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Review Article

Exploring the Adverse Effects of Fenugreek in Humans: A Scoping Review

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What's Known

- Fenugreek (*Trigonella foenum-graecum*) is a plant that has been widely used both as a culinary spice and a medicinal herb.

What's New

- The most frequently reported adverse effect associated with oral fenugreek ingestion is mild gastrointestinal discomfort.
- Other documented adverse events include hypoglycemia, suspected hypokalemia, allergic reactions, a maple syrup-like odor in the sweat or urine of mothers and breastfed infants, and interactions with specific medications.

Abstract

Background: *Trigonella foenum-graecum*, commonly known as fenugreek, is used both as a spice and a medicinal herb. While numerous studies investigated its therapeutic effects, this scoping review aimed to explore the reported adverse effects associated with fenugreek consumption in humans.

Methods: A systematic search of several scientific databases was conducted, including Google Scholar, Web of Science, PubMed/PMC-MEDLINE, Scopus, and Science Direct, from January 1990 to September 2024. The search utilized keywords such as "Fenugreek", "Adverse Effects", "Clinical Trial", and "Case Report", or "Case Series". References of retrieved articles were also screened.

Results: The review included 60 articles. Of these, 14 clinical trials reported adverse effects, 23 reported none, and 13 did not provide information on adverse effects. Additionally, 10 case reports or case series (reported in eight articles) detailed allergic reactions or hypersensitivity signs and symptoms. The most common adverse effect was mild gastrointestinal discomfort following oral consumption. Other reported effects included hypoglycemia, potential hypokalemia, allergic reactions, a maple syrup odor in the urine, sweat, or skin of infants and mothers, and interactions with certain medications.

Conclusion: Fenugreek is generally considered safe, with most reported side effects being mild and self-limiting. No fatalities have been attributed to its use. This evidence might be valuable for both the general public and healthcare professionals.

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Introduction

In recent years, public interest in complementary and alternative medicine (CAM) has grown significantly. Concurrently, global research publications on the application of CAM in clinical practice have increased. The use of herbal medicines and medicinal plants for common illnesses is becoming more popular, aligning with the rising integration of CAM alongside modern conventional treatments for a wide range of conditions.[1-4]

This growing attention from both patients and the scientific community is partly due to the incomplete success of conventional medications in treating or managing numerous common ailments, including gynecological disorders, type 2 diabetes mellitus, male reproductive problems, hyperlipidemia, cardiovascular conditions, and COVID-19.[5-10] Furthermore, several studies

documented a patient perception that the herbal and natural remedies are safer than synthetic pharmaceutical alternatives.[5-10]

Fenugreek (*Trigonella foenum-graecum L.*) is an annual plant from the *Fabaceae* family, native to some regions of Asia, Africa, southern Europe, and also Canada. The plant typically reaches 30-60 cm in height and features trifoliate green leaves. Its flowers produce slender, boat-shaped pods, each containing an average of 10-20 green-brown seeds.[11] Fenugreek seeds and leaves are used variously as a spice, food additive, flavoring, condiment, preservative, and vegetable.[12] For example, the seeds and leaves are utilized in diverse culinary applications, including Iranian stews, Swiss cheese flavoring, German syrup and bitter rum, and Egyptian mixed seed powder for flatbread. They are also used in curries, as dyes, and—when roasted—as a coffee substitute in Africa, while young seedlings are consumed as a vegetable.[11, 13]

The pharmacotherapeutic potential of fenugreek is derived from its rich array of bioactive components, including steroids, polyphenols, alkaloids, saponins, hydrocarbons, and galactomannan fiber. Furthermore, the plant contains substantial quantities of furostanolic saponins, such as trigoneoside, isoorientin, vitexin, and isovitexin. The seeds are a source of triglycerides, fatty acids, polysaccharides, notably a high concentration of galactomannan and flavone C-glycosides.[14-17] Nutritionally, fenugreek is rich in vitamin A, B_1, B_2, C, niacin, and nicotinic acid.[18] The seeds contain 28.4% protein, 9.3% fiber, and 7.1% fat,[19] in addition to minerals such as magnesium, iron, copper, chromium, and calcium.[20]

Fenugreek seed oil contains omega-6 fatty acids, which are beneficial in managing coronary heart disease, inflammation, and cancer. It also contains palmitic acid, pinene, and other components with antioxidant activity.[21] The oligosaccharides in fenugreek seeds are known to confer health benefits in type 2 diabetes by preventing the rapid absorption of monosaccharides,[17] and fenugreek supplementation has been shown to significantly improve both fasting and postprandial blood glucose levels.[22] Furthermore, diosgenin, a compound found in fenugreek, seems to prevent colon cancer[23] and has beneficial effects in hyperlipidemic patients.[24] Fenugreek extract was also demonstrated to increase serum total testosterone levels in males.[25] A saponin-rich fenugreek extract can generate multi-bioactive extracts that inhibit pancreatic lipase and cholesterol bioaccessibility, potentially leading to a hypocholesterolemic effect.[26] Additionally, fenugreek seed is recognized for its ability to improve breast milk production.[27]

Given the increasing popularity of using herbal medicine to treat various diseases and conditions,[5, 9, 28, 29] there is a growing need to evaluate and report the adverse effects of medicinal plants such as fenugreek. Therefore, this scoping review aimed to comprehensively examine human studies on fenugreek consumption, including clinical trials, case reports, and case series, to identify any associated adverse effects. The findings of this study could provide valuable information for a wide audience, particularly for patients who use fenugreek as an herbal remedy.

Materials and Methods

Study Design

This scoping review aimed to collect information on the adverse effects associated with fenugreeks consumption in human studies. A systematic search was conducted using various keywords and related MeSH terms, such as "Trigonellas," "*Trigonella foenum-graecum*", "*Trigonella foenum graecum*", "Fenugreek", "Fenugreeks", "Foenumgraecum", "Adverse Effects", "Clinical Trial", and "Case Report" and "Case Series" in multiple databases and search engines, such as Google Scholar, Web of Science, PubMed, Scopus, and Science Direct, from January 1990 to September 2024. The reference lists of retrieved articles were also screened.

The study included only English-published articles that documented the adverse effects of fenugreeks on humans. Animal studies, non-English publications, and articles for which the full text was unavailable were excluded. The eligible articles were reviewed, and relevant data were extracted and recorded in Microsoft Excel software (Microsoft Press, Redmond, WA, USA). Finally, the included articles were categorized as clinical trials, case reports, or case series.

Data Extraction

For clinical trials, the extracted data included: the health status of the participants, the number of subjects in the fenugreek and control groups, the formulation, dosage, and administration schedule of fenugreek, the interval between consumption and follow-up, concomitant interventions, study design, and any reported adverse effects. For case reports and case series, the extracted information included article title, patient demographics (age, sex), health status, medical history, clinical examination

findings, as well as the formulation, dosage, administration schedule, and reported adverse effects of fenugreek. Following the review and data extraction, the studies were categorized, and the adverse effects observed in the selected studies were summarized using the available data and tables.

The study protocol was approved by the Research Ethics Committee of Shiraz University of Medical Sciences (code: IR.SUMS.MED.REC.1399.420).

Results

Based on the inclusion criteria, the relevant data from the selected articles were organized into tables. The final review included 60 articles, comprising 50 clinical trials and 10 case reports.

Clinical Trial Articles

Of the 50 clinical trials, 14 reported adverse effects associated with fenugreek consumption, 23 reported no adverse effects, and the remaining 13 did not mention adverse effects.

As shown in table 1, among the 14 clinical trials reporting adverse effects, 57 out of 384 participants in the fenugreek group experienced them. These studies involved healthy individuals,[30] women with low libido,[31] lactating women,[32] overweight patients,[33] and individuals with type 1 and type 2 diabetes.[34, 35]

These reported adverse effects included gastrointestinal complications, such as reflux, abdominal pain, diarrhea, mild abdominal distention, hunger, appetite loss, and nausea. Other complications included migraine exacerbation, maple syrup odor in urine or sweat, frequent urination, dizziness, increased need for sanitary napkins, and hypoglycemia. The most prevalent adverse effect was urine with a maple syrup odor.

The treatment duration varied across studies, ranging from a single dose of fenugreek leaf aqueous extract to a 12-week regimen of fenugreek seed capsules.

As shown in table 2, 23 clinical trial articles reported no adverse effects. The majority of these studies investigated type 2 diabetes and utilized fenugreek seed powder.

Research on the effects of fenugreek has been conducted across diverse populations. These included studies on individuals with dysmenorrhea (n=3), polycystic ovary syndrome (n=2), Parkinson's disease (n=1), pre-diabetes (n=1), and testosterone deficiency (n=1), as well as on healthy men (n=2) and mechanically ventilated patients (n=1). The duration of these interventions ranged from 3 days to 6 months.

As shown in table 3, 13 clinical trials on fenugreek consumption, involving over 500 participants, reported no adverse effects. The studies investigated a range of health conditions, including type 2 diabetes, obesity, menopausal symptoms, hernia surgery, lactation, low libido in women, and gingivitis.

The duration of these studies varied, with the shortest being a two-day investigation using a 10% fenugreek transdermal patch on hernia surgery wounds. The longest was a 6-month trial involving patients with type 2 diabetes.

Table 1: Adverse effects associated with *Trigonella foenum-graecum* (fenugreek) in clinical trials

Authors/ year of publication	Country	Participants	Health status	Preparation and dosage	Duration of treatment	Adverse effects reported from the fenugreek group	Adverse effects reported in the control group
Steel et al., 2011[36]	Australia	30	Healthy men	Testophen tablets contain 300 mg of fenugreek powder two times a day	6 weeks	Three cases of mild stomach pain before meals	Was not observed
Rao et al., 2015[37]	Australia	40	Women with low libido	600 mg of fenugreek seed extract per day	In two consecutive menstrual periods	Two cases of exacerbation of migraine, two cases of reflux	Was not observed
Rao et al., 2020[31]	Australia	50	Benign prostatic hyperplasia	600 mg of fenugreek seed extract per day	12 weeks	Three cases of reflux	One case of reflux
Najdi et al., 2019[38]	Saudi Arabia	5	Type 2 diabetes that was treated with metformin	2 g of fenugreek in capsule form (one 500 mL capsule after breakfast, two capsules after lunch, and one capsule after dinner)	12 weeks	One case of hypoglycemia	Was not observed

Authors/ year of publication	Country	Participants	Health status	Preparation and dosage	Duration of treatment	Adverse effects reported from the fenugreek group	Adverse effects reported in the control group
Bumrungpert et al., 2018[32]	Thailand	25	Lactating lady	3 capsules (200 mg fenugreek seeds, 120 mg ginger, 100 mg turmeric) 3 times a day	4 weeks	Two cases of flatulence, two cases of urine with the odor of maple syrup	Two cases of urine with the odor of maple syrup
Chevassus et al., 2009[33]	France	24	Healthy	Fenugreek tablets (one group, 588 mg, and another group, 1176 mg)	3-14 days with 14 days in between	One case of heartburn, two cases of the specific smell of urine	Was not observed
Chevassus et al., 2010[39]	France	19	Overweight	Fenugreek tablets contain 1176 mg of hydroalcoholic extract of fenugreek seeds daily	6 weeks	Four cases of mild gastrointestinal symptoms, one case of a specific odor of urine and sweat	Was not observed
Emtiazy et al., 2018[40]	Iran	28	Mild asthma	Ten mL of fenugreek seed extract syrup, two times a day	4 weeks	Two cases of increased sanitary napkin use during menstruation	Was not observed
Sharma et al., 1990[34]	India	10	Type 1 diabetes	50 g of fenugreek seed powder, two times a day, at lunch and dinner, added to bread	10 days	Four cases of gastrointestinal symptoms, including diarrhea and bloating	Was not observed
Gupta et al., 2001[35]	India	12	Type 2 diabetes	1 g of hydroalcoholic extract of fenugreek seeds in capsule form	2 months	Five people with mild abdominal distension	Was not observed
Abdel-Barry et al., 2000[30]	Iraq	20	Healthy	40 mg per Kg bodyweight of fenugreek leaf extract in 10 mL of boiled water	A single dose	Four cases felt hungry, four cases of frequent urination, and four cases of dizziness.	Was not observed
Lu et al., 2008[41]	China	46	Type 2 diabetes	Six 35% pills from seeds three times a day	12 weeks	Two cases of nausea and one case of diarrhea	Was not observed
Sudheeran et al., 2016[42]	India	20	Healthy	500 mg capsules, including 300 mg of fiber and 200 mg of turmeric, two times daily before breakfast and at bedtime	30 days	Two cases of decreased appetite	One case of gastro-intestinal problems
Mirgoaybayat et al.,[43]	Iran	55	Polycystic Ovary Syndrome	Take 333 mg of fenugreek capsules three times a day (Mootta capsules contain 333 mg of dry fenugreek extract, standardized to contain 53.7% trigonelline, the key phytochemical compound in fenugreek)	2 months	Six (10.9%) cases of nausea	32 (58.2%) cases of nausea, 16 (29.1) cases of headache

Table 2: Clinical trials with no associated adverse effects from *Trigonella foenum-graecum* (fenugreek) administration

Authors/ year of publication	Country	Number of participants in the fenugreek group	Health status of the fenugreek group	Preparation and dosage	Duration of the treatment
Shamshad et al., 2016[44]	India	44	Involved in menopausal symptoms	250 mg capsules of fenugreek seed extract twice a day for a week and four times a day for 12 weeks	90 days
Swaroop et al., 2015[45]	USA	50	Polycystic ovary	500 mg capsules of fenugreek seed extract two times a day	90 days
Nathan et al., 2013[46]	India	25	Parkinson	300 mg of fenugreek seed extract two times a day	6 months
Florentin et al., 2019[47]	Greece	50	Pre-diabetes	Tablets containing bergamot extract 500 mg, fenugreek seed extract 200 mg, and olive leaf extract 100 mg once a day	6 months
Verma et al., 2016[48]	India	77	Type 2 diabetes	500 mg capsules of fenugreek seed extract two times a day	90 days
Geberemeskel et al., 2019[49]	Ethiopia	57	Type 2 diabetes	25 mg of fenugreek seed extract solution two times a day	1 month
Madar et al., 1988[50]	Israel	21	Type 2 diabetes	15 g of fenugreek seeds mixed with water	7 days
Younesy et al., 2014[51]	Iran	51	Dysmenorrhea	900 mg capsules of fenugreek seed powder three times a day	The first three days of menstruation
Losso et al., 2009[52]	USA	10	Type 2 diabetes	9% of bread wheat flour replaced with 2.5 g of fenugreek seed powder (1 slice, two times a day)	1 week
Inanmdar et al., 2016[53]	India	20	Primary dysmenorrhea	Three capsules equivalent to 3 g of fenugreek seeds	The first 3 days of menstruation
Park et al., 2018[54]	Korea	44	Testosterone deficiency syndrome	200 mg capsules of fenugreek seeds two times a day	8 weeks
Hassanzadeh et al., 2013[55]	Iran	23	Polycystic ovary	500 mg capsules of fenugreek seed extract two times a day	2 months
Rao et al., 2016[56]	Australia	55	Healthy men	600 mg daily fenugreek seed extract	12 weeks
Maheshwari et al., 2017[57]	India	50	Healthy men	500 mg capsules of fenugreek seeds after breakfast	12 weeks
Rao et al., 2020[31]	Australia	40	Type 2 diabetes mellitus	Used two chapatis twice a day, 6 days/week for a daily dose of 5.45 g of an *Nigella sativa* /fenugreek combination	12 weeks
Hausenblas et al., 2021[58]	USA	19	Healthy men	Fenugreek 400 mg/d	60 days
Zarghi et al., 2021[59]	Iran	33	Mechanically ventilated patients hospitalized	3 mg of fenugreek seed powder with a gavage solution twice daily	5 days
Foroumandi et al., 2023[60]	Iran	41	Alzheimer's disease	Received 5 mL oral seed extract of fenugreek (equivalent to 500 mg of dry extract) added to the similar routine treatment, including Donepezil (5 mg twice a day) and Sertraline (50 mg once a day).	4 months
Gupta et al., 2024[16]	India	42	Type 2 diabetes	Use 1000 mg (500 mg×2) daily (Fenfuro®) capsules, that was a novel Fenugreek seed extract with >45% furostanolic saponins	12 weeks
Lee-Ødegård et al., 2024[61]	Norway	600 mg (n=21), 1200 mg (n=25) and 1800 mg (n=27)	Men with reduced energy and libido related to non-optimal testosterone levels	Taking 3 tablets daily, 600 mg (n=21), 1200 mg (n=25), and 1800 mg (n=27) of fenugreek extract and essential nutrients.[a]	12 weeks
Hota D et al., 2024[16, 62]	India	204 (total patients)	Type 2 diabetes	Fenfuro® in the dosage of 500 mg twice daily along with metformin	12 weeks
Singh et al., 2023[63]	India	113	Pre-menopausal women with polycystic ovary syndrome (PCOS)	Furocyst® (2 capsules of 500 mg/day)	90 days

a. No reported side effects, but with a slight increase in serum concentrations of ALAT and creatinine

Table 3: Clinical trials of *Trigonella foenum-graecum* (fenugreek), not reporting adverse effects

Authors/ year of publication	Country	Fenugreek group participant	Health status of the fenugreek group	Preparation and dosage	Duration of the treatment
Robert et al., 2016[64]	Malaysia	10	Healthy	Buns and flatbreads each contain 10% fenugreek seed powder with 50 g of glucose and 250 mL of water daily.	6 times
Sundaram et al., 2018[65]	India	40	Uncontrolled type 2 diabetes treated with metformin, with chronic periodontal disease	12.5 g of fenugreek powder before breakfast and lunch	1 month
Ansari et al., 2019[66]	Iran	30	After transdermal local patch hernia surgery	10% fenugreek daily	2 days
Bordia et al., 1997[67]	India	20	Non-insulin-dependent diabetes mellitus (NIDDM) and coronary artery disease	2.5 g twice a day	3 months
	India	20	Non-insulin-dependent diabetes mellitus (NIDDM) without coronary artery disease	2.5 g twice a day	3 months
	India	20	Healthy	2.5 g twice a day	3 months
Ghasemi et al., 2015[27]	Iran	39	Healthy breastfeeding mothers	7.5 g of fenugreek seed powder with 3 g of black tea three times a day	4 weeks
Kassaian et al., 2009[68]	Iran	11	Type 2 diabetes	10 g of fenugreek seed powder soaked in water daily	8 weeks
Kassaian et al., 2009[68]	Iran	7	Type 2 diabetes	10 g of fenugreek seed powder in yogurt daily	8 weeks
Ranad et al., 2017[69]	India	30	Type 2 diabetes	10 g of fenugreek seeds soaked in water	6 months
Kiss et al., 2018[70]	Hungary	8	Healthy	500 mg capsules, the first day two capsules in two meals at noon and evening, the last day two capsules in the evening, and on other days two capsules three times a day	11 days
Mathern et al., 2009[71]	USA	18	Fat	Extracts of 4 and 8 g of fenugreek fiber in beer	3 days
Steels et al., 2017[72]	Australia	54	Menopausal symptoms	600 mg of seed extract without fenugreek pod daily	12 weeks
Palacios et al., 2019[73]	Spain	29	Women with low libido	Tablets contain 300 mg of fenugreek extract two times a day	2 months
Mehrzadi et al., 2020[74]	Iran	150	Type 2 diabetes	Traditional herbal capsules including 115 mg fenugreek, caper, rosehip, *Securigera securidaca*, *Silybum marianum* (milk thistle), nettle, and *Caucasian whortleberry* daily	3 months
Varghese et al., 2021[75]	Karnataka	15	Gingivitis	Use toothpaste daily, two times (morning and at night) in a pea-size amount	14 days

Case Reports and Case Series Articles

As detailed in table 4, ten case reports were qualified, reviewed, and analyzed. The cases involved seven females and three males, with ages ranging from infancy to 67 years.

The most commonly reported adverse effects of fenugreek were allergic reactions, including pruritus, shortness of breath, rhinorrhea, diarrhea, angioedema, cough, and anaphylaxis (seven cases). Almost all cases reported a history of allergies to other substances, such as peas, peanuts, and coriander. In one case, the topical application of a fenugreek ointment to the scalp for dandruff resulted in syncope.

One case of Stevens-Johnson syndrome and toxic epidermal necrosis was reported in a 32-year-old woman. The reaction, presenting as blisters and sores on her face and upper torso, occurred 1 month postpartum after she had taken a fenugreek-containing medication to stimulate lactation.

In another report, a newborn boy exhibited a maple syrup odor from his skin and diaper area after his mother had consumed fenugreek during early labor.

Another case described a 67-year-old woman with atrial fibrillation whose international normalized ratio (INR) increased following the consumption of fenugreek and Boldo drops while on warfarin therapy.

In another report, symptoms suggestive of serotonin syndrome, including hyperreflexia, tachycardia, nausea, and anxiety, were observed in a 38-year-old woman with psychosis.

Table 4: Reported adverse events of *Trigonella foenum-graecum* (fenugreek) in case reports and series

Authors/ year of publication	Country	Sex	Age	Health status	How to expose	Adverse effects	Result
Patil et al., 1997[76]	India	Woman	37	Mild asthma - pea allergy	Open and smell the glass containing fenugreek	Runny nose and eyes, cough, fainting	Treated
Patil et al., 1997[76]	India	Woman	45	Asthma - Dandruff with a history of wheezing after eating fenugreek	Fenugreek seed ointment on the scalp	Angioedema of the face, runny nose, and numbness of the head	Treated
Bentele-Jaberg et al., 2015[77]	Switzerland	Woman	32	1 month after delivery	Eat medicine made from fenugreek seeds	Blisters and sores on the face and upper body, with involvement of the mouth, lips, and tongue	Treated
Joseph et al., 2018[78]	USA	Man	14	Healthy	Eat food containing fenugreek	Urticaria, chest tightness, abdominal pain, vomiting	Treated
Korman et al., 2001[79]	Israel	Man	Infant	Healthy	The baby's mother consumed fenugreek in the first hours of labor pains	The smell of maple syrup from the skin and diaper area	Treated
Lambert et al., 2001[80]	Canada	Woman	67	Atrial fibrillation on warfarin	A fenugreek capsule with ten drops of Boldo after a meal	Increase INR	Treated
Aurich et al., 2019[81]	Germany	Woman	34	Atopic dermatitis, asthma, peanut allergy	Eat a Chinese soup containing fenugreek	Facial flushing, angioedema, shortness of breath, nausea, and diarrhea	Treated
Doolabh et al., 2019[82]	Australia	Woman	38	Psychosis on sertraline during breastfeeding	Use fenugreek supplements to increase breastfeeding	Symptoms of serotonin syndrome include hyperreflexia, nausea, anxiety, and tachycardia	Treated
Ohnuma et al., 1998[83]	Japan	Woman	26	Healthy	Use curry powder containing fenugreek	Itching, diarrhea, wheezing	Treated
Ebo et al., 2006[84]	Belgium	Man	25	Healthy with a history of allergies to fenugreek and coriander in occupational exposure	Eat a loaf of bread containing fenugreek and coriander	Anaphylactic reactions include generalized urticaria, conjunctivitis, bronchospasm angioedema	Treated

The symptoms emerged after she consumed a fenugreek supplement to augment lactation while taking sertraline and breastfeeding.

Discussion

The utilization of herbal remedies, herbal medicinal products, and supplements has surged significantly over the past three decades. It is estimated that at least 80% of the world's population relies on these products for several aspects of healthcare, including preventive, therapeutic, or palliative care.[85, 86] The use of herbal products is deeply entrenched in the traditional medicinal practices of many cultures for disease prevention and treatment.[87] Although the World Health Organization (WHO) acknowledges herbal products as a vital component of the healthcare system, growing apprehensions exist regarding their quality and safety.[88] Herbal products are generally not subject to stringent regulation, as they are often classified as dietary supplements, thereby evading the rigorous scrutiny required for pharmaceutical drugs. Despite a widespread public perception that herbal remedies are inherently safe, numerous studies indicated that they could cause mild to severe, clinically significant adverse effects.[28, 89]

Nowadays, the market for non-registered health-related products consists primarily of herbal remedies and food supplements. In this context, official or governmental systems often fail to comprehensively document their adverse effects, which are typically reported on a case-by-case basis. Research revealed that consumers might experience adverse events from herbal food supplements, particularly when they received insufficient information about these products.[90-93]

Fenugreek is commonly used as a food flavoring and is also consumed traditionally to prevent or treat certain diseases.[94, 95] While numerous systematic reviews have examined its efficacy[19, 96, 97] and toxicity,[98] no previous review has specifically focused on its adverse effects. This study is the first to systematically extract and summarize the adverse effects reported across various study types. This study illustrated the potential negative consequences associated with fenugreek consumption.

The most significant and well-documented adverse effects were allergic and hypersensitivity reactions, including angioedema, anaphylaxis, Stevens-Johnson syndrome, and toxic epidermal necrolysis. The clinical significance of these reactions is underscored by their documentation in dedicated case reports and case series. Other less common but notable adverse effects included serotonin syndrome, a maple syrup odor in infants, elevated INR level, dizziness, syncope, and other similar symptoms. However, the most frequently reported adverse effects were gastrointestinal problems, which were often mild and required no treatment. According to the included articles, all patients who experienced adverse effects from fenugreek recovered completely, with many cases resolving without intervention.

Several mechanisms could be suggested for the adverse effects associated with fenugreek. Gastrointestinal effects, such as indigestion, abdominal distention, and bloating, are likely attributable to its high fiber content.[99] This high fiber content may also interfere with the absorption of concurrently administered oral medications. Consequently, it is advisable to avoid combining fenugreek with oral drugs, particularly those with a narrow therapeutic index. The hypoglycemic activity of fenugreek, which occurs through the stimulation of insulin signaling pathways[100] and the inhibition of carbohydrate digestion and absorption by its soluble dietary fiber,[101] poses a risk of hypoglycemia. Therefore, diabetic patients should use fenugreek with caution, and long-term use might necessitate an adjustment of their insulin dose. Moreover, fenugreek consumption was associated with reduced serum levels of potassium.[76] Evidence showed that when used concomitantly with diuretics or other hypokalemic agents, fenugreek might potentially contribute to hypokalemia.[102, 103]

Dizziness associated with fenugreek use might result from a significant decrease in systolic blood pressure[101] or from hypoglycemia-induced neurological symptoms due to its activity on insulin receptors.[22] Moreover, concomitant use of fenugreek with antiarrhythmic drugs, diuretics, laxatives, or mineralocorticoids might increase the risk of hypokalemia and potentiate cardiac glycoside toxicity. Fenugreek seed extracts exhibited both central nervous system (CNS) stimulant and depressant activities,[77, 78] which could potentially trigger seizures in individuals with epilepsy.

The most frequently reported significant complications were allergic reactions to fenugreek.[76-78, 81, 83, 84] As fenugreek belongs to the Fabaceae family, individuals with allergies to peanuts, peas, or coriander should use it with caution due to the potential for cross-reactivity. Fenugreek might also interact with serotonergic drugs, such as selective serotonin reuptake inhibitor (SSRI), increasing the risk of serotonin syndrome.[82] A case report noted that fenugreek could elevate the INR, a critical consideration for patients taking warfarin.[80] A rare, benign, yet well-documented effect is a maple syrup odor in the urine or sweat of infants or mothers following maternal consumption.[79] Finally, the safety of long-term fenugreek use remains uncertain due to a lack of extensive studies.

This study had several limitations. As a scoping review, it did not incorporate critical steps of a systematic review, such as a formal quality assessment of the included studies, an evaluation of the risk of bias, or the use of independent reviewers for article selection and data extraction. Furthermore, the overall quality of the evidence was not assessed using a tool such as GRADE. The review was also limited by its exclusion of animal studies, experimental studies, case-control studies, cross-sectional studies, and cohort studies. Consequently, the authors recommend that future research consider these limitations.

It is important to note that a meta-analysis was not an objective of this study. In addition, while some of the included studies did not report any adverse events, this could not be taken as definitive proof of their absence. The authors suggested that a future systematic review and meta-analysis (including network meta-analysis) could provide more robust insights into the adverse effects of fenugreek and its supplements. Finally, further studies are strongly recommended to investigate the mechanisms underlying fenugreek's adverse effects and to assess the relationship between dosage, severity, and the incidence of these side effects.

Conclusion

Fenugreek and its supplements are commonly used worldwide as both a vegetable and an herbal remedy. Although widely perceived

as safe, several studies demonstrated that it could cause adverse effects, including allergic and hypersensitivity reactions, gastrointestinal complaints, headache, dizziness, hypoglycemia, elevated INR levels in plasma, and hypokalemia. However, it is crucial to note that no documented fatalities or cases requiring aggressive medical intervention were attributed to fenugreek use.

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Authors' Contribution

E.AA: Study design, conception, data gathering, data analysis, data interpretation, drafting and reviewing critically; MM.P: Study design, data analysis, data interpretation, and reviewing critically; R.Z: Data analysis and drafting; M.MJ: Data gathering and drafting; Th.R: Study design and reviewing critically; M.P: Study design, conception, data gathering, data analysis, data interpretation and reviewing critically; All authors approved the final the version of the manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of AI

Artificial intelligence (QuillBot) was used solely for language editing. The authors are fully responsible for the content and integrity of the manuscript.

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