Original Article

Phytochemical And Pharmacological Activity Of Trigonella Foenum Graceum And Its Impact On Polycystic Ovarian Syndrome: A Comprehensive Review

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Abstract

The main cause of infertility worldwide is PCOS, an endocrine disorder caused by increased levels of androgens (male hormones) in females of reproductive age. The various treatments include lifestyle changes, ovulation induction, high testosterone therapy, insulin sensitizer, myoinositol, folic acid, and vitamin D supplementation and surgical intervention. However, due to drug side effects, there has been an increase in the use of herbal medicines. Herbs and spices are some of the best sources of organic compounds and are necessary for a healthy lifestyle. Fenugreek, a member of the Fabaceae family and one of the oldest spices, is frequently used in traditional herbal remedies and food preparations. It has a wide range of pharmacological properties due to its abundance of diverse phytoconstituents, including antibacterial, antioxidative, anti-parasitic, hypocholesterolemic, anti-fertility hypertensive, hyperthyroidism, etc., Many clinical studies elucidated that the fenugreek seed consumption improved menstrual cycle regularity, reduced polycystic appearing ovaries, decreases the ovarian volume, cysts and significantly increase the follicular stimulating hormone (FSH) and luteinizing hormone (LH) levels. Additionally, it has been noticed complete cyst dissolution, a significant reduction in cyst size, and the return of a routine menstrual cycle. In order to assess the safety and pharmacological mechanisms of fenugreek seeds in PCOS, additional preclinical and clinical studies with a larger sample size and a more structured methodology are imperative.

Keywords: Fenugreek, Phytochemistry, Antioxidant, PCOS, infertility, reproductive health

Introduction

Natural products have enormous nutritional and health benefits due to their high content of vitamins, minerals, amino acids, proteins, fibres, phenolic compounds, antioxidants, and bioactive metabolites. These substances also serve as fresh starting points for the creation of new drugs, especially when the production of synthetic drugs already in use fails to reach their full pharmacological potential (Khan et al., 2020; Goni et al., 2021). Due to their numerous

drawbacks, including their negative side effects, slow response, and high price, synthetic drugs also have a very low success rate. As a result, new natural therapeutic drugs must address these issues with synthetic drugs (Rahman et al., 2020).

Herbs and spices are some of the best sources of organic compounds and are necessary for a healthy lifestyle. Furthermore, it was stated that "medicine and food have a common origin" simultaneously. Herbs and spices have long been used extensively in the practice of cooking as food additives (Freitas et al., 2021). They are now an essential component of many traditional herbal remedies and different healthcare products. Their mildly toxic natural pharmacological properties aid in regenerating biological tissues, slowing the ageing process, and treating metabolic disorders, cardiac disorders, neurodegenerative diseases, and other conditions (Singh et al., 2021). In order to prevent dyslipidemia and obesity, consuming functional food also increases the activity of nuclear transcription factors called peroxisome proliferator-activated receptors, which are involved in lipid metabolism (Freitas et al., 2021). They are therefore the most popular natural immune boosters.

Fenugreek

Fenugreek, a member of the Fabaceae family and one of the oldest spices, is frequently used in traditional herbal remedies and food preparations (Snehlata & Payal, 2012). The Greek word for this plant, Trigonella, means "three angled," which describes its triangular flowers. The herb is grown all over the world, depending on the edaphoclimatic conditions, including in India, North Africa, Mediterranean Europe, Russia, the Middle East, China, Pakistan, Iran, Afghanistan, Australia, Canada, Argentina, and the United States. India is the world's largest producer of fenugreek, but due to its high domestic consumption, it does not contribute significantly to the global fenugreek trade. Figure: 1 depicts the fenugreek plant and seeds (Mandal & DebMandal, 2016; Zandi et al., 2017).

The herb is a flavorful, yearly forage legume crop that is widely used as a traditional spice. It has reportedly been used in Tibetan and Chinese medicine as well as Indian Ayurvedic medicine in the past. Fenugreek was used for embalming mummies for the first time in history, according to Egyptian papyrus from 1500 B.C. Additionally, they reported using this plant as a lactation stimulant (Snehlata & Payal, 2012). Trigonella seeds are an addition to bread making in African cuisine. Galactomannan, which is found in seeds, is a plentiful source of soluble dietary fibres that increases the bread's nutritional value and physicochemical stability. The leaves and seeds are mostly used to flavour foods like cheese, curries, seasonings, pickles, maple syrup, chutneys, and dietary supplements because of their potent aroma. Green leaves can also be consumed raw while the seeds are ground to create pastes or curry powder (Liu et al., 2012).

According to reports, nutritional supplements are essential for preventing gastrointestinal diseases and maintaining general gastrointestinal health. They have also been shown to be effective in treating a variety of conditions, including cancer, diabetes, menstrual pain, abdominal cramps, asthma, emphysema, pneumonia, microbial infection, hormonal imbalance, and inflammation. Fenugreek seeds are used in pharmaceutical and nutraceutical products due to their abundance of antioxidant compounds (Snehlata & Payal, 2012).

Figure: 1 fenugreek plant & seeds

The botanical description

The Fabaceae family includes the significant medicinal herb Trigonella foenum-graecum. It is an annual herb that measures 0.3–0.8 m (1-2 ft) in length and is aromatic. Trifoliate, 20–25 mm long, toothed, gray–green, obovate leaves are present on the long, slender stem. The Scientific classification was shown in table:1. Obovate to oblanceolate leaflets can be found on the long-stalked leaves. Flowers range from white to yellow and are papilionaceous. They flower in the middle of summer, from June to July. The sword-shaped, yellow to brown, sessile, axillary raceme flowers produce 10-15 cm long, thin, slender pods with a curved beak-like tip. Each mature pod produces 10 to 20 brown, 5 mm long, oblong or square-shaped hard seeds. The seeds are used as a spice and have high economic value (Snehlata & Payal, 2012).

Table; 1 scientific classification

Scientific classification of fenugreek	
Kingdom	Plantae
Class	Mangnoliopsida
Order	Fabales
Family	Fabaceae
Subfamily	Papilionaceae
Genus	Trigonella
Species	foenum-graecum

Distribution

According to C. Linnaeus, the genus Trigonella should have 260 species, but the exact total species count is still up for debate. There are currently only 18 species of Trigonella known. Fenugreek, also known as T. foenum-graecum, is one of them and is a species that is widely cultivated (Zandi et al., 2017). Although it originated in Central Asia,South-Eastern Europe, Western Asia, Northern Africa, and the Mediterranean region, it is now widely cultivated almost everywhere in the world, including India,Pakistan, Canada, Russia, Afghanistan, Egypt,Morocco, South East Asia, Ethiopia, Argentina, Iran, Chile, Australia, and the United States,China among other places. It was once cultivated as fodder in North Africa. It is primarily grown in the European countries of Austria, Hungary, Belgium, France,and Spain. Naturally, it can also be found in semi-highland and highland areas on field roadsides, uncultivated

land, dry grasslands and hillsides. In India, Rajasthan, Punjab,Gujarat, Haryana, Utter Pradesh, Madhya Pradesh, Uttaranchal,and Maharashtra are the principal growing regions for trigonella. According to Kenny et al. (2013) and Zandi et al. (2017), Rajasthan alone makes a significant contribution more than 80% of India's total fenugreek production.

Phytochemistry:

Trigonella foenum-graecum is a prolific source of various nutrients, including alkaloids, amino acids,phenolic acids, fatty acids, flavonoids, polysaccharides, triterpenoids, fibres, fixed oils, coumarins, and steroidal saponins and vitamins. Fenugreek contains steroidal saponins such as disogenin, gitogenin, neogitogenin, saponaretin, and others. Fenugreek's main bioactive is trigonelline. Choline, coumarins (trigocoumarin, trimethyl coumarin, and scopoletin), fenugreekine, nicotinic acid, phytic acid, gentianine, apigenin, luteolin, orientin, kaempferol, quercetin, vitexin, caffeic acid, and furostanol saponins, also known as trigoneoside, are other compounds found in the plant. Numerous sex hormones are thought to have diosgenin as a precursor (Steels et al., 2011; Tejaswini et al., 2012; Talapatra & Talapatra, 2015).

Nutritional importance

Fenugreek has a different nutritional profile depending on the edaphoclimatic and harvesting conditions in each region. Fenugreek is an extremely nutritious plant that can be used for a variety of things, including vegetables, food, beverages, cosmetics, fragrances, and other industrial uses. Alkaloids like trigonelline, nicotinic acid, and others are found in the stem. Mucilage, proteins (tryptophan and lysine), fibres, alkaloids, flavonoids, fixed and volatile oils, and proteins are all abundant in seeds. Mannose and galactose make up its gum. Alkaloids, Oil and steroidal saponins are what give fenugreek seeds their bitter flavour. Additionally, they contain vitamins (A, B1, C), sitosterol, n-alkanes, sesquiterpenes, and cholesterol. Trace elements that they also contain include Ca, Cu, Fe, Zn, K, Mg, P, Na, and Mn. They also contain a sizable portion of free amino acids (4-hydroxy isoleucine, arginine, lysine, and histidine), as well as mucilaginous fibre and galactomannan, two types of carbohydrates (Snehlata & Payal, 2012; Zandi et al., 2017). As a result, they can be used as a great food source to maintain good health.

Pharmacological activities

In various cultural cuisines, fenugreek is primarily used as a spice or food additive. In addition to its nutritional value, it is well known for having a wide range of therapeutic properties. It has a wide range of pharmacological properties due to its abundance of diverse phytoconstituents, including antibacterial, antioxidative, antifungal, antiviral, antiatherogenic, antidiabetic, anti-parasitic, hypocholesterolemic,anti-fertility hypertensive, antiulcerogenic, antitumor, immunomodulatory, antineoplastic, anti-inflammatory, antipyretic, , antiseptic, arthritis, hyperthyroidism, etc., According to reports, the steroid saponins are effective anti-inflammatory and lactation-stimulating substances. While the 3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) and Lactate dehydrogenase (LDH) leakage assay demonstrated its role in glucose transporter-4 (GLUT-4) translocation without any toxicity symptoms, the enzyme-linked immunosorbant assay (ELISA) disclosed the cytotoxicity of the Trigonella extract. Additionally, fever appetite stimulation, flatulence, diabetes, wound healing and inflammation have all been reported to benefit from its use (Snehlata & Payal, 2012; Tejaswini et al., 2012; Mandal & DebMandal, 2016).

Effect of fenugreek on polycystic ovary syndrome (PCOS)

PCOS and its prevalence

One of the most prevalent conditions that affect both the metabolic and reproductive systems is polycystic ovary syndrome. The most prominent symptoms of PCOS are hyper-androgenism, chronic an ovulation, and irregular menstrual cycles (Eshre, 2004; Ozcan Dag et al., 2017). The prevalence of polycystic ovaries is 28%, while that of PCOS is 10%, according to the Rotterdam criteria (Bozdag et al., 2016). There is no single effective treatment for this disorder because the pathogenesis is still unclear, despite the fact that it likely has epigenetic roots (Celik et al., 2012).

The main cause of infertility worldwide is PCOS, an endocrine disorder caused by increased levels of androgens (male hormones) in females of reproductive age. A number of clinical symptoms, including irregular menstruation, infertility, androgen growth, hirsutism, insulin resistance, acne, weight gain, and ovarian cysts, are linked to PCOS. In various societies, PCOS prevalence has been estimated to range from 2.2-26%. A hormonal imbalance-related condition that can lead to infertility is known as Stein-Leventhal Syndrome or chronic oligoanovulation. Normally, ovarian follicles release fully developed eggs, but in PCOS, the underdeveloped egg gets trapped and forms cysts inside the swollen follicle instead of being released (Norman et al., 2007; Helvaci et al., 2014).

The prevalence of PCOS worldwide has been the subject of numerous studies. Due to differences in the population being studied, restrictions on sampling, protocols used, and a lack of standardized definitions for the phenotype, results have been observed even when using the same diagnostic criteria. Most PCOS cases are reported in women in their 20s and 30s who complain of having trouble getting pregnant. Menstrual disorders like oligomenorrhea or amenorrhea, hirsutism, obesity, a rapid increase in weight or difficulty losing weight, other symptoms of type 2 diabetes, oily skin, acne, and trouble getting pregnant are among the symptoms of PCOS. It can also lead to psychological and social issues (Celiket al., 2012; Seaman et al., 2004).

Pathogenesis

Ovarian dysfunction, elevated insulin levels, and dysfunction of the hypothalamus-pituitary-adrenal axis all seem to be important in the development of PCOS. PCOS is a condition marked by abnormal ovarian steroid secretion, which may be linked to insulin resistance, as well as abnormal gonadotropin secretion, including abnormal levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). LH function is elevated and androgen synthesis is stimulated by insulin. In PCOS patients, the ovaries overproduce dehydroepiandrosterone, androstenedione, and testosterone (Messinis, 2005).

PCOS women have been shown to secrete an excessive amount of the adrenal precursor androgen. The development of the severe endocrine and metabolic disturbances linked to PCOS may be significantly influenced pathologically by hyperandrogenism. A glycoprotein called sex hormone-binding globulin (SHBG) has the ability to control the bioavailability of sex steroid hormone, and levels of SHBG are associated with an increased risk of PCOS. Due to the presence of insulin resistance, PCOS women with low SHBG levels were more likely to have hyperandrogenism, type 2 diabetes, insulin resistance, glucose intolerance, obesity, infertility, and cardiovascular disease (CVD). Classic PCOS (Phenotypes A and B), Ovulatory PCOS (Phenotype C), and Nonhyperandrogenic PCOS are the three phenotypes that have been identified for this condition (Phenotype D). Each patient should receive treatment that is specific to their phenotype and expectations, such as their desire for pregnancy (Tannus, 2015).

Importance of herbs on PCOS treatment

Patients with PCOS have undergone a variety of treatments, including lifestyle changes, ovulation induction, high testosterone therapy, insulin sensitizer, myoinositol, folic acid, and vitamin D supplementation, assisted reproductive technology therapy, and surgical intervention. Metformin is the primary treatment for women with PCOS who have insulin resistance and glucose intolerance, but a study found that pioglitazone significantly improved menstrual cycle and ovulation in PCOS patients more effectively than metformin did. Clomiphene Citrate is yet another medication

recommended (CC). CC, a non-steroidal selective oestrogen receptor modulator, stimulates ovulation effectively but has an unsatisfactory pregnancy rate (Vrbikova and Cibula, 2005; Balen et al., 2016; Abu et al., 2016).

However, due to drug side effects, there has been an increase in the use of herbal medicines as natural antioxidants and anti-inflammatory agents to control hypertension and hyperlipidemia and to regulate metabolism. The use of medicinal herbs may be crucial in the treatment of PCOS. The conditions of PCOS patients are improved by these medicinal herbs' steroidogenic response, which expresses oestrogen receptor protein, decreases androgens, increases glucose uptake, and increases glucose uptake. Approximately 40% of adults now benefit from complementary treatments as a result of recent growth in their use. Women are more likely than men to use complementary medicine, particularly for self-care. Evidence suggests that 40% of non-pregnant/non-postpartum women use complementary medicine, compared to 37% and 28%, respectively, for pregnant and postpartum women. Traditional Persian and Chinese medicine were the first to use herbal medicine as a complementary therapy (Lunny CA, Fraseret al., 2010; Bishop et al., 2011).

Impact of Fenugreek on PCOS

Fenugreek has historically been used in Ayurvedic and Chinese medicine. Numerous medical conditions, including indigestion, labour induction, and immune booster, were addressed in the application. Fenugreek seeds may have hypoglycemic, antiplasmodiac, anticarcinogenic, anti-hyperlipidemic, anti-hair loss, antinociceptive, weight-loss aiding, and gastro protective properties, according to preliminary animal and human trials. Fenugreek should be avoided during pregnancy due to its oestrogen content and capacity to stimulate the uterus (Hosseinkhani et al., 2017).

Bashtian et al. (2013) performed a randomized, double-blind, placebo-controlled study on 58 female patients with oligo-anovulatory PCOS. These PCOS patients received an eight-week course of treatment that included hydroalcoholic extract of Trigonella seed and metformin as an adjuvant. The PAO (polycystic appearing ovaries) were significantly reduced and the menstrual cycle was significantly improved when metformin was administered as an adjunctive therapy for the extract.

FurocystTM, a brand-new Trigonella seed extract, was studied by Swaroop et al. (2015) for its effectiveness in treating PCOS. 50 premenopausal women between the ages of 18 and 45 participated in a post-marketing surveillance trial that was open-labeled, one-armed, non-randomized, and examined. Furocyst was administered to the women twice daily (500 mg per capsule) for a total of 90 days. The therapy produced a marked decrease in ovarian volume, cysts, and a marked increase in follicular stimulating hormone (FSH) and luteinizing hormone (LH) levels. Additionally, they noticed complete cyst dissolution, a significant reduction in cyst size, and the return of a routine menstrual cycle in about 46%, 36%, and 71% of the population, respectively. 12 percent of the women were also able to get pregnant after the treatment period was over.

The recent single-blind, randomized, controlled trial was performed in which fenugreek seed powder was used for 90 days to treat 90 premenopausal women with PCOS. The subjects underwent regular monitoring for any side effects related to the administration of fenugreek seed powder while also receiving advice about diet and exercise. Vital clinical assessments of the human subjects were performed at the beginning of the study and by the 90th day of the trial. Evaluation of BMI, LHFSH, ovarian size, menstrual regularity, and FBG were all clinical estimations. Overall findings showed that raw fenugreek seed administration for a prolonged period of time was particularly effective for PCOS-affected women. Three months of fenugreek seed consumption improved menstrual cycle regularity, egg maturation, decreased ovarian volume, and reduced infertility (Abbasi and Abbasi ,2019).

Conclusion

On the basis of recent clinical evidence, fenugreek may be beneficial in the management of PCOS. However, some restrictions, such as a small sample size and brief study duration, make it uncertain whether they are effective. In order to assess the safety and pharmacological mechanisms of fenugreek seeds in PCOS, additional preclinical and clinical studies with a larger sample size and a more structured methodology are imperative.

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