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Medicinal plants with lactogenic effect: A review

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Abstract

Milk production is essential for optimal feeding of infants. The most common lactogenic drugs are dopamine 2 antagonists, oxytocin, recombinant bovine somatotropin (rBST), thyrotropin releasing hormone (TRH) and estrogenic drugs. However, many medicinal plants possess lactogenic effects in humans and animals. The current review focused on medicinal plants with lactogenic effect as natural sources of galactogogues characterized by efficacy and safety.

Keywords: Galactogogues; Lactogenic; Medicinal Plants; Prolactin; Milk Production

1. Introduction

Milk production is essential for optimal feeding of infants with direct effect on growth, development, and health in neonatal period [1].

Galactogogues are substances used to induce, maintain, and increase milk production. Most common drugs used to enhance milk productions were dopamine 2 antagonists (metoclopramide, domperidone, chlorpromazine, sulpiride), oxytocin, recombinant bovine somatotropin (rBST), thyrotropin releasing hormone (TRH) and estrogenic drugs [2].

The probable mechanism of action of dopamine 2 antagonists, including binding of antagonist to dopamine 2receptor in the pituitary, induce prolactin gene expression, increased blood prolactin, increased the synthetic rate of milk protein and stimulate the proliferation of mammary epithelial cells [3-7].

Oxytocin induces contraction of the myoepithelial cells, via a G protein receptor. It also induces exocytosis of milk in mammary epithelial cells by increasing intracellular calcium. Both increase milk production [8-10].

The recombinant bovine somatotropin (rBST) possessed direct effects on basal metabolic rate and breast parenchyma; the effect on the mammary epithelial cells is mediated by rBST/ST-R complex, which stimulates JAK2/STAT5 pathway, promotes and upregulates IRS/PI3K/(AKT/PKB)/mTOR and Ras/Raf/(MAPK/ERK) pathways which induce cell proliferation and survival and increase milk protein synthesis [11-14].

Estrogen possesses D2R inhibition and induces prolactin gene expression in anterior pituitary lactotrophic cells and milk production in mammary epithelial cells[915-19].

Lactogenic effect of many plants has been studied and there is evidence that they increased milk production and safe in humans and animals [20-23].

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2. Medicinal plants with lactogenic effect

2.1. *Allium sativum*

Allium sativum is given to enhance gestation and lactation. A naturally prepared galactagogue mixtures containing garlic increased prolactin level and milk production [24-25].

2.2. *Arundo donax*

A commercial bolus made of a mixture of several powdered plants including *Arundo donax* improved milk yield in dairy cows, which was attributed to the presence of components reported to be galactogogues[26-28].

2.3. *Asparagus racemosus*

The milk yield and fat corrected milk yield were found to be significantly higher ($P<0.05$) in *Asparagus racemosus* supplemented cows. Average milk fat%, SNF%, total solid% and protein% were significantly higher [29].

A randomized double-blind clinical trial showed that *Asparagus racemosus* possessed galactogogue effect in lactating mothers. The oral administration of *Asparagus racemosus* led to more than three-fold increase in the prolactin hormone level of the treated subjects as compared to the control group. The primary findings were corroborated by the secondary outcome measures(mothers' weight, babies' weight, subjective satisfaction of mothers and well-being and happiness of babies) and were found to be statistically significant ($p < 0.05$) [30].

A multicentric, randomized, double blind, placebo controlled parallel study showed that *Asparagus racemosus* increased serum prolactin levels (primary outcome variable), increased milk production and enhanced weight gain of infant [31].

2.4. *Coleus amboinicus*

Coleus amboinicus supplementation increased breast milk production without compromising the nutritional quality of the breast milk. Lactating women receiving *Coleus amboinicus* supplementation had a 65% increase in milk volume during the last two weeks of supplementation (from Day 14 to Day 28). The residual effects of *Coleus amboinicus* supplementation were seen even after the supplementation had ended for one month [32].

2.5. *Cyperus rotundus*

The lactogenic property of aqueous extract of *Cyperus rotundus* rhizome was evaluated it rats. Oral administration of 300 and 600mg of the extract induced about 23% and 40% more milk respectively in experimental rats as compared to the control group. Weight gain by pups and mother rats of treated groups were significantly higher following administration of the extract. Protein and carbohydrate content of mammary gland tissue were also significantly more than control group. The extract stimulated the synthesis of prolactin significantly and enhanced lobuloalveolar development with milk secretion [33].

2.6. *Euphorbia hirta*

The powdered plant given to female guinea pigs before puberty, increased the development of the mammary glands and induced secretion [35-36].

Euphorbia hirta aqueous leaf extract administration increased milk production in lactating rats. At a dose of200 mg/kg, the extract was significantly increased milk production (40.92%) ($p< 0.0001$). The extract at a dose 200 mg/kg also significantly increased the biosynthesis of prolactin in virgin rats ($P < 0.0001$). Histological study revealed that the extract induced the development of the lobuloalveolar system of the mammary glands [37].

2.7. *Falcaria vulgaris*

The effects of *Falcaria vulgaris* on the on the milk production parameters was investigated in female rats. It significantly increased diameter and number of alveoli, prolactin hormone level and prolactin receptor gene expression compared to control group ($p < 0.05$) [38].

2.8. *Ficus semicordata*

9.4 kg of fodder eaten per day by buffaloes increased milk yield by 0.36 kg day [39].

2.9. *Gossypium species*

Cottonseed feeding enhances the milk production in buffaloes significantly (P<0.0l)in comparison to commercial concentrate mixture fed control group animals [40-42].

2.10. *Hibiscus sabdariffa*

The lactogenic effect of ethanolic seed extract of *Hibiscus sabdariffa* was investigated by administering extract and metoclopramide in albino rats. The extracts were administered at varying doses (200, 400, 800 and 1600mg/kg) for six days orally. The ethanolic seed extract of *Hibiscus sabdariffa* possessed lactogenic effect. It caused significant increase (p<.01) in serum prolactin levels in a dose dependent manner. The doses of 800 and 1600 mg/kg seemed more effective with serum prolactin levels of 15.74±0.8 and 17±0.6 respectively, compared to control 6.68 ±0.5 ng/ml [43-44].

2.11. *Lepidium sativum*

The total milk yields for the period of 5 months in the buffaloes received diet supplemented with *Lepidium sativum* seed powder were increased dose dependently [45-46].

Lepidium sativum seeds were usually supplemented in the diet of lactating women to increase the milk secretion during post-natal period [47-49].

2.12. *Medicago sativa*

Medicago sativa feed increased milk yield, lowered fat, and increased milk protein in dairy cows [50-51].

2.13. *Moringa oleifera*

Moringa oleifera capsule intake increased milk production by increasing serum prolactin levels. It caused significant increase in the weight of infants [52-55].

2.14. *Musa paradisiaca*

Rats treated with aqueous extract produced higher milk than control and ethanol groups. Aqueous extract increased milk production by 25%, while petroleum ether extract by 18%. The mean of yields produced by the rats during suckling period for aqueous, petroleum ether, ethanol extracts and control were 4.62±2.45, 4.37±1.93, 3.65±1.89 and 3.69±1.79 g/pup/ day [56].

2.15. *Nigella sativa*

The galactagogue action of *Nigella sativa* seeds was investigated in mice. Lactating mice were switched onto *Nigella sativa* containing diet from the day of labour and for 15days.*Nigella sativa* significantly (P<0.0l) increased serum prolactin level and the weight of the Litter compared with control group. Breast tissues of lactating mice kept on *Nigella sativa* contain ing diet showed larger acini, thicker epithelia and hyperactivity [57].

The galactagogue effect of *Nigella sativa* was also studied in female rats. The aqueous (0.5 g/kg) and ethanolic extracts (1 g/kg) increased milk production significantly ($p < 0.001$), producing about 31.3% and 37.6% more milk than control, respectively. The pups gained more weight with the aqueous (0.5 g/kg, $p < 0.01$) and ethanolic extracts (1 g/kg, $p < 0.05$) [58].

2.16. *Pimpinella anisum*

The effect of aqueous and ethanolic extracts of the seeds on milk production in rats was evaluated by measuring the pups' weights during the suckling period. The aqueous (1 g/kg) and ethanolic extracts (1 g/kg) increased the milk production significantly ($p < 0.001$), with about 68.1% and 81% more milk being produced, respectively. The pups gained weight during the study period with the aqueous (0.5 and 1 g/kg, $p < 0.05$) and ethanolic (0.5 and 1 g/kg, $p < 0.01$) extracts [59].

2.17. *Phoenix dactylifera*

Date juice increases milk production in 20 breastfeeding mothers. Breast milk production after consuming date palm juice was significantly higher than before consuming (Þ<0.001) [60].

Date fruit consumption was beneficial for promoting and increasing breast milk quantity in breastfeeding mothers. Breastfeeding mothers received 10 date fruits/day showed11% increase in breast milk quantity from baseline to week 2, and a 23% increase from baseline to week 4 ($p< 0.05$)[61].

Suspension of palm fruit at doses of 1 g/kg and 2 g/kg on day 10 and day 22 of breastfeeding increased mothers prolactin significantly compared to the control group. Date consumption dose-dependently increased the insulin-like growth factor (IGF-1),in the mothers and their litters. Malondialdehyde (MDA), as a marker of lipid peroxidation, decreased and glutathione (GSH) increased due to date palm intake [62].

The effects of consumption of fenugreek herbal tea or palm dates on breast milk production were investigated in puerperal women. Breast milk volume at 3 days postpartum and percentage weight change were statistically significant either dates or fenugreek groups and control group $p<0.001$, $p=0.001$ respectively. On the seventh day, newborns in date's group showed an increase in weight while those in fenugreek or control groups were still below their birth weight ($p=0.001$)[63].

2.18. *Silybum marianum*

Women orally treated for 63 days with *Silybum marianum* standardized extract improve the daily milk production in healthy women 85.94% after delivery, without affecting milk quality. No drop out, nor unwanted effects were reported. Compliance and tolerability were also very good [64].

2.19. *Teramnus labialis*

The lactogenic activity of methanolic extract of *Teramnus labialis* fruit was investigated in female rats. Oral administration of the extract, dose- dependently increased the milk yield, body weight of pups as well as mother rat, glycogen, and protein content as well as serum prolactin and cortisol level as compared to the control animals [65].

2.20. *Trigonella foenum-graceum*

Galactagogue mix supplementation containing fenugreek enhanced breast milk production in women and increased infant birth weight gain in early postnatal days [24, 66].

Maternal galactagogue effect of herbal supplementation herbal tea containing fenugreek significantly enhanced breast milk production in mothers and enhanced fetal weight gain [67-68].

Polyherbal formula (contains extract of *Sauropus androgynous, Trigonella foenum-graceum* and *Moringa oleifera*)(52.5 and 105 mg/kg/day)significantly increased milk production of lactating rats ($p < 0.05$). The levels of mRNA expression of α-lactalbumin (LALBA) as well as aquaporin (AQP) were significantly upregulated by 105 mg/kg/day of polyherbal formula or 2.7 mg/kg of domperidone administration ($p < 0.0001$). Histopathological analysis of mammary glands shows that alveoli diameter was increase 14.59 and 19.33% at 105 mg/kg of polyherbal formula and 2.7 mg/kg of domperidone treatment, respectively [69].

The fenugreek supplemented buffaloes diet caused higher daily milk yield compared to control group. The average total milk yield (liters) of lactating buffaloes up to 12 week 28.52% higher in treatment group than the control group, with no significant difference in milk components and also no significant difference in average serum calcium, serum cholesterol, serum total protein, serum albumin and serum globulin concentrations between the groups [70].

2.21. *Vitis vinifera*

The galactagogue action of the crude phenolic extracts of the grape seed (*Vitis vinifera*) was studied in mice. The crude phenolic extract of *Vitis vinifera* seeds in a dose of significantly increased serum prolactin level in a dose dependent manner, the maximum effect was recorded when the crude phenolic extract used in a dose of 400mg/kg. The weight of the litter of the females treated with 400mg/kg was significantly ($P<0.05$) higher than those of female of control group. The section of the mammary tissue of the mice treated with crude phenolic extract of Vitis *vinifera* seed showed larger acini, thicker epithelia, and more secretory activity, compared to the mammary tissue of the lactating mice in the control group [71].

2.22. *Zingiber officinale*

Women receive dried ginger for 7 days postpartum have higher milk volume than the placebo group (191.0 ± 71.2 ml/day versus 135.0 ± 61.5 ml/day, $p < 0.01$). The mean serum prolactin levels were similar in both groups. No side effects were recorded in ginger group [72].

3. Conclusion

Insufficient milk production by mothers is a real challenge in breast-feeding of infants. There are very few recommended synthetic drugs to increase lactation. There is no enough information for clinicians and mothers to make informed decisions on the efficacy safety and usage of lactogenic herbs. The current review highlighted the medicinal plant with lactogenic effects.

Compliance with ethical standards

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