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Exploring the Hypoglycemic Mechanism and Milk Production Effects of Fenugreek: A Systematic Review

Yasmine Terbeche[1], Gatien Messire[2], Sabine Berteina-Raboin[2*], Ammar Amirouche[3], Amine Benyamina[3], Raphaël Serreau[4,5*]

Abstract

This scoping review comprehensively explores the existing literature on fenugreek (Trigonella foenum-graecum), a versatile herb known for its culinary and traditional medicinal uses. The review focuses on two key aspects: the hypoglycemic mechanism of fenugreek and its impact on milk production in breastfeeding women. By systematically analyzing and synthesizing the available evidence, this review aims to enhance our understanding of fenugreek's potential applications and identify research gaps for future systematic reviews. The search strategy targeted English-language animal studies published within the last five years that specifically investigated fenugreek's hypoglycemic mechanism and its effects on milk production. A total of 15,236 articles were initially identified from databases such as PubMed, Sci finder and ScienceDirect. After a rigorous selection process, including thorough evaluation of titles, abstracts, and full-texts, a subset of articles (including those titled "Impact of Fenugreek on Milk Production in Rodent Models of Lactation Challenge" and "Fenugreek Stimulates the Expression of Genes Involved in Milk Synthesis and Milk Flow through Modulation of Insulin/GH/IGF-1 Axis and Oxytocin Secretion") were included for detailed analysis. The findings 18 articles from the included studies demonstrate promising results regarding fenugreek's potential to stimulate milk production and regulate blood glucose levels.

However, further research is necessary to unravel the underlying molecular pathways, establish optimal dosage guidelines, and assess long-term side effects. Overall, this scoping review offers valuable insights for lactating women seeking to enhance milk production and individuals managing blood sugar levels, providing potential alternative approaches for supporting lactation and glycemic control.

Keywords: Fenugreek; Milk Production; Milk Composition; Galactagogue; Insulin; Hypoglycemic; Constituents; Diabetes; Breastfeeding

Introduction

There are numerous phytotherapy products claiming a galactological effect, either in the form of pure extracts or as mixtures of various plants [1]. They are consumed in various forms (infusions, powders, capsules). One of the main plants used with the best galactogenic effects is fenugreek. Fenugreek, scientifically known as Trigonella foenum-graecum L., is an herbaceous plant native to the Mediterranean basin (Figure 1).

Its seeds have been widely used in cooking and traditional medicine for centuries. Fenugreek has been the subject of much scientific research

Affiliation:

[1]Faculté de pharmacie, université Paris Saclay, 17 avenue des Sciences, 91400 ORSAY

[2]Institut de Chimie Organique et Analytique (ICOA), Université d'Orléans, UMR-CNRS 7311, BP 6759, Rue de Chartres, CEDEX 2, 45067 Orléans, France

[3]Unité de Recherche PSYCOMADD-Psychiatrie Comorbidités Addictions, APHP Université Paris Saclay, Hôpital Paul-Brousse, 12 Avenue Paul Vaillant Couturier, 94804 Villejuif, France

[4]Unité de Recherche PSYCOMADD, APHP Université Paris Saclay, Hôpital Paul-Brousse, 12 Avenue Paul Vaillant Couturier, 94804 Villejuif, France

[5]Addictologie EPSM Georges DAUMEZON, GHT Loiret, 1 Route de Chanteau, 45400 Fleury les Aubrais, France

***Corresponding Author**

Raphaël Serreau, Unité de Recherche PSYCOMADD, APHP Université Paris Saclay, Hôpital Paul-Brousse, 12 Avenue Paul Vaillant Couturier, 94804 Villejuif, France.

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because of its potential medicinal properties, including its effect on milk production in breastfeeding women and its hypoglycemic effects. The use of fenugreek to increase milk production in breastfeeding women has been a topic of interest for centuries. While some women report significant results, the scientific evidence on the effectiveness of fenugreek to stimulate lactation is still limited and mixed. However, there are studies that have shown that fenugreek can increase milk production in rat or rabbit models of lactation challenges [2, 3-9].

In addition to its potential benefits for breastfeeding women, fenugreek has also been investigated for its hypo-glycemic effects. Several studies have explored the mechanisms by which fenugreek may lower blood glucose levels. The hypoglycemic effects of fenugreek have been observed in animal models, showing promising results in managing blood sugar levels [10-12].

This scoping review aims to explore the extent of the literature available on the hypoglycemic mechanism of fenugreek and its use to increase milk production in breastfeeding women. By identifying research trends and gaps in the literature, this scoping review will contribute to a better understanding of the potential uses of fenugreek and identify relevant research questions for future systematic reviews. The findings from this review may have implications for both lactating women seeking to enhance milk production and individuals managing blood sugar levels.

Methods

For the methodology employed to conduct this systematic review, we intentionally chose an exploratory and systematic approach to comprehensively map the current understanding of the hypoglycemic mechanism of fenugreek and its effects on milk production. This method enabled us to gather relevant information from scientific literature in a comprehensive manner. We utilized several academic databases, including PubMed, Scifinder and ScienceDirect, to retrieve relevant articles for our scoping review. By utilizing these databases, we ensured access to a broad spectrum of academic literature, maximizing the likelihood of capturing relevant studies related to the hypoglycemic mechanism of fenugreek and its impact on milk production.

We employed a systematic approach to develop the search strategy used to identify relevant articles for our scoping review. Specific keywords and search terms such as "fenugreek", "hypoglycemic mechanism, diabetes or galactogogue" and "milk production" were carefully chosen to target our research topic.

To optimize the search results, we utilized the following terms using the Boolean operator AND and OR, to combine the search terms effectively. Based on search results obtained from PubMed, Scifinder and ScienceDirect, a total of 15,236 articles, reviews, clinical trials, book chapters and others were identified using various combinations of fenugreek-related keywords. These keywords included "fenugreek", "fenugreek galactogogue", "fenugreek diabetes", “fenugreek diabetes galactogogue“, "fenugreek galactogogue milk" and “fenugreek diabetes galactogogue milk“. The literature was studied by the authors followed the standards PRISMA guidelines (Figure 2).

The search was conducted in two ways, the first using the keywords fenugreek, galatogogue and milk, the second using the keywords fenugreek, diabetes, galacotogogue and milk. In addition, to refine the search, specific limitations were applied. Language filters were used to select articles for inclusion in our systematic review and to include only English-language articles, to ensure accessibility to relevant literature. Articles had to have been published within the last ten years up to 2023, including August 2023, allowing us to take into account the most recent research. Book chapters were also excluded and we were left with a total of 221 articles. After conducting the initial search of the selected databases, we carefully screened the 221 articles on the basis of their titles and abstracts to identify the 18 selected articles that were relevant to our topic. Articles had to be focused on animal or human studies examining the specific hypoglycemic mechanism of fenugreek and milk production. We also excluded studies investigating other aspects of fenugreek, such as its hypocholesterolemic, anti-inflammatory and antioxidant effects, as these were not directly related to our research question. These search strategies were meticulously designed to produce accurate and pertinent results, ensuring that only relevant articles were included in our analysis. Twenty-six articles were added to this study in relation to the different molecules cited as being at the origin of the biological impact of this cereal in the different articles selected, or to explain the tests or concepts indicated in the 18 articles. These new

Figure 1: Fenugreek (T. foenum graecum L.) plant of the Fabaceae family.

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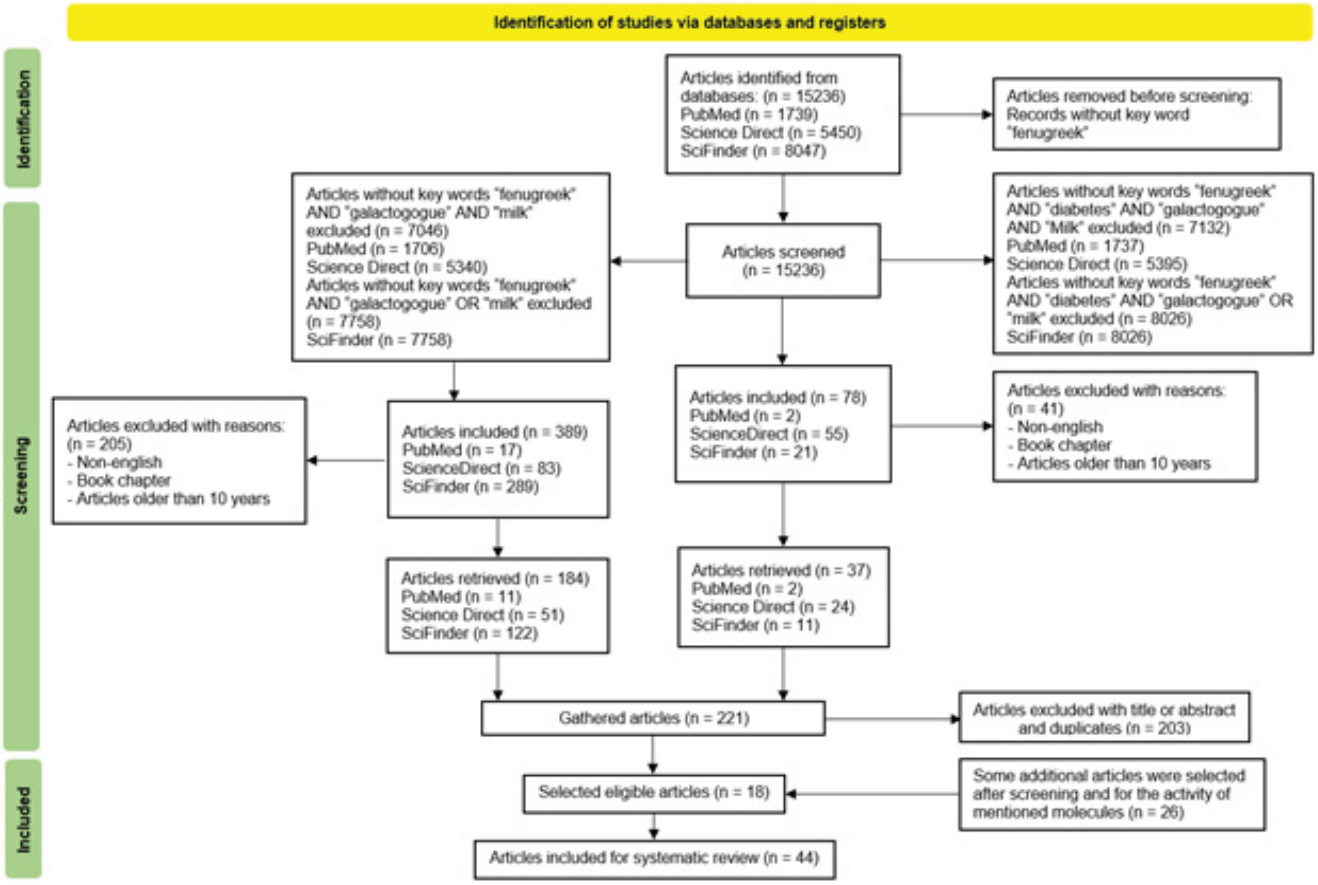

Figure 2: PRISMA flow diagram.

references may predate the criteria for sorting articles "within the last ten years up to 2023". This brings the total number of articles mentioned in this systematic review to 44.

The articles that were deemed potentially relevant, such as for example, "Impact of Fenugreek on Milk Production in Rodent Models of Lactation Challenge" [3] and "Fenugreek Stimulates the Expression of Genes Involved in Milk Synthesis and Milk Flow through Modulation of Insulin/GH/IGF-1 Axis and Oxytocin Secretion" [10] were included for a comprehensive evaluation of their content. To conduct this thorough evaluation, we obtained and carefully read the selected articles in their entirety. We assessed their methodology, research objectives, findings, and their relevance to our topic of interest: the hypoglycemic mechanism of fenugreek and its impact on milk production. Using these criteria, we excluded articles that did not address our research question or focused on unrelated aspects of fenugreek.

The articles identified cover a wide range of topics, including the hypoglycemic effects of fenugreek, its potential as a galactogogue to promote milk production, and its general medicinal properties. The large number of research and review articles suggests the importance and interest of studying the effects of fenugreek in different contexts. The present study encompasses three separate sources of information, which together highlight the therapeutic potential of fenugreek.

Results

The first study focused on the impact of fenugreek on milk production in rodent models of lactation problems. It revealed that fenugreek supplementation led to a significant increase in milk production and subsequently improved the growth of the offspring, without any adverse effect on the metabolic profiles of the dams and their litters [2]. The second study investigated the underlying molecular mechanisms associated with the effects of fenugreek on milk synthesis and secretion. It revealed that fenugreek supplementation resulted in a significant increase in the genes involved in macronutrient synthesis and energy metabolism in the mammary glands of lactating rats. In addition, there was a concomitant increase in the secretion of oxytocin, which is crucial for milk ejection [10]. Finally, a comprehensive study examined the pharmacological properties and therapeutic applications of fenugreek. It discussed the rich phytochemical composition of fenugreek, which contributes to its various medicinal properties [13]. In particular, the study highlighted the hypoglycemic effects of fenugreek observed in human

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and animal studies, including improved glycemic control and insulin resistance. This study also suggests that combining fenugreek with anti-diabetic drugs could improve their effectiveness in managing blood sugar levels. In summary, these studies and the review collectively contribute to our understanding of the potential benefits of fenugreek in terms of improving milk production, modulating milk synthesis and hypoglycemic effects. The galactogogue effect discussed below appeared significant in humans in some studies [14-16] and rather limited in others [17], but some studies did not meet the necessary conditions, such as the absence of a placebo [14], for example. We thought it useful to begin by listing the compounds present in fenugreek that have been reported to be involved in lactation processes, before proceeding with our study.

A closer look at the molecules present in this plant reveals large quantities of galactomannans (dietary fiber, Figure 3), followed by saponins (dioscin, diosgenin and gitogenin, potential steroid hormone precursors, Figure 4), flavonoids (quercetin, quercetin-3-O-glucoside and vitexin), alkaloids (including trigonelline, one of the plant's most important metabolites, with cholesterol-lowering and lipid-lowering properties) and the amino acid 4-hydroxyisoleucine, one of the major amino acids in milk proteins (Figure 5). Among these compounds, which may play a role in the still poorly understood mechanisms of action in milk production, flavonoids, which have antioxidant effects and are potential phytoestrogens, and saponins have both an activating effect on prolactin and growth hormone production [17-21], while alkaloids and 4-hydroxyisoleucine have an activating effect on insulin and, in particular, increase the sensitivity of the mammary gland to insulin, thus stimulating lactocytes [22]. Among the steroidal saponins, diosgenin stimulates prolactin secretion [15, 17-22] and contributes to the plant's estrogenic action. It should be noted that it is generally this increased secretion that is put forward to explain fenugreek's galactogogue effect.

Flavonoids such as quercetin and vitexin have been reported as estrogen agonists and dopamine antagonists [17]. 4-Hydroxyisoleucine and trigonelline are considered activators of insulin secretion in pancreatic cells [22-24]. The various compounds present in fenugreek could therefore have a concomitant effect on the mammary gland [17, 19-21].

Fenugreek, a legume widely used in the diet in some countries and in chin, can be used as a dietary supplement and in traditional medicines, particularly Chinese and Mediterranean, to increase milk production without any particular restrictions [25]. It has been tested in humans at doses of 25 gr without showing any effects on various parameters, apart from a few laxative side effects in the case of high consumption [26, 27]. The intake of this dietary supplement should be monitored in the case of collateral intake of certain treatments, given its therapeutic anti-diabetic effects [25-28]. Further experimental and clinical studies are required before it can be recommended as a treatment for low milk production [29].

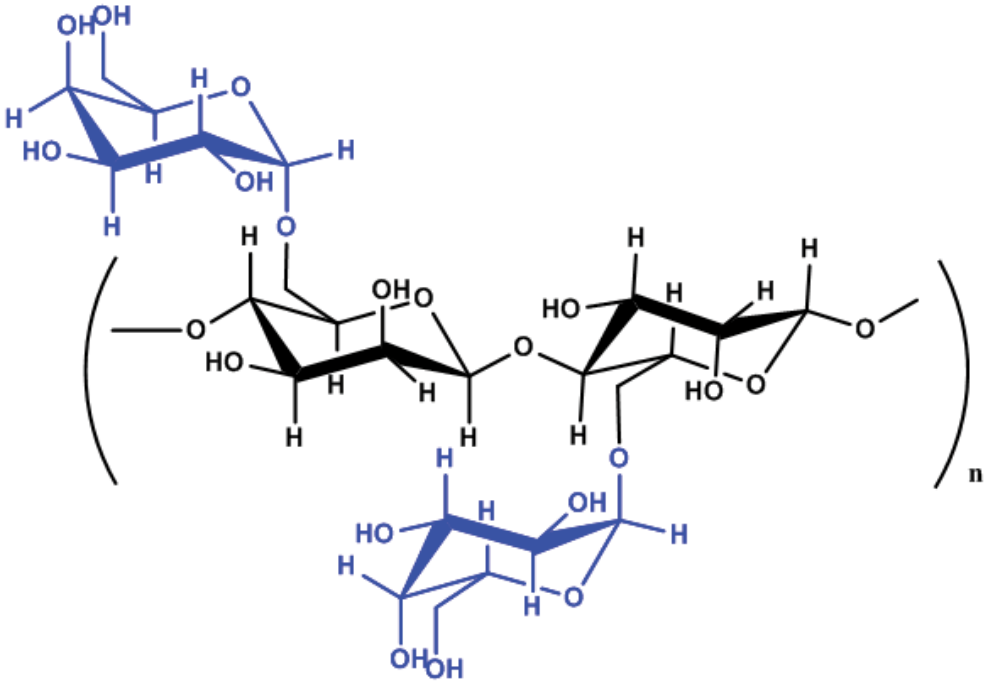

Figure 3: Dietary fiber found in fenugreek, the galactomannan 1:1, chain of mannoses linked at β (1-4) and grafted with galactoses in α (1-6).

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The exact mechanisms of action of fenugreek on milk production and on the various causes of lactation difficulties [12] remain to be demonstrated and will be discussed below, although recent clinical studies [16, 30-34] provide some answers to these questions.

In the animal experiments described in the two articles [2, 10], pregnant Sprague-Dawley rats were individually housed in cages with wood chips, maintaining a controlled environment with a constant temperature of 22 ± 1°C, relative humidity of 50% ± 3%, and a fixed 12-hour light dark cycle. The dams were divided into different groups based on their diets and litter sizes. In the first study, the groups included dams fed a standard normal 20% protein diet (NP) with either 8 or 12 pups, dams fed a low-protein diet 8% (LP) with 8 pups, and dams fed NP diet with 12 pups supplemented with fenugreek (NPF). In the second study, the dams were randomly assigned to receive either a control diet alone (CTL) or the control diet supplemented with fenugreek extract (FEN) at a dosage of 1 g/kg body weight/day. Throughout the experiments, various samples were collected at specific time points. Milk samples were collected from lactating dams at specific lactation days, while blood samples were obtained from both dams and pups for further analysis. Additionally, urine samples were collected from the pups, and tissue samples, including mammary glands and pituitary glands, were collected from both dams and offspring. Milk flow, a critical parameter, was measured using the deuterated water enrichment method [35]. Various analyses, such as protein assays, enzymatic assays for lactose concentration, gas chromatography for fatty acid analysis, and liquid chromatography coupled with mass spectrometry for trigonelline quantification, were performed on the collected samples. Statistical analyses were conducted using a combination of parametric and non-parametric tests, including ANOVA, post-hoc tests, correlation tests, and linear regression analysis. The experimental protocols were approved by the Animal Ethics Committee, and the studies were conducted in compliance with institutional guidelines and regulations [2, 10].

The synthesis of results from these two studies provides key insights into the impact of fenugreek on milk production in mammals. The study titled 'Impact of Fenugreek on Milk Production in Rodent Models of Lactation Challenge' confirms the galactagogue effect of fenugreek in another mammalian model, suggesting its potential benefits for humans. It demonstrates that fenugreek has a galactagogue effect, particularly in situations where there are no physiological impairments in milk production, such as when there is an increase in litter size. However, fenugreek does not show the same effect in cases of maternal dietary protein restriction, indicating its inability to overcome lactation impairment caused by undernutrition. Therefore, fenugreek supplementation may enhance milk production in scenarios with insufficient maternal milk production due to factors like maternal stress, breastfeeding management difficulties, first-time mothers, or when breastfeeding twins. However, fenugreek is unlikely to be effective in situations affecting lactation physiology, such as undernutrition, mammary hypoplasia, or hormonal deregulation [2].

There was a significant correlation between fenugreek consumption and milk production, for total milk production $R2=0.87$ with $p<0.001$ and milk consumption by pups $R2=0.82$ with $p<0.001$ [2]. These data come from the study carried out under three different conditions of physiology and lactation: NP:8, NP:12 and LP:8, as described above.

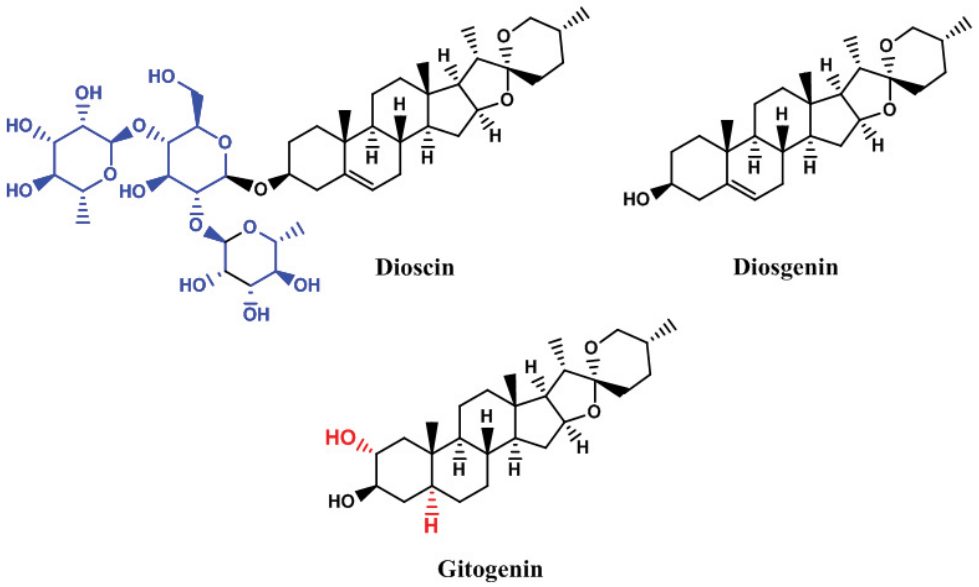

Figure 4: Saponins found in fenugreek and involved in therapeutic activities.

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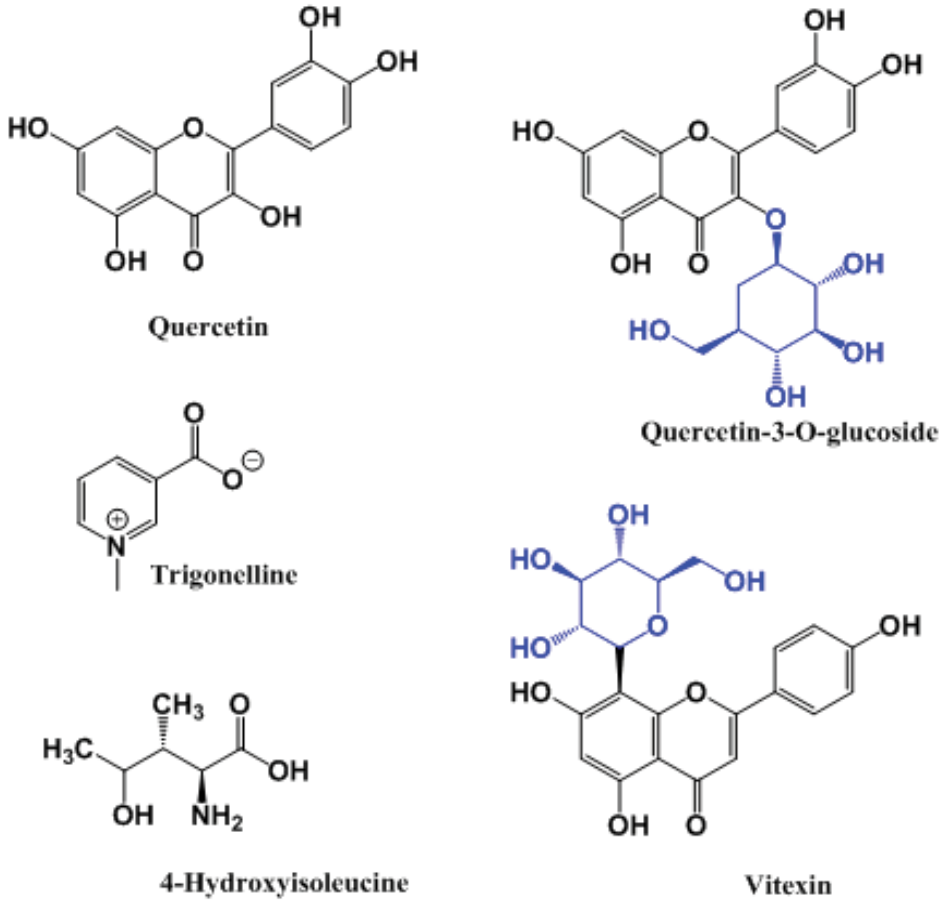

Figure 5: Flavonoids, alkaloids and amino acid found in fenugreek and involved in therapeutic activities.

Sevrin et al. [2] showed, on one hand, that increasing litter size had`Additionally, the study found no adverse metabolic effects on dams or offspring, and there is preliminary evidence suggesting that fenugreek may even improve insulin sensitivity in the long term. The significant 16% increase in milk production attributed to fenugreek warrants the design of clinical trials in breastfeeding women. Fenugreek seeds have been shown to possess hypoglycemic effects in individuals with both type 1 and type 2 diabetes mellitus [2, 10, 36-38]. Type 1 and type 2 diabetes are two of the fastest-growing diseases, with a current prevalence of 10.5% and 536.6 million people living with the disease in 2021. WHO estimates that this prevalence will reach 12.2% in 2045 (783.2 million people) [39]. Type 2 diabetes mellitus is a metabolic disorder in which the pancreas does not produce enough insulin, or its targets do not respond to conventional insulin concentration. The result is chronic hyperglycemia, which is likely to become a public health problem in the near future, given the various pathologies it can lead to [40]. The prevalence of type 2 diabetes accounts for more than 90-95% of all cases of diabetes [16]. The synthetic drugs used to treat type 2 diabetes are effective but, like all medicines, they have undesirable side-effects and a certain toxicity. The use of natural products, while not necessarily risk-free, is better accepted by patients, and their availability seems less subject to the production problems encountered by some drugs in recent years. The interesting clinical study conducted by Geberemeskel et al. [16] involved 95 patients, 49 of whom received treatment with 25 mg fenugreek powder solution, and a control group of 46 patients who received placebo, for 30 consecutive days. All patients had abnormal blood glucose levels ≥180 mg/dL, as well as an abnormal lipid profile (total cholesterol, triglycerides, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol). The results showed that fenugreek reduced total cholesterol by 13.6% and triglycerides by 23.53%, but increased high-density lipoprotein cholesterol by 21.7%, while low-density lipoprotein cholesterol was reduced by 23.4%, significantly improving the ratio of high-density lipoprotein cholesterol to low-density lipoprotein cholesterol. These results therefore suggest that *Trigonella foenum-graecum* seed powder solution has a potential anti-dyslipidemic effect at a dose of 25 mg, although the mechanism of action is not well defined. These effects can be attributed to the dietary fiber content present in fenugreek, with some of the fiber being soluble. This soluble fiber is associated with a reduction in glycemic

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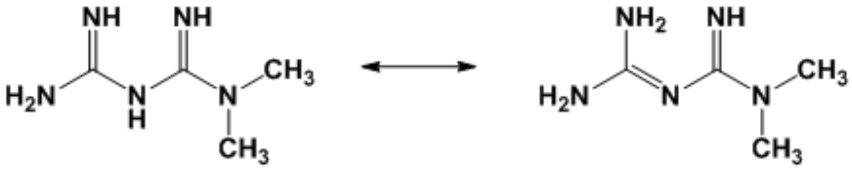

Figure 6: Chemical structure of metformin and tautomeric form.

effects. Incorporating fenugreek-based therapeutic foods into the diet has demonstrated significant impacts on blood sugar levels in patients with non- insulin-dependent diabetes. In one study, the administration of 30 gr of fenugreek-based therapeutic food for approximately one month resulted in a noteworthy decrease in blood sugar levels [41]. The fenugreek seeds themselves contain 45.4% dietary fiber, with 13.3% being soluble and 32% insoluble [13].

The mechanisms underlying fenugreek's hypoglycemic effects are still not fully understood. However, it has been suggested that the soluble fraction rich in galactomannan found in fenugreek plays a crucial role. This fraction is believed to slow gastric emptying and delay glucose absorption in the small intestine, thereby contributing to the hypoglycemic activity. The gum present in fenugreek seeds, composed of galactose and mannose in a 1:1 ration (Figure 3), is also associated with a reduction in glycemic effects [13]. Several studies have provided evidence supporting the hypoglycemic effects of fenugreek. It has been shown to improve glucose tolerance and peripheral utilization in patients with noninsulin-dependent diabetes and type 2 diabetes [38]. In experiments with alloxan-induced diabetic mice, dialyzed fenugreek seed extract exhibited a comparable reduction in glucose levels to that of insulin [38]. Moreover, fenugreek has demonstrated the ability to enhance glycemic control, reduce insulin resistance, and increase insulin signaling and sensitivity in rats fed a fructose-rich diet [38]. In type 2 diabetic rats, fenugreek supplementation was associated with lower serum glucose levels and increased hepatic glycogen content [38]. Additionally, fenugreek may enhance the bioavailability of other antidiabetic medications, such as metformin (Figure 6), when administered concomitantly [10].

While the precise biochemical mechanisms underlying fenugreek's hypoglycemic effects require further investigation, the soluble fraction rich in galactomannan appears to play a significant role in slowing gastric emptying and delaying glucose absorption [42]. Additionally, fenugreek may exert its hypoglycemic effects by improving glucose tolerance and insulin signaling in muscle and adipose cells [38]. Continued research is necessary to gain a comprehensive understanding of fenugreek's mechanisms of action in regulating glycemic levels[10].

Fenugreek supplementation has been investigated for its potential to stimulate milk production in lactating females by modulating the insulin/GH/IGF-1 axis. The study aimed to explore the molecular mechanisms underlying fenugreek's effect on milk synthesis and examined the genes involved in this process [10]. The results revealed that fenugreek supplementation led to a significant increase in milk yield, with a 15.3% higher milk production observed in animals receiving fenugreek compared to the control group. Furthermore, the expression of genes related to the synthesis of milk lipids, lactose, proteins, and energy metabolism was upregulated in the fenugreek-supplemented animals [10].

To understand how fenugreek acts at the molecular level, the authors investigated the gene expression in the mammary and pituitary glands. They also assessed the influence of lactation time on fenugreek's efficacy by using statistical models to isolate the specific effect of the dietary intervention. The results demonstrated that fenugreek supplementation had a significant impact on gene expression associated with milk synthesis, independent of lactation time [10].

The underlying molecular mechanisms of fenugreek's role in stimulating milk production are believed to involve the activation of the insulin/GH/IGF-1 axis, leading to increased sensitivity of the mammary glands to these hormones. Additionally, fenugreek may extend the duration of peak lactation rather than intensifying it. The upregulation of genes involved in milk lipid, lactose, protein synthesis, and energy metabolism supports the notion that fenugreek enhances milk production by enhancing hormonal activity and regulating gene expression associated with milk synthesis. These findings highlight the potential of fenugreek as a natural supplement to promote milk production in lactating females [10].

Discussion

The present scoping review explored the hypoglycemic mechanism of fenugreek and its impact on milk production in breastfeeding women. The review aimed to identify research trends, evaluate the available evidence, and identify potential research questions for future systematic reviews. The findings from the selected articles shed light on the potential benefits of fenugreek in terms of hypoglycemic effects and

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milk production. The studies included in this review provided insights into the potential use of fenugreek as a galactagogue to enhance milk production in lactating females. The study titled "Impact of Fenugreek on Milk Production in Rodent Models of Lactation Challenge" demonstrated that fenugreek supplementation led to a significant increase in milk production in rodent models, particularly in situations where there were no physiological impairments in milk production. The findings suggest that fenugreek may be effective in enhancing milk production in scenarios with insufficient maternal milk production due to factors like maternal stress, breastfeeding management difficulties, first-time mothers, or when breastfeeding twins. However, the study also indicated that fenugreek may not be effective in situations affecting lactation physiology, such as undernutrition, mammary hypoplasia, or hormonal deregulation. This suggests that fenugreek supplementation may have limitations in cases where there are underlying physiological issues affecting milk production [2].

The study further revealed that fenugreek supplementation had no significant effect on the amino acid concentrations in breast milk, indicating that fenugreek's effect on milk production does not involve significant changes in the amino acid composition of breast milk. Additionally, the study found no adverse metabolic effects on dams or offspring, suggesting that fenugreek supplementation is generally safe for lactating females and their offspring. These findings provide valuable insights into the potential benefits and safety considerations of using fenugreek as a galactagogue [2]. Regarding the hypoglycemic effects of fenugreek, several studies have provided evidence supporting its efficacy. As far as the hypoglycaemic effects of fenugreek are concerned, several studies have demonstrated its effectiveness. Even at low concentrations, just 25 mg a day, according to a clinical study conducted on 95 patients [16], it significantly reduces total cholesterol and triglycerides, and considerably improves the ratio of high-density lipoprotein cholesterol to low-density lipoprotein cholesterol, which is particularly interesting for the treatment of diabetes mellitus [2, 10, 16, 34]. Fenugreek has been shown to improve glucose tolerance and peripheral utilization in individuals with non-insulin-dependent diabetes and type 2 diabetes [16, 43].

The soluble fraction rich in galactomannan found in fenugreek is believed to play a crucial role in slowing gastric emptying and delaying glucose absorption, contributing to its hypoglycemic activity. The gum present in fenugreek seeds, composed of galactose and mannose, is also associated with a reduction in glycemic effects [13].

These mechanisms, along with fenugreek's potential to enhance glycemic control, reduce insulin resistance, and increase insulin signaling and sensitivity; suggest its potential as an adjunct therapy for individuals with diabetes [2, 10, 16, 34]. While the precise biochemical mechanisms underlying fenugreek's hypoglycemic effects require further investigation, the findings suggest that fenugreek supplementation may offer benefits in managing blood sugar levels [10].

However, it is important to note that most studies included in this review were conducted on animal models, mainly rats. Few placebo-controlled clinical trials have yet been carried out on the hypoglycemic effect of this promising seed, and further research is needed to confirm the efficacy and safety of fenugreek supplementation in humans, particularly breastfeeding women and people with diabetes. Overall, this scoping review highlights the potential of fenugreek in enhancing milk production and its hypoglycemic effects. However, the limitations of the included studies and the need for further research in human subjects should be considered. Future studies should focus on conducting well-designed clinical trials to evaluate the efficacy, optimal dosage, and long-term effects of fenugreek supplementation in lactating women and individuals with diabetes [2, 10].

Additionally, investigations into the molecular mechanisms underlying fenugreek's effects on milk synthesis and glucose metabolism would provide a deeper understanding of its therapeutic potential [10]. Findings have implications for lactating women seeking to enhance milk production and individuals managing blood sugar levels, offering potential alternative approaches for supporting lactation and glycemic control.

Conclusion

In conclusion, the scoping review conducted on fenugreek has provided insights into its hypoglycemic mechanisms and its impact on milk production in breastfeeding women. The reviewed studies have shown promising results regarding the effectiveness of fenugreek in stimulating milk production and regulating blood glucose levels. However, further research is needed to deepen our understanding of the molecular pathways involved and determine the optimal dosage and long-term effects of fenugreek supplementation. The potential implications of fenugreek for supporting lactation and glycemic control are promising, but it is important to note that the included studies primarily involved animal models, and well-designed clinical trials on human subjects are required to confirm these effects. In summary, fenugreek offers an intriguing avenue to explore for breastfeeding women and individuals with diabetes, providing potential alternative approaches to support lactation and manage blood sugar levels.

Author Contributions

Conceptualization, Y.T., G.M., S.B-R. and R.S.; methodology, Y.T., G.M., S.B-R., A.A., A.B. and R.S.;

validation, Y.T., G.M., S.B-R., A.A., A.B. and R.S.; formal analysis, Y.T., G.M., S.B-R., A.A., A.B., and R.S.; investigation, Y.T., G.M., S.B-R., A.A., A.B. and R.S.; resources, S.B-R., A.A., A.B., and R.S.; data curation, Y.T., G.M., S.B-R., A.A., A.B. and R.S.; writing—original draft preparation, T.Y., S.B-R. and R.S.; writing—review and editing, Y.T., G.M., S.B-R., A.A., A.B., and R.S.; supervision, S.B-R. and R.S.; project administration, R.S. All authors have read and agreed to the published version of the manuscript.

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References

1. Bazzano AN, Hofer R, Thibeau S, et al. A Review of Herbal and Pharmaceutical Galactagogues for Breast-Feeding. Ochsner J 16 (2016): 511-524.
2. Sevrin T, Alexandre-Gouabau MC, Castellano B, et al. Impact of Fenugreek on Milk Production in Rodent Models of Lactation Challenge. Nutrients 11 (2019): 2571.
3. Petit P, Sauvaire Y, Ponsin G, et al. Effects of a fenugreek seed extract on feeding behaviour in the rat: metabolic-endocrine correlates. Pharmacol. Biochem. Behav. 1993, 45, 369–374.
4. KumarP, Bhandari U, Jamadagni S. Fenugreek seed extract inhibit fat accumulation and ameliorates dyslipidemia in high fat diet-induced obese rats. Biomed. Res. Int 2014 (2014): 606021.
5. Al-Chalabii IMS. Diosgenin effect on rats and mice ovaries. J. Fac. Med. Baghdad 47 (2005): 296-301.
6. Shim SH, Lee EJ, Kim JS, et al. Rat growth-hormone release stimulators from fenugreek seeds. Chem. Biodivers 5 (2008): 1753-1761.
7. Abdel-Rahman H, Fathalla SI, Ezzat Assayed M, et al. Physiological Studies on the Effect of Fenugreek on Productive Performance of White New-Zealand Rabbit Does. Food Nutr. Sci 07 (2016): 1276-1289.
8. Eiben Cs, Rashwan AA, Kustos K, et al. Effect of Anise and Fenugreek supplementation on performance of rabbit does. Proceedings - 8th World Rabbit Congress – September 7-10, 2004 – Puebla, Mexico (2004): 805-810.
9. Turkyilmaz C, Onal E, Hirfanoglu IM, et al. The effect of galactagogue herbal tea on breast milk production and short-term catch-up of birth weight in the first week of life. J. Altern. Complement. Med17 (2011): 139-142.
10. Sevrin T, Boquien CY, Gandon A, et al. Fenugreek Stimulates the Expression of Genes Involved in Milk Synthesis and Milk Flow through Modulation of Insulin/GH/IGF-1 Axis and Oxytocin Secretion. Genes 11 (2020): 1208.
11. Khan TM, Wu DB, Dolzhenko AV. Effectiveness of fenugreek as a galactagogue: A network meta-analysis. Phytother. Res 32 (2018): 402-412.
12. Foong SC, Tan ML, Marasco LA, et al. Oral galactagogues (natural therapies or drugs) for increasing breast milk production in mothers of non-hospitalised term infants. Cochrane Database Syst. Rev 5 (2020): CD011505.
13. Visuvanathan T, Than LTL, Stanslas J, et al. Revisiting Trigonella foenum-graecum L. : Pharmacology and Therapeutic Potentialities. Plants 11 (2022): 1450.
14. El Sakka A, Salama M, Salama K. The Effect of Fenugreek Herbal Tea and Palm Dates on Breast Milk Production and Infant Weight. J. Pediatr. Sci 6 (2014): e202.
15. Ghasemi V, Kheirkhah M, Vahedi M. The Effect of Herbal Tea Containing Fenugreek Seed on the Signs of Breast Milk Sufficiency in Iranian Girl Infants. Iran. Red. Crescent. Med. J 17 (2015): e21848-e21848.
16. Geberemeskel GA, Debebe YG, Nguse NA. Clinical Study. Antidiabetic Effect of Fenugreek Seed Powder Solution (Trigonella foenum-graecum L.) on Hyperlipidemia in Diabetic Patients. J. Diabetes Res (2019): ID 8507453.
17. Abdou RM, Fathey M. Evaluation of early postpartum fenugreek supplementation on expressed breast milk volume and prolactin levels variation. Gaz. Egyp. Paediatr. Assoc 66 (2018): 57-60.
18. Petit PR, Sauvaire YD, Hillaire-Buys DM, et al. Steroid saponins from fenugreek seeds: Extraction, purification, and pharmacological investigation on feeding behavior and plasma cholesterol. Steroids 60 (1995): 674-680.
19. Gudelsky GA, Nansel DD, Porter JC. Role of estrogen in the dopaminergic control of prolactin secretion. Endocrinology 108 (1981): 440-444.
20. Sreeja S, Anju VS, Sreeja S. In vitro estrogenic activities of fenugreek Trigonella foenum graecum seeds. Indian J. Med. Res 131 (2010): 814-819.
21. Chen Y, Tang YM, Yu SL, et al. Advances in the pharmacological activities and mechanisms of diosgenin. Chin. J. Nat. Med 13 (2015): 578-587.
22. Fuller S, Stephens JM. Diosgenin, 4-Hydroxyisoleucine, and Fiber from Fenugreek: Mechanisms of Actions and Potential Effects on Metabolic Syndrome. Adv. Nutr 6 (2015): 189-197.
23. Zhou J, Zhou S, Zeng S. Experimental diabetes treated with trigonelline: effect on β cell and pancreatic oxidative

parameters. Fundam. Clin. Pharmacol 27 (2013): 279-287.

24. Broca C, Gross R, Petit P, et al. 4-Hydroxyisoleucine: experimental evidence of its insulinotropic and antidiabetic properties. Am. J. Physiol 277 (1999): E617-E623.

25. National Library of Medicine. Drugs and Lactation Database (LactMed®) [Internet]. Bethesda (MD): National Institute of Child Health and Human Development; 2006. Fenugreek (2023).

26. Bahmani M, Shirzad H, Mirhosseini M, et al. A Review on Ethnobotanical and Therapeutic Uses of Fenugreek (Trigonella foenum-graceum L). J. Evid. Based Complementary Altern Med 21 (2016): 53-62.

27. Kandhare AD, Thakurdesai PA, Wangikar P, et al. A systematic literature review of fenugreek seed toxicity by using ToxRTool: evidence from preclinical and clinical studies. Heliyon 5 (2019): e01536.

28. Ouzir M, El Bairi K, Amzazi S. Toxicological properties of fenugreek (Trigonella foenum graecum). Food Chem. Toxicol 96 (2016): 145-154.

29. Forinash AB, Yancey AM, Barnes KN, et al. The use of galactogogues in the breastfeeding mother. Ann. Pharmacother 46 (2012): 1392-1404.

30. Hassani SS, Fallahi-Arezodar F, Esmaeili SS, et al. Effect of Fenugreek Use on Fasting Blood Glucose, Glycosylated Hemoglobin, Body Mass Index, Waist Circumference, Blood Pressure and Quality of Life in Patients with Type 2 Diabetes Mellitus: A Randomized, Double-Blinded, Placebo-Controlled Clinical Trials. Galen. Med. J 8 (2019): e1432.

31. Neelakantan N, Narayanan M, De Souza RJ, et al. Effect of fenugreek (Trigonella foenum-graecum L.) intake on glycemia: a meta-analysis of clinical trials. Nutr. J 13 (2014): 7.

32. Najdi RA, Hagras MM, Kamel FO, et al. A randomized controlled clinical trial evaluating the effect of Trigonella foenum-graecum (fenugreek) versus glibenclamide in patients with diabetes. Afr. Health Sci 19 (2019): 1594-1601.

33. Rao AS, Hegde S, Pacioretty LM, et al. Nigella sativa and Trigonella foenum-graecum supplemented chapatis safely improve HbA1c, body weight, waist circumference, blood lipids and fatty liver in overweight and diabetic subjects: A twelve-week safety and efficacy study. J. Med. Food 23 (2020): 905-919.

34. Verma N, Usman K, Patel N, et al. A multicenter clinical study to determine the efficacy of a novel fenugreek seed (Trigonella foenum-graecum) extract (Fenfuro™) in patients with type 2 diabetes. Food Nutr. Res 60 (2016): 32382.

35. Sevrin T, Alexandre-Gouabau MC, Darmaun D, et al. Use of water turnover method to measure mother's milk flow in a rat model: Application to dams receiving a low protein diet during gestation and lactation. PLoS ONE 12 (2017): e0180550.

36. Ota A, Ulrich P. An Overview of Herbal Products and Secondary Metabolites Used for Management of Type two Diabetes. Front. Pharmacol 8 (2017): 436.

37. Hannan JM, Ali L, Rokeya B, et al. Soluble dietary fibre fraction of Trigonella foenum-graecum (fenugreek) seed improves glucose homeostasis in animal models of type 1 and type 2 diabetes by delaying carbohydrate digestion and absorption, and enhancing insulin action. Br. J. Nutr 97 (2007): 514-521.

38. Roberts KT. The potential of fenugreek (Trigonella foenum-graecum) as a functional food and nutraceutical and its effects on glycemia and lipidemia. J. Med. Food 14 (2011): 1485-1489.

39. Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res. Clin. Pract 183 (2022) : 109119.

40. Kumar K, Kumar S, Datta A, et al. Effect of fenugreek seeds on glycemia and dyslipidemia in patients with type 2 diabetes mellitus. Int. J. Med. Sci. Public Health 4 (2015): 997-1000.

41. Losso JN, Holliday DL, Finley JW, et al. Fenugreek bread: a treatment for diabetes mellitus. J. Med. Food 12 (2009): 1046-1049.

42. Xue WL, Li XS, Zhang J, et al. Effect of Trigonella foenum-graecum (fenugreek) extract on blood glucose, blood lipid and hemorheological properties in streptozotocin-induced diabetic rats. Asia. Pac. J. Clin. Nutr 1 (2007): 422-426.

43. Gaddam A, Galla C, Thummisetti S, et al. Role of Fenugreek in the prevention of type 2 diabetes mellitus in prediabetes. J. Diabetes Metab. Disord 14 (2015): 74.