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REVIEW ARTICLE
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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 tranditional 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-hypophyseal-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.

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

Common name	Botanical name	Family	Parts used	Chemical constituents	Effects	Reference
Alfalfa	*Medicago sativa*	Fabaceae	Leaves	Alkaloids (stachydrine, 1-homostachydrine), coumesterol, flavonoids, iso-flavonoids, carotenoids, phenolic acids and minerals (Fe, Ca, K, P and Zn).	Estrogenic and lactogenic stimulant, presence of "TRH-like material " in turn stimulates prolactin release.	[7]
Anise	*Pimpinella anisum*	Umbelliferae	Seeds	*Trans*-anethole, estragole, *γ*-hymachalen, *p*-anisaldehyde, and methyl chavicol.	Anti-spasmodic, mildly estrogenic.	[8,9]
Black cohosh	*Cimicifuga resebosa*	Ranunculaceae	Root (dried, not fresh)	Triterpene glycosides (actein, cimigoside, cimifugine, macrotin, racemoside), isoflavones (formononetin) and isoferulic acid.	Emmenagogue, anti-spasmodic, alterative, nervine, hypotensive.	[10]
Black seed/ Black cumin	*Nigella sativa*	Ranunculaceae	Seeds	Nigellicine, nigellidine, thymol , nigellimine oxide, thymoquinone, di-thymoquinone, oxy-coumarin, thymo-hydroquinone, nigellone, arvacrol, α-hedrin, flavinoids, steryl-glucoside, tannins, essential fatty acids, essential amino acids, ascorbic acid and minerals (Fe and Ca).	Analgesic, anti-inflammatory, galactopoetic, improves FCR in buffalo and lambs.	[11]
Blessed thistle	*Cnicus benedictus*	Asteraceae	Flowering tops, leaves, seeds	Sesquiterpene lactone (cnicin).	Effective galactogogue with red raspberry and fenugreek acts as ruminotorics and increases blood flow to the mammary gland improves post partum hemorrhage.	[8]
Borage	*Borago officinalis*	Boraginaceae	Leaf and flower	Pyrrolizidine alkaloids (amabiline, supinine, lycopsamine, intermedine), choline, minerals (K and Ca) and oil rich in ω_3 fatty acids.	Effective galactagogue, restorative effect on adrenal cortex.	[12]
Caraway	*Carum carvi*	Umbelliferae	Seeds	Andlimonene, thujone, pinen, carvone, dihydrocarvone, carveol, dihydrocarveol, flavonoids (quercetin), limonene, germacrene D and trans-dihydrocarvone.	Post-partum galactagogue and lactational herbs.	[13]
Chaste berry	*Vitex agnuscastus*	Verbenaceae	Fruit	Iridoid glycosides (agnoside, aucubin) flavonoids (casticin, kampferol, quercetagetin, vitexin), progesterone, hydroxy-progesterone, testosterone, epi-testosterone, androstenedione, alkaloids (viticin), volatile oil (1,8-cineol, limes, linalool, terpinyl acetate, alpha pinenes, beta pinenes), palmitic acid, oleic acid, linoleic acid and stearic acid.	Normalizing effect on progesterone function of the pituitary gland stimulates prolactin production, uterine tonic, and hyper-prolactinemia.	[8]
Dill	*Anethum graveolens*	Umbelliferae	Seed	Carvone, dihydro-carvone, eugenol, limonene, phellandrene, anethole, carvole, myristicin, *x*-pinene, flavonoids (kaempferol, vicenin blucuronide), coumarins (esculetin, scopoletin, bergapten, umbelliferone) and xanthone (dillanoside).	Anti-spasmodic, anti-inflammatory, galactogogue. Contraindicated for low sodium diets.	[14]
Fennel	*Foeniculum volgare*	Apiaceae	Seed	Anethole, fenchone, flavonoids and coumarins.	Carminative, anti-spasmodic, anti-inflammatory, promote milk ejection, stimulates milk flow, and increases udder milk production. Contraindicated due to its allergic and estrogenic effects.	[8]
Fenugreek	*Trigonella foenumgraecum*	Fabaceae	Seed	Elemene, selinene, furanone, dihydro-benzofuran, muurolene, dihydro-actinidiolide, Alkaloids (trigonelline, gentianine, carpaine), saponins (diosgenin, yamogenin, gitogenin, tigogenin), flavonoids (vitexin, isovitexin, orientin, vicenins, quercetin, luteolin) and galactomannan.	Anti-inflammatory, anti-spasmodic, emmenagogue, galactogogue, hypotensive, oxytocic, stimulate milk ducts of mammary gland tissue, promotes milk ejection, Contraindicated in pregnancy due to its uterotonic effect.	[7,8,15]
Levant cotton	*Gossypium herbaceum*	Malvaceae	Root	Alkaloids, flavones, β-sitosterol, α-amyrin, terpene and naphthalene derivative gossypol.	Abortifacient, uterotonic, ecbolic, galactogogue.	[7]
Goat's Rue	*Galegas officinalis*	Papilionaceae	Dried aerial parts	*Galegin,* peganine, flavonoids and saponins.	Stimulate breast growth, improve milk yield, moderately regulate estrogen levels, toxic to sheep.	[7,8]
Ixbut	*Euphorbia lancifolia*	Euphorbiaceae	Dried aerial parts	Sesquiterpenes, eleinol, ingenol, 3-angelate, kaempferol, scopoletin, kaempferol 3-O-glucopyranoside, quercetin, vanillic acid, p-hydroxycinnamic acid, protocatechuic acid, dihydroxycoumarin, β-sitosterol, brevifolin, daucosterol, piceatannol, jolkinolide β, D-glucopyranoside, octacosyl cis-ferulate, ethylbrevifolin carboxylate, octacosyl trans-ferulate and chrysophanol.	Ancient Mayan galactogogue, double the volume of milk, no effect on mammary gland, milk composition.	[16]
Jivanti	*Leptadenia reticulate*	Asparagaceae	Root	Leptadenol, triacontane, cetyl alcohol, leptidin-1 and sitosterol.	Increase milk yield and correct milk irregularity.	[3,17]
Marshmallow	*Althaea officinalis*	Malvaceae	Root and leaf	D-glucan, diosmetin glucosides, flavanoids (kaempferol, quercitin), polyphenolic acids (syringic, caffeic, salicyclic, vanillic), pectin, asparagine and tannins.	Synergistic galactogogue effect with alfalfa, blessed thistle and fenugreek.	[18]

Table-1: Continue from page no.

Common name	Botanical name	Family	Parts used	Chemical constituents	Effects	Reference
Milk thistle	*Silybum marianum*	Asteraceae	Leaves and seeds	Flavonoids/ flavonolignans, silymarin (silybin, silibinin, silidianin, silychristin, apigenin, isosylibin, dehydrosilybin, deoxysilycristin, deoxysildianin, siliandrin, silybinome, silybonol, silyhermin, neosilyhermin), myristic, oleic, palmitic and stearic acids.	Galactogogue, cholagogue, increase milk supply, side effects include allergy and diarrhoea.	[7,8]
Stinging Nettle	*Utica diotica*	Urticaceae	Aerial parts	Vitamin (A, B complexes, C, D), minerals(Fe, P, K, S, Mg), fiber, acetylcholine, histamine and serotonin.	Stimulate milk production, increase the flow of milk.	[7]
Raspberry/ Red raspberry	*Rubus idaeus*	Rosaceae	Leaves and fruits	Polypeptides, flavonoids, glycosides of kaempferol and quercitin, tannins, pectin, fructose,volatile oil, citric acid, malic acid, vitamin (A, B complex, C, E), and minerals (Fe, Ca, K, P).	Galactogogue effect uncertain, help the uterus to recover and regain its size and shape quickly following parturition.	[19]
Red Clover	*Trifolium pratense*	Papilionaceae	Flower	Isoflavones (biochanin A, daidzein, formononnetin, genistein, pratensein, trifoside) flavonoids (pectolinarin, trifoliin, isoquercitrin), clovamides; L-Dopa-caffeic acid conjugates, coumarins (coumestrol, medicagol, coumarin), galactomannan, resins, minerals, vitamins and phyto-alexins.	Estrogenic effect, mild stomachic, use non-fermented only, contradicted in pregnancy.	[20]
Saw Palmetto	*Serenoa repens*	Palmae	Fruit	Polysaccharides (galactose, arabinose), Vitamin (B-complex, C, D), minerals (Mg, Mn, Fe, Si, Zn), 25% fatty acids (caproic, lauric, palmitic) 75% neutral fats and sterols.	Excellent treatment for agalactia, mammary gland enlargement.	[21]
Shatapuspha	*Anethum sowa*	Umbelliferaceae	Flower head	Anethole, estragole, fenchone, β-sitosterol, carvone, limonene, eugenol, α-phellandrene, flavonoids, coumarins, tri-terpenes, phenolic acids and umbelliferones.	Galactogogue, anethole is responsible for sedative effect.	[14]
Shatavari	*Asparagus racemosus*	Liliaceae	Root	Shatavarin1-IV, quercetin, rutin and hyperoside.	Prevent infertility and miscarriage, increase milk supply and weight of the mammary glands, inhibits involution of lobulo-alveolar tissue and maintained milk secretion.	[3]
Vervain	*Verbena officinalis*	Verbenaceae	Aerial parts	Iridoid glycosides (verbenin, verbenalin, bastatoside), tannin, volatile oils (citral, geraniol, limonene, verbenone), saponin, mucilage and alkaloid.	galactagogue	[22]
Vidarikanda	*Ipomoea digitata*	Convolvulaceae	Tuberous root	Pterocarpanone, hydroxyl-tuberosome, oxy-methyl tuberosine and pterocaspero-hydro tuberosine.	Galactogogue, cholagogue.	[23]

An effective nutritional regimen and use of herbal galactogogues act synergistically to enhance milk yield which would prompt a good augmentation in productivity of dairy herd. Herbal galactogogues act through interactions with dopamine receptors by exerting an influence through adreno-hypothalamo-hypophyseal-gonadal axis resulting in enhanced prolactin concentration and thereby augmenting milk production [6]. Yet there is another set of herbal source like alfa alfa, aniseed and raspberry act by exerting a synergistic effect by promoting appetite, controlling stress and increasing productivity as they are rich in vitamins, minerals and anti-oxidants. Oat straw, dandelion, vervain, marshmallow, lemon balm, pot marigold, chamomile are the herbal supplements those act as galactogogues, 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 galactopoesis are compiled in Table-1 [7-23].

Natural lead compounds

Phytochemical screening of plants extracts either with organic or aquous solvents has revealed the presence of numerous active principle including α-linolenic acid, stearidonic acid, ascorbic acid, domperidone, metoclopramide, risperdal, sulpiride (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, isopelletierine, anaferine, andrograpolide, pregnane derivatives etc which contribute to galactapoetic 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-modulative, and cardio-protective effect [25]. Although, phytophenols 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 galacatagogues under commercial use

Anifed [34], Galog, Galactin, Immu-21 [35], Leptaden, Payapro [36], Ruchamax (appetizer, resto-

Table-2: Phytochemical groups with effect on galactopoiesis [26-33].

Lead compound	Mechanism of action	References
Alkaloids	Help in letting down of milk.	[8,26]
Isoflavones	Increases milk yield as well as fat, protein and lactose percentage of milk.	[27]
Polyphenols	Improve milk yield, concentration of milk protein and ovulation rate, prevent bloat in cattle, reduce gastrointestinal nematode numbers and fly strike.	[28]
Saponin	Ruminotoric, improves the health status as well as productivity.	[29]
Stearidonic Acid,	Improve rumen bio-hydrogenation with proper ruminal protection to achieve impressive increases in the omega 3 fatty acids in the milk.	[30]
α-linolenic acid	Ruminotoric, alter the milk fat composition and the oxidative stability of the fat as well.	[31]
Tannins	Anthelmintic, Ruminotoric, improves protein digestion and health status.	[32,33]

Table-3: Commercial drugs available in market used as galactogogues.

Brand name	Composition as per the label	Dosage	Company
Alfimilk	Prebiotic, rumen protected vitamins, ionophores.	10g OD	Vetnex
Ksheeradhara	Calcium lactate gluconate, lactobacillus sp. vitamins, proteins.	50g daily	Brilliant
Lactofat	*Asparagus racemosus, Leptadena reticulata, Nardostachys jatamansi*, lactobacillus species, vitamins.	30g per day	Dosch
Lepta milk forte	Herbal aqueous extract, vitamins, minerals.	30-40ml bid	Concept
Payapro	*Leptadena reticulata, Nigella sativa, Foeniculam vulgare,Pueraria tuberosa, Glycerriza globra, Cuminum cyminum* and *Asparagus racemosus.*	4 boli daily	Ayurvet
Ruchamax	*Allium sativum*, *Azadirachta indica, Calotrophis orocera, Centratherum anthelmenticum, Eclipta elba, Commiphora mukul, Embelica ribes, Piper longum*, *Picorrhiza kurora* and *Zinziber officinale.*	15 gm OD	Ayurvet
Leptaden	*Asparagus racemosus and Leptadena reticulate.*	10-15 tabs bid	Alarsin
DudhNahar	*Acacia catechu, Acacia nilotica, Anethum graveolens, Asparagus racemosus, Coriandrum sativum, Cuminum cyminum, Foeniculum vulgare, Leptadena reticulata, Lepidium sativum, Celosia argentea, Sesamum indicum and Tinospora cordifolia* with jiggery (unrefined sugar) and natural clay.	40 biscuits daily herbal	Abhumka

rative, carminative, stomachic and tonic), and Calshakti platina [3] are some of the herbal galactogogues manufactured by different pharmaceuticals to safeguard the health of the animal and the ultimate user. *Leptadenia retiulata* (Jivanti) and *Asparagus racemosus* (Shatavari) are very commonly incorporated in the preparation of these pharmaceuticals due to their promising effect. Some of the commonly used polyherbal preparations along with their dose, brand name and name of the manufacturing company are described as in Table-3.

Besides above, other herbal preparations like Dugdhdan (Cattle remedies), Lactovet and Milkvet (Rakesh), Lactomore (Indian herbs), Galactin Vet (Himalaya), Galog bolus and Milk It (Natural remedies), Galactomax (Century), Increlac bolus (TTK), Milkfit and Milkmore (Arosol), Milkomax (Neospark), Milktab (Cipla) and Lactoboon (Lyka) are frequently used by goalas to boost their milk production.

Use and future prospect of herbal galactogogues

As many herbal plants contain large number of chemical active principles, having galactogenic properties; can be used as herbal medicine for of 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 (*Galega officianalis*), Milk thistle (*Silybum marianum*), Giant Cane (*Arundo donax*), Abuta or Laghu Patha (*Cissampelos pareira*), and extracts of Bhringraj *or* false daisy (*Eclipta alba*), Black Nightshade (*Solanum 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 galactogogue, a report of complete animal health history as well as its productive and reprodu-

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 ursi*), Senna leaf (*Cassia* spp.), Black Cohosh (*Cimifugia 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 conformation.

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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