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Phytochemicals and Mechanisms of Herbal Galactagogues in Lactation

Jelsita Nova, Nadia Shabira Amima

Master's Program in Midwifery, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia

Breastfeeding is crucial for infant health and development, as well as maternal well-being, yet global exclusive breastfeeding rates remain below targets due to factors like insufficient milk supply. Galactagogues, including herbal compounds, are explored as potential therapeutic options to stimulate, sustain, and enhance milk production, though comprehensive scientific research on their phytochemical components and underlying mechanisms is still limited. This review explores the phytochemical composition and mechanisms of action of several herbal galactagogues, including *Trigonella foenum-graecum* (fenugreek), *Vitis vinifera* (grape seed), *Moringa oleifera*, and *Camellia sinensis* (green tea). These herbs exert their lactogenic effects through diverse pathways such as prolactin stimulation, oxytocin release, enhancement of mammary alveolar development, and anti-inflammatory actions in mammary epithelial cells. Key mechanisms involve hormonal regulation via the insulin/GH/IGF-1 axis, modulation of AKT/mTOR signaling, and antioxidant responses. Most evidence is derived from animal studies and molecular research, with limited clinical data available in humans.
Summary: Herbal galactagogues have promising lactogenic potential through multifaceted biochemical mechanisms, but more clinical trials in humans are needed to confirm efficacy, optimize dosing, and evaluate long-term safety for lactating women.

Keywords: Herbal galactagogues, lactation, phytochemicals, prolactin, oxytocin, fenugreek, *Moringa oleifera*, green tea

Introduction

Breastfeeding offers the best foundation for lifetime healthy nutrition and is essential for a child's health and wellbeing.[1,2] The World Health Organization (WHO) recommends exclusive breastfeeding for the first six months of life, followed by appropriate supplemental feeding until the child is two years old or older.[3] Breastfeeding supports good brain function, early development, and normal physical growth in addition to increasing child survival and offering defense against acute and chronic diseases.[4]

In addition to its benefits for infants, breastfeeding also has a major positive impact on mothers' health. Research has shown that it can help prevent postpartum hemorrhage and depression, as well as lower long-term risks including breast and ovarian cancer, heart disease, and type 2 diabetes.[4,5] Despite widespread recognition of its health benefits, the global rate of exclusive breastfeeding remains below expectations. Currently, only 37% of infants under six months are exclusively breastfed, which falls short of the global nutrition target set by the WHO to reach at least 50% by 2025.[4,6]

Corresponding Author:
Jelsita Nova
Master Program in Midwifery
Faculty of Medicine, Universitas Padjajaran
Jl. Professor Eyckman No.38, Bandung 40161, Indonesia
e-mail: jelsita24001@mail.unpad.ac.id

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Although breastfeeding is marketed as a convenient and natural way to feed babies, some women are unable to do so exclusively.[7] Several studies indicate that even when mothers are motivated, well-informed, supported, and use proper breastfeeding techniques, approximately 5% may still face difficulties in producing sufficient breast milk.[8,9] Impaired lactation may result from either insufficient lactation, in which a mother is unable to produce enough breast milk to exclusively feed her infant, or delayed lactogenesis, defined as the initiation of copious milk production occurring more than 72 hours after delivery.[7] Delaying the start of milk production increases the likelihood that breastfeeding will be stopped early and puts neonates at higher risk of excessive weight loss, which necessitates the use of baby formula.[10-12]

Women with low milk supply and adoptive mothers who wish to induce lactation may turn to galactagogues as potential therapeutic options.[13] Galactogogues refer to either synthetic substances or plant-derived compounds that help stimulate, sustain, and enhance milk production. Their effects involve intricate interactions between physical and physiological factors within the body. Many natural galactagogues are primarily used based on cultural traditions. Although some of their effects have been evaluated in both human and animal studies, there is still a lack of comprehensive scientific research exploring their phytochemical components and underlying mechanisms.[14] Thus, the purpose of this study is to analyze the phytochemical components of popular herbal galactagogues and provide an overview of the state of knowledge on their mechanisms of lactation support.

Result and Disscusion

Lactation Physiology and Hormonal Regulation

Lactation represents the final functional phase of the reproductive process. During pregnancy, the breasts develop and prepare to provide full nutrition to the baby once the placenta is released. During this complex process, the mammary glands adapt to support the infant's survival. Lactogenesis is generally divided into two major stages.

The first stage, known as secretory differentiation, occurs from mid-pregnancy (approximately 16 weeks of gestation). During this phase, the mammary glands undergo morphological and biochemical differentiation, rendering them theoretically capable of producing milk. However, secretory activity is largely inhibited by the elevated levels of circulating progesterone in most mammals and by estrogen in humans. Increases in plasma lactose and α-lactalbumin levels serve as indicators of this phase, and in some mothers, colostrum may already be expressed before delivery.

The second stage, referred to as secretory activation, begins immediately after birth in response to a rapid decline in progesterone levels following placental expulsion. This event triggers the transformation of the mammary epithelium into an active secretory state, marked by a substantial increase in milk volume within 3 to 4 days postpartum (lactogenesis II). About 100 mL of milk is produced in the first 24 hours, 500–750 mL per day by days 4–5, and 600–700 mL per day by day 8. During this process, the composition of breast milk undergoes notable changes, including decreased sodium and chloride concentrations and increased lactose levels.[18]

Lactose plays a crucial role in driving milk volume through its osmotic effect. Meanwhile, immunological components such as secretory IgA and lactoferrin experience a decrease in concentration as milk volume increases, although their absolute quantities remain relatively constant.[18] Prolactin and oxytocin are two hormones that are directly involved in lactation. During breastfeeding, there is an increase in intramammary pressure and milk flow as a reflex response to suckling. Stimulation of the neurohypophysis results in the release of oxytocin, which is then carried through the bloodstream to the capillaries in the breast, where oxytocin triggers contraction of the myoepithelium and ejects the breast milk from the ductal system.[19]

Oxytocin plays a central role in the milk ejection reflex (let-down reflex). This reflex is initiated when nipple stimulation sends neural impulses to the central nervous system, leading to the release of oxytocin from the posterior pituitary into the bloodstream. In addition to suckling, oxytocin release can also be triggered by sensory cues such as the infant's sight, sound, or smell.[17] The anterior pituitary contains specialized cells called lactotrophs, which are responsible for synthesizing prolactin. During pregnancy, the population of these cells increases to support breast development and prepare the body for lactation.

Prolactin contributes to the regulation of milk production by supporting the transcription of casein mRNA and promoting the synthesis of α-lactalbumin, a key regulatory component of the lactose synthase enzyme complex. It also enhances lipoprotein lipase activity within mammary gland tissues, facilitating While prolactin is involved in numerous physiological processes, its primary roles are to promote milk synthesis and to support the development of mammary gland structures within the breast. It facilitates the growth of mammary alveoli the sites within the gland where milk is produced and activates alveolar epithelial cells to generate key milk components, including lactose, the main carbohydrate, Including lactose, the primary milk carbohydrate, and casein, a significant milk protein.

The serum progesterone level decreases after delivery, which permits the mammary alveolar cells' prolactin receptors to be up-regulated and facilitate lactogenesis. Prolactin levels will not consistently stay high even after delivery. Milk production can be regulated because prolactin levels increase specifically in response to nipple stimulation. Prolactin levels continue to rise as long as breastfeeding is continued. Mammary gland milk production decreases and prolactin levels drop to a basal level when the mother is not nursing. Prolactin levels drop to non-pregnant levels after one to two weeks if the mother does not nurse her child.[16]

Lactogenic Phytochemicals and Their Mechanisms of Action

The effects of herbal galactagogues are thought to be linked to their phytoestrogenic activity, with certain compounds potentially mimicking the action of 17β-estradiol (E2), a natural estrogen known to stimulate the proliferation of mammary epithelial cells.[20] These compounds may promote milk ejection, enhance the protein content of milk, and support lactation by stimulating the release of prolactin.[21] One example of a herbal galactagogue is fenugreek. Fenugreek seed appears to be the most common form used as a galactagogue. It contains a wide variety of polyphenols, including quercetin, diosgenin, rutin, vitexin, isovitexin, graecunins and other saponins, and coumarin.

Fenugreek is believed to enhance milk production primarily by activating the insulin/GH/IGF-1 signaling pathway, thereby increasing the mammary gland's responsiveness to these hormones. As a result, the synthesis of milk proteins and lactose may be largely regulated via the protein Kinase B (AKT)/mechanistic Target of Rapamycin (mTOR) signaling cascade, whereas lipid synthesis and energy metabolism in the mammary tissue appear to be influenced by Liver X Receptor Alpha (LXRα), Peroxisome Proliferator-Activated Receptor Gamma (PPARγ), and potentially Insulin-Like Growth Factor 1 Receptor (IGF1R). In addition, fenugreek might facilitate milk let-down by boosting oxytocin release from the pituitary gland. Nonetheless, these findings based on gene expression still require validation through proteomic and histological investigations.[22]

Grape seeds (*Vitis vinifera*) are a rich source of phytochemicals, including gallic acid, monomeric flavan-3-ols such as catechin, epicatechin, gallocatechin, epigallocatechin, and epicatechin 3-O-gallate, as well as proanthocyanidins in the form of dimers, trimers, and higher-order polymers. These compounds have been linked to increased prolactin (PRL) signaling, which contributes to the enlargement of mammary alveoli despite a relatively low alveolar count. In addition, the flavonoids in Grape Seed Extract (GSE) have been shown to promote the expression of nutrient-sensing genes such as sirtuin (Sirt1), Peroxisome Proliferator-Activated Receptor Gamma Co-activator 1 Alpha (PGC-1α), Nuclear Respiratory Factor (NRF)1, Transcription Factor A Mitochondrial (TFAM), and Mitofusin (Mfn) 1, and to enhance mitochondrial biogenesis in kidney cells. Altogether, these molecular effects suggest that GSE may improve energy metabolism within Mammary Epithelial Cells (MECs). This outcome was observed in research involving dairy cows, indicating the potential role of GSE in supporting milk production in bovine species.[23]

A separate study in lactating goats demonstrated more direct lactogenic effects of flavonoids and phenolic acids. Supplementation with *Moringa oleifera*, a plant rich in compounds such as kaempferol, myricetin, quercetin, gallic acid, ellagic acid, and chlorogenic acid, resulted in elevated levels of prolactin and oxytocin in the bloodstream. These hormonal changes led to an increase in alveolar diameter and upregulation of key lactation-related proteins, including alpha-lactalbumin (LALBA) and aquaporins, thereby enhancing milk production. Notably, the combination of alpha-lactalbumin and beta-1,4-galactosyltransferase (B4GALT1) forms the lactose synthase complex, which plays an essential role in synthesizing lactose, the main factor influencing milk volume.[24]

Green tea (*Camellia sinensis*) contains several major catechins, such as epigallocatechin-3-gallate (EGCG), epigallocatechin (EGC), epicatechin-3-gallate (ECG), and epicatechin (EC), all of which are known for their potent biological activities. In lactating dairy cows with hyperketonemia, supplementation with green tea extract (GTE) has been associated with modulation of key lactogenic pathways, particularly those involving TGF beta signaling and cellular oxygen metabolism. Additionally, GTE intake significantly reduced the expression of pro-inflammatory cytokines such as IL1 beta, IL6, and TNF alpha. These findings provide evidence that, under metabolic stress conditions, GTE may contribute to reduced inflammation and oxidative stress, while helping to preserve mammary gland integrity in bovine species.[25]

The EC which is abundant in cocoa, grapes, tea, and various other fruits and vegetables, has been shown to reduce the expression of inflammatory mediators such as Cyclooxygenase-2 (COX2) and Nitric Oxide Synthase (NOS2) (inducible nitric oxide synthase) in bovine Mammary Alveolar Cell (MAC)-T cells, and to lower several pro-inflammatory cytokines (such as TNFα, IL1β, and IL6) in the mammary glands of lipopolysaccharide (LPS)-stimulated mice and MAC-T cells, through reduced phosphorylation and nuclear translocation ofNuclear Factor Kappa B (NF-κβ). This suggests that EC may enhance antioxidant capacity in the mammary gland during lactation, thereby supporting milk production.[26] The proposed molecular mechanisms of selected herbal galactagogues are illustrated in **Figure 1.**

Based on the available evidence, herbal galactagogues appear to influence lactation through several interconnected molecular pathways. However, most of these findings

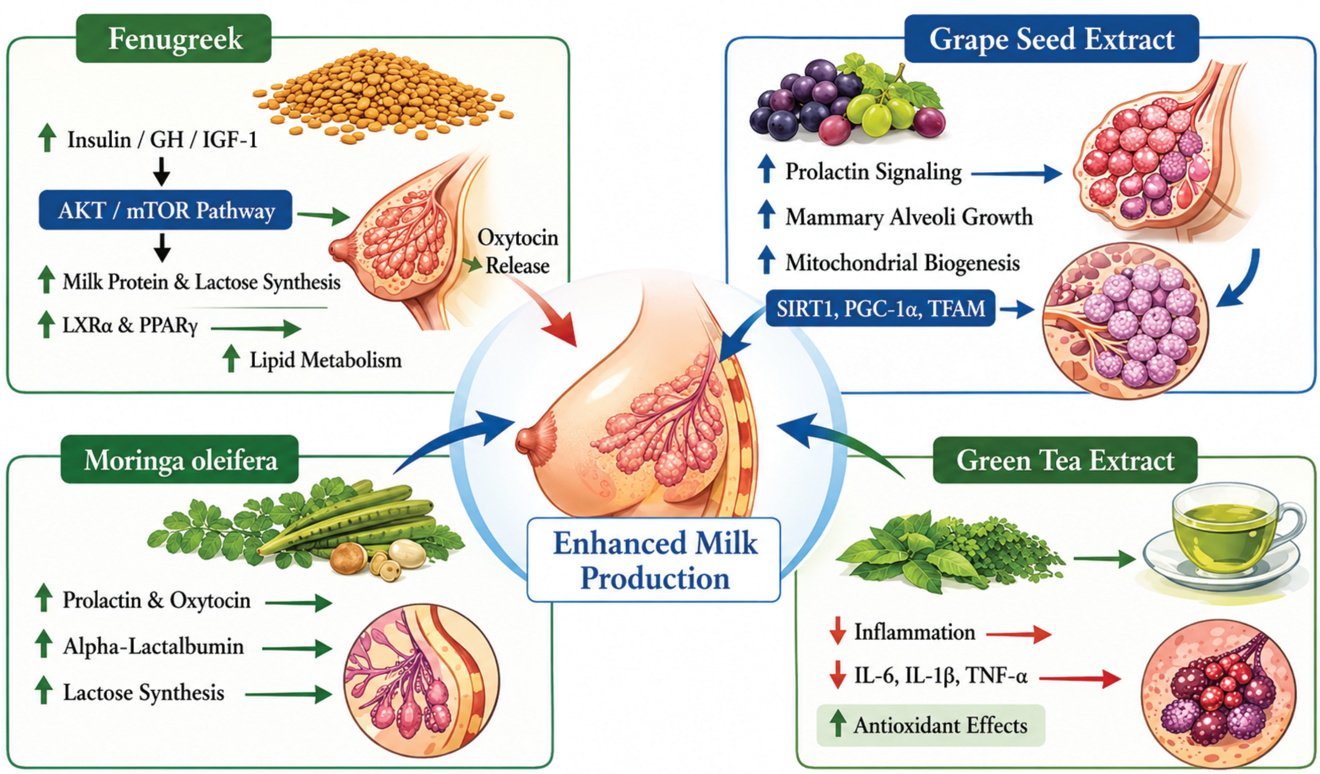

Figure 1. Mechanisms of herbal galactagogues.

Table 1. Comparison of herbal galactagogues.

Herbal Galactagogue	Key Phytochemicals	Primary Mechanisms of Action	Reference
Trigonella foenum-graecum	Quercetin, rutin, vitexin, isovitexin, graecunins, diosgenin, and coumarin	Activates insulin/GH/IGF-1 signaling, stimulates oxytocin release, and regulates milk protein synthesis through the AKT/mTOR pathway	[22]
Vitis vinifera	Gallic acid, catechin, epicatechin, gallocatechin, epigallocatechin, epicatechin 3-O-gallate, and proanthocyanidins	Enhances prolactin (PRL) signaling and improves mitochondrial biogenesis and energy metabolism in mammary epithelial cells (MECs)	[23,25]
Moringa oleifera	Kaempferol, myricetin, quercetin, gallic acid, ellagic acid, and chlorogenic acid	Increases serum prolactin and oxytocin levels, enlarges alveolar diameter, and upregulates alpha-lactalbumin (LALBA) expression	[24]
Camellia sinensis	Epigallocatechin-3-gallate (EGCG), epigallocatechin (EGC), epicatechin-3-gallate (ECG), and epicatechin (EC)	Modulates TGF-β signaling, suppresses pro-inflammatory cytokines (IL-1β, IL-6, TNF-α), and preserves mammary gland integrity	[25]

are still largely derived from studies in animal models, particularly mammals. As shown in **Figure 1**, each compound may act through different but overlapping mechanisms, such as modulation of prolactin and oxytocin signaling, activation of the AKT/mTOR pathway, improvement of cellular energy metabolism, and reduction of inflammatory responses, which together contribute to enhanced milk production. To provide a clearer comparison of the primary findings, the characteristics and mechanisms of selected herbal galactagogues are summarized in **Table 1.**

Conclusion

Herbal galactagogues contain phytochemicals that influence key hormonal and molecular pathways involved in milk production. These include stimulation of prolactin and oxytocin, enhancement of alveolar development, and anti-inflammatory actions in the mammary gland. Most evidence comes from animal models, with limited clinical data in humans. Further human studies are needed to validate these findings, determine optimal dosing, and confirm long-term safety in lactating women.

Authors' Contribution

Manuscript was proposed, drafted and designed by JN and NSA. All authors made manuscript revisions and finalized the last version of the manuscript.

Conflict of Interest

The authors declare no competing interests.

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