytochemicals are established as frontline antioxidants to combat oxidative stress by scavenging free radicals in lactating cows, they also play a vital role in milk augmentation process. Phytochemical groups with effect on galactopoiesis have been summarized in the Table-2 [26-33].

**Herbal galactagogues under commercial use**

Anifed [34], Galog, Galactin, Immu-21 [35], Leptaden, Payapro [36], Ruchamax (appetizer, restorative, anti-allergic, hypo-lipidaemic, anti-cancer, anti-mutagenic, hepato-protective, immune-modulatory, and cardio-protective effect [25]. Although, phytochemicals are established as frontline antioxidants to combat oxidative stress by scavenging free radicals in lactating cows, they also play a vital role in milk augmentation process. Phytochemical groups with effect on galactopoiesis have been summarized in the Table-2 [26-33].

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Asparagus racemosus, Leptadenia reticulata, Nardostachys jatamansi, lactobacillus species, vitamins.

Leptadenia reticulata, Nigella sativa, Foeniculam vulgare, Pueraria tuberosa, Glycenza glabra, Cuminum cyminum and Asparagus racemosus.

Allium sativum, Azadirachta indica, Calotrophis orocora, Centratherum anthelmenticum, Eclipta elba, Comnniphora mukul, Embelica ribes, Piper longum, Piccroriza kuroara and Zinziber officinale.

Asparagus racemosus and Leptadena reticulate, Nardostachys jatamansi, Anethum graveolens, Asparagus racemosus, Coriandrum sativum, Cuminum cyminum, Foeniculum vulgare, Leptadenia reticulata, Lepidium sativum, Celosia argentea, Sesamum indicum and Tinospora cordifolia with jaggery (unrefined sugar) and natural clay.

As many herbal plants contain large number of chemical active principles, having galactogenic properties; can be used as herbal medicine for the letting-down of milk in milch animals. Among these, Fenugreek (Trigonella foenum graecum), Fennel (Foeniculum vulgare), Raspberry leaf/Red Raspberry (Rubus idaeus), Nettle (URTica dioica) and Nettle leaf (UTica urens), Blessed thistle (Cnicus benedictus), Chaste berry (Vitex agnus-castus), Alfalfa (Medicago sativa), Black cohosh (Cimicifuga resebosa), Dill (Anethum graveolens), Goat's Rue (Galage officianalis), Milk thistle (Silbyum marianum), Giant Cane (Arundo donax), Abuta or Laghu Patha (Cismampelos pareira), and extracts of Bhringraj or false daisy (Eclipta alba), Black Nightshade (Solum nigrum), Jivanti (Leptadenia reticulata), Ashwagandha and Shatavari (Asparagus racemosus) plant ingredients have been emphasized in Ayurveda to induce lactogenesis and lactation. So, a thorough, critical and scientific evaluation is necessary to include theses herbs as potent herbal galactogogues. A bulk of literatures have spoken about the isolation of active principles of herbs through in vitro study, thus questioning about their safety and efficacy as such, because the theoretical concerns have not been proved in vivo experience. Judging an herb by individual constituents does not take into account the possible ameliorating effects of its other constituents. Again these herbs can be potentially toxic if not used properly at proper dose, drug form and through specified route of administration. Just because they are natural, doesn’t mean they are entirely safe. Standardization of methods and quality control data on safety and efficacy are essential for the understanding of the use of these herbs. Hence, it is high time that further research on pharmacokinetics, dose rate, long and/or short-term detrimental effects of these agents on the metabolic rate of related body tissues should be done, before marketing them as large/ small ruminant medicine. Again, it is imperative to probe into actual mode of action in order to exploit the compounds responsible for the observed galactopoetic activity by focusing on the target organ. The research dents on indigenous herbal products/medicinal plants as galactogogues need patent rights in order to have foreign recognition [10]. Worldwide figure presents, hundreds of plants used as galactogogue have estrogenic, oxytocic or other reproductive hormonal effects in laboratory conditions [37]. Before selecting any galactogogues, a report of complete animal health history as well as its productive and reproducing.
ctive status, including any medical conditions, history of parity, current medications is important before administration of any drug. The therapeutic approach is to detect the root cause of the agalactia so as to administer a medication or herb that seems to target the same.

**Anti-galactogogues**

Certain herbs, termed as anti-galactogogue, are contraindicated during lactation as their constituents are excreted as milk residues which can be toxic. Alkaloids containing plants like Alkanet (*Alkanna tinctoria*), BORAGE (*Borago officinalis*), Butterbur (*Petasites hybridus*), Coltsfoot (*Tussilago farfara*), Comfrey (*Symphytum officinale*), Joe-pye weed (*Eupatorium purpureum*), and Indian snake root (*Rauwolfia serpentine*) are highly hepatotoxic and are readily excreted through milk [19]. Alder buckthorn (*Rhamnus frangula*), Cascara sagrada (*Rhamnus purshiana*), Aloe (*Aloe barbadensis*), Alder buckthorn (*Rhamnus frangula*), Bearberry (*Arctostaphylos Urv urst*), Senna leaf (*Cassia spp.*), Black Cohosh (*Cimifuga racemosa*), Prickly ash bark (*Zanthoxylum americanum*) and Pulsatilla plant (*Anemone pulsatilla*) contain some toxic irritants as well as rich in anthraquinones and hence act as intestinal irritants and purgatives causing adverse effect on digestive system. Dong Quai (*Angelica sinensis*) has an estrogenic effect, so it is not recommended in milch animals [38].

Antigalactagogue herbs (opposite to herbs with galactagogue properties) viz. Bilberry (*Vaccinium myrtillus*), Black Walnut (*Juglans nigra*), Mugwort (*Artemisia vulgaris*), Osha (*Ligusticum porteri*), Parsley leaves (*Petroselinum crispum*), Peppermint oil (*Mentha piperita*), Sage (*Salvia officinalis*) and *Helicteres isora* *L.* prevent or decrease the secretion of milk and are recommended against postpartum mastitis and lessen engorgement [39-42]. But, still yet the mechanisms of actions of above plants/herbs need experimental actions for confirmation.

**Conclusion**

Galactogogues provide a rich and ever-evolving research topic at prevailing time. Use of plant and synthetic products to enhance lactation are widespread and numerous literatures in the medical sector have been published about the efficacy of various galactogogues. We have documented an overview of the most widely used plants that are used as galactogogues in veterinary practice. Still there exists a further need to deepen the horizon of research on the phytochemical composition of the herbs, their mode of action, and furthermore to assess the lethal dose as well as explain how further studies might be conducted to bridge the gap between common uses and lack of studies on the safety and effectiveness of these herbs in lactation. Hence, an optimal standardization and dosing recommendations of these herbal galactogogues by an explicit clarification in pre-clinical and clinical studies through *in-vitro* and *in-vivo* experimentations is needed before they are being harvested as a potential new drug in the market.

**Authors’ contributions**

IM prepared the initial version of the manuscript. MRS and DJ assisted in literature collection and edited the final manuscript. IM, MRS and PCB drafted and revised the manuscript for critical scientific corrections. All authors read and approved the final manuscript.

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**Competing interests**

The authors declare that they have no competing interests.

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