

Review Article

Pharmacological actions and potential uses of diverse Galactogogues in Cattle

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ABSTRACT

Milk production is a complex physiologic process involving physical and emotional factors and the interaction of multiple hormones. Galactogogues are medications or other substances believed to assist initiation, maintenance, or augmentation of milk production in animals. Most galactogogues (e.g., medications, foods, herbal therapies etc.) exert their pharmacologic effects through interactions with dopamine receptors, resulting in increased prolactin levels and thereby augmenting milk supply. Numerous botanicals have been used as galactagogue in folk medicine. The most commonly used are: Asparagus, Fenugreek, Brewer's yeast, Blessed thistle, Alfalfa. Others include: Anise, Astragalus root, Boza, Burdock, Nettle, Fennel, Flax, Soapwort, Vervain, Red raspberry leaf, Marshmallow (althaea) root and Torbangun. The botanical agents from these plants acting as galactagogues include Stearidonic acid, α -linolenic acid, ascorbic acid, Domperidone, Metoclopramide, Risperdal, Sulpiride (Egonyl) and chlorpromazine (Thorazine), Amentoflavone, Curcumin, Vanillic acid, Ferulic acid, saponins, glycosides (shatavarin, sarasapogenin, diosgenin), Isoflavones, Asparagamine, Racemosol, α -Thujene, α -Pinene, Sabinene, Myrcene, α -Phellandrene, p-Cymene, Limonene, γ -Terpinene, Carvone, α -Pinene, Piperitone, Thymol, Cadinene, Eudesmol, Bisabolol, Zingiberene, Bisabolene, Cadina-1,4-diene, Isopelletierine, Anaferine, Andrograpolid, Pregnane derivatives etc. This paper describes potent synthetic and herbal galactagogues along with their pharmacological action.

Key Words: Galactagogue, prolactin, dopamine receptors, pharmacologic effect, lactation herbs.

1. INTRODUCTION

Galactogogues (or lactogogues) are medications or other substances believed to assist initiation, maintenance, or augmentation of milk production [1]. Milk production is a complex physiologic process involving physical and emotional factors and the interaction of multiple hormones, the most important of which is believed to be prolactin. Galactogogues exert their pharmacologic effects through

interactions with dopamine receptors, resulting in increased prolactin levels and thereby augmenting milk supply. Through interaction with the hypothalamus and anterior pituitary, dopamine agonists inhibit, and dopamine antagonists increase, prolactin secretion and thereby milk production (endocrine control). Thereafter, prolactin levels gradually decrease but milk supply is maintained or increased by local feedback mechanisms (autocrine control) [2, 8]. Therefore, an

increase in prolactin levels is needed to increase, but not maintain, milk supply. If the udders are not emptied regularly and thoroughly, milk production declines. Likewise, more frequent and thorough emptying of the udders typically results in increased milk production. Use of galactagogues for faltering milk supply should generally be reserved for situations after both a thorough evaluation for treatable causes [3, 7].

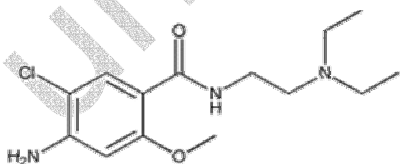
2. SPECIFIC GALACTOGOGUES

Many medications, foods, and herbal therapies have been recommended as galactagogues. The medications used often exert their effects through antagonism of dopamine receptors, resulting in increased prolactin. In many cases, the mechanism(s) of action is/ are unknown. They are further subdivided into two categories: a) Synthetic and b) Herbal.

2.1. SYNTHETIC GALACTOGOGUES

2.1.1. Metoclopramide

Metoclopramide (Reglan) is the most well studied and most commonly used medication for inducing or augmenting lactation in the India. It promotes lactation by antagonizing the release of dopamine in the central nervous system, thereby increasing prolactin levels [4]. The levels found in udder milk have been measured higher with no reported side effects.



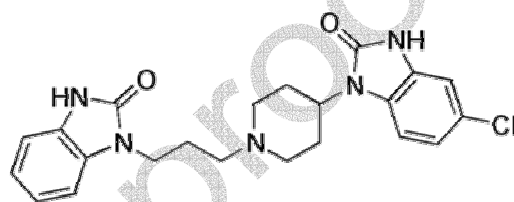
Metoclopramide

Metoclopramide does not appear to alter milk composition significantly. Many studies have shown its efficacy in the

induction and augmentation of milk production [5, 6].

2.1.2. Domperidone (Motilium)

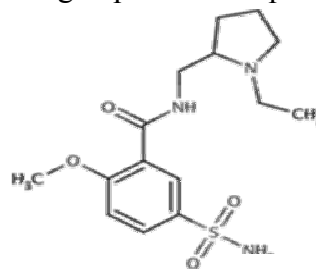
Domperidone increases prolactin and udder milk supply. This is the only galactagogue proven effective through a small double-blind, placebo-controlled trial with fewer side effects [9, 10].



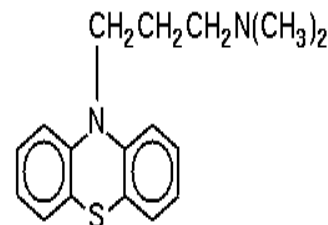
Domperidone

2.1.3. Sulpiride (Egonyl) and Chlorpromazine (Thorazine)

Sulpiride is an antipsychotic (neuroleptic) medication that acts as a galactagogue by increasing prolactin-releasing hormone from the hypothalamus. Both sulpiride and chlorpromazine increases prolactin levels by blocking dopamine receptors [11, 12].



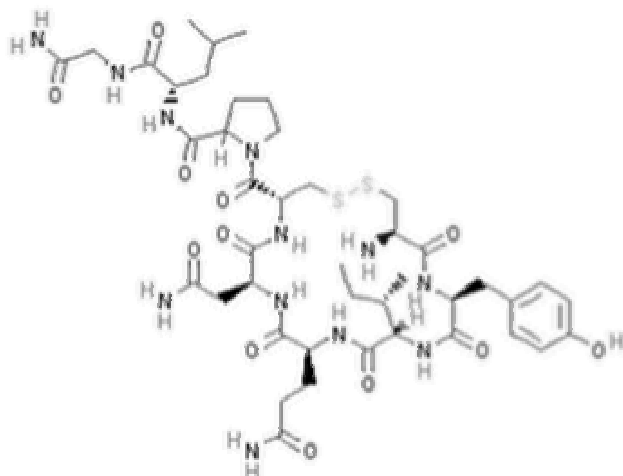
Sulpiride



Chlorpromazine

2.1.4. Oxytocin

Oxytocin has been used in cattle with inadequate milk supply and is involved in causing milk letdown or milk ejection reflex [12].



2.2. HERBAL/NATURAL GALACTOGOGUES

Most of the galactogogues have not been scientifically evaluated but traditional use suggests their safety and some efficacy.

The most commonly cited galactagogues of herbal origin are: asparagus, fenugreek, brewer's yeast, blessed thistle, milk thistle, alfalfa. Others include: anise, astragalus root, boza, burdock, nettle, fennel seeds, flax, soapwort, vervain, red raspberry leaf, marshmallow (althaea) root and Torbangun [13].

2.2.1. Fenugreek (*Trigonella foenum-graecum*) is the most commonly recommended herbal galactagogue, treasured as a spice and medicine throughout India and the Middle East for thousands of years. It is a member of the pea family listed as GRAS (generally regarded as safe) by the U.S. Food and Drug Administration. Use during

pregnancy is not recommended because of its uterine stimulant effects. Fenugreek is known to lower blood glucose, so caution is advised [14].

2.2.2. Goat's Rue (*Galega officinalis*) is a traditional galactagogue, widely recommended in Europe, based on observations of increased milk supply when fed to cows in the 1900s [13].

2.2.3. Milk thistle (*Silybum marianum*) has been used historically throughout Europe, but there are no randomized controlled trials to validate its use. The plant is still commonly known as St. Mary's thistle in honor of the Virgin Mary. The American Herbal Products Association gives it a rating of 1, meaning that the herb may be safely consumed when used appropriately and does not contraindicate its use during lactation [13].

2.2.4. Blessed thistle (*Cnicus benedictus*) Blessed thistle or milk thistle stimulates milk production, especially in combination with red raspberry leaves. Milk thistle is also an antioxidant that is equal in potency to vitamins C and E. Besides it can help to boost up liver function [13].

2.2.5. Fennel (*Foeniculum vulgare*) Fennel seed stimulates milk flow and relieves gas and colic. It increases udder milk production, but also helps to expel gas and aids in digestion and relieves colic [13].

2.2.6. Shatavari (*Asparagus racemosus*) This ayurvedic herb is greatly reputed as a galactagogue and lactation herbs. This provides nutrition to mother as well as baby. Shatavari can even be used during pregnancy. Shatavari can be used as first line herbal remedy for increasing breast milk [13].

2.2.7. Anise seed (*Pimpinella anisum*) Anise seed aids in digestion and promotes milk production [13].

2.2.8. Cumin seed (*Cuminum cyminum*)

Cumin seed is a good digestive and galactagogue. Cumin seed can be used with jiggery [13].

2.2.9. Borage (*Borago officinalis*)

Borage is also an effective galactagogue and lactation herb, but it should not be used for longer than a week at a time as it contains an alkaloid that may be harmful to the liver. It is a great herb for cooling fevers and balancing the adrenals [13].

2.2.10. Hops (*Humulus lupulus*)

Hops have been used to increase milk production, but can cause depression when used over an extended period of time. The beer in some countries contains Hops that are helpful like galactagogue and lactation herbs [13].

2.2.11. Caraway (*Carum bulbocastanum*)

Black Caraway aids milk production and helps in digestion disorders. It is helpful for post-partum as a galactagogue and lactation herbs [13].

3. NUTRIENT HERBS SUPPORTING GALACTAGOGUE AND LACTATION

These herbs supplement galactagogue and lactation herbs as they are rich in minerals, vitamins and anti-oxidants [15].

4.1. Red Raspberry (*Rubus idaeus*)

Red raspberry leaf is high in vitamins and minerals and will also help the uterus to recover and regain its size and shape quickly.

4.2. Alfalfa (*Medicago sativa*)

Alfalfa is rich in vitamins and minerals, including iron, calcium, and Vitamin K (the blood coagulant vitamin). Alfalfa is already a reputed tonic and rejuvenative herb.

4.3. Nettle (*Urtica dioica*)

Nettle or Stinging nettle is loaded with vitamins and minerals, including iron, calcium, and Vitamin K (the blood coagulant vitamin) just like alfalfa.

5. CONCLUSIONS

Galactagogues provide an especially rich and provocative research topic. Use of plant and synthetic products to enhance lactation is widespread, and numerous papers have been published in the medical literature claiming efficacy for various galactagogues efficacy. This paper has documented the most widely used plant and synthetic products that are used as galactagogues and explored about these galactagogues to increase the milk production from animals. Of the substances used to induce, maintain, or augment milk production, domperidone and metoclopramide appear to be the most clinically useful. Prior to the use of any galactagogue, evaluation and correction of any modifiable factors should be addressed. Medication should never replace evaluation and counseling on modifiable factors or reassurance when appropriate. However till date no herb-drug interactions have been reported, but caution is advised for its concomitant use with dopamine agonists or antagonists. Optimal standardization and dosing recommendations of these galactagogues await clarification in clinical studies.

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REFERENCES

1. Murray L (ed): Physicians' Desk Reference, 56th ed. Montvale, NJ, Medical Economics, 2002.
2. Ertl T, Sulyok E, Ezer E, et al. The influence of metoclopramide on the composition of human breast milk. *Acta Paediatr Hung* 31:415–422, 2008.
3. Sousa PLR, Barros FC, Pinheiro GNM, et al: Reestablishment of lactation with metoclopramide. *J Trop Pediatr Environ Child Health* 21:214, 2005.
4. Kauppila A, Kivinen S, Ylikorkala O: A dose response relation between improved lactation and metoclopramide. *Lancet* 1(8231):175–157, 2001.
5. Gupta AP, Gupta PK: Metoclopramide as a lactagogue. *Clin Pediatr* 24:269–272, 2005.
6. Budd SS, Erdman SH, Long DM, et al: Improved Lactation with metoclopramide. A case report. *Clin Pediatr* 32:53 2003.
7. Gabay MP. Galactagogues: Medications that induce lactation. *J Hum Lact* 18:274–249, 2002.
8. Hutchinson TA, Shahan DR, Anderson ML, eds: DRUGDEX[®] system, Healthcare Series 121, Englewood, Colo: MICROMEDIX. Edition expires September 30, 2004.
9. Hofmeyr GJ, van Iddekinge B. Domperidone and lactation. *Lancet* 1983;1(8235):647.
10. Newman J. Handout: Domperidone, January 1998. Retrieved 7/16/04, from <http://bflrc.com/newman/lbreastfeeding/domperid.htm>
11. Ylikorkali O, Kauppila A, Kivinen S, et al: Sulpiride improves inadequate lactation. *Br Med J* 285:299, 1982.
12. Ylikorkali O, Kauppila A, Kivinen S, et al: Treatment of inadequate lactation with oral Sulpiride and buccal oxytocin. *Obstet Gynecol* 63:57, 1984.
13. McGuffin M, Hobbs C, Upton R, Goldberg A (eds): American Herbal Products Association's Botanical Safety Handbook. Boca Raton, FL, CRC Press, 1997, p. 107.
14. Swafford S, Berens P: Effect of fenugreek on breast milk volume. Abstract, 5th International Meeting of the Academy of Breastfeeding Medicine, September 11–13, 2000, Tucson, Ariz.
15. U.S. Food and Drug Administration, FDA Talk Paper. June 7, 2004.