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PHYTOCHEMICAL COMPOSITION AND MEDICINAL USES OF TRIGONELLA FOENUM-GRAECUM (FENUGREEK) WITH SPECIAL ASSESSMENT AGAINST SARS-COV-2 INFECTION

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ABSTRACT
Trigonella foenum-graecum (Fenugreek) is an important leafy vegetable crop with its seeds being used as spices in Asian and South west European countries. The plant mainly contains polyphenols, flavonoids, polysaccharides, alkaloids, glycosides, saponin, anthraquinone, tannins, phenol, and carbohydrates. The plant exhibit significant pharmacological activities as anti-diabetic, anti-cancer, antioxidant, anti-obesity, antihypertensive, anti-inflammatory, anti-arthritis, antimicrobial, antiviral, and hypotensive. The plant also possesses various medicinal properties and used in respiratory problems, reproductive disorders, fever, carminative, antacid, stomach disorders, hepatoprotective, wound healer, and anti-dysentery. Recent researches have justified the plant as a suitable candidate against SARS-CoV-2 virus responsible for Covid-19 pandemic. This comprehensive review highlights the morphology, and phytochemical composition of plant. The important pharmacological and medicinal activities of the plants are also discussed.

KEYWORDS: Fenugreek, phytochemical, pharmacological, medicinal applications.

1. INTRODUCTION

Traditional medicines are an important resource for health in communities around the world. According to WHO, 170 countries or 88% are reported to use traditional medicine as cost-effective, safe, and equitable use. More than 40% of pharmaceutical preparations are based on natural products and various landmark drugs, originated from plant-derived medicines.[1] The active ingredients present in plants and their phytochemistry, helps in dosage decision and targeting the ailments making relevant to pharmaceutical drug discovery.[2] The studies on phytochemical composition of plants and herbs, helps in identifying the chief ingredients and enhancing their pharmaceutical and medicinal value.[3-5] The proper documentation of plants and their medicinal significance make easier the communities to gain knowledge about their traditional and complimentary uses.[6,7]

Trigonella foenum-graecum (Fenugreek) belonging to family Fabaceae is an important herb native to the Asia, Mediterranean and Europe. The plant leaves are used as green leafy vegetables, whereas seeds with bitter taste as spices and also possess medicinal property.[8,9] The plant mainly originated in Western Asia and South-Eastern Europe has been used over 2500 years as fodder, and major parts of the world as edible or medicinal applications.[10-12] India occupies a significant position with state of Rajasthan leading in the plant production. The whole plant is consumed in form of vegetable whereas the seeds are used as spice condiments and flavoring agents. The plant generally occurs in uncultivated ground, field verges, and hillsides in highland regions. In Mediterranean region, the plant is grown as both rainfed and irrigated crop, whereas in Indian continent it is a winter crop. The plant generally prefers cool dry, climate, well drained loam soils, with pH 5.3-8.2. The seeds require 8-27^{0}c warm temperature with a full sunlight and annual rainfall 400-1500 mm.[10,13,14]

2. Plant Descriptions

The plants are erect, smooth, loosely branched, herbaceous, drought resistant 40-80 cm or even 3 feet tall. The leaves are compound, alternate, trifoliate, light green 7-12 cm long having oval leaflet. The flowers are papillonaceous, with lemon-yellow or white in color. Stems are single or branched, and 50 cm in height. The pods are small, straight, 15 cm long, curved bilobed containing 10-20 yellowish brown seeds (Fig. 1). The seeds are oblong, 6-8 mm long with spicy odor.[10,12,15] The plant can be propagated from seed sown at a depth of 1–2 cm with 3 inches gap between individual and 8–18 inches between rows.[13]

Fig. 1: *Trigonella foenum-graecum* (Fenugreek) plant leaves and seeds.

3. Phytochemical Compositions

The research conducted in the past have isolated more than 100 phytochemicals from the plant.[16] The phytochemical analysis reveals the presence of alkaloids, steroids, saponins, flavonoids, polyphenols, lipids, amino acids, carbohydrates, and hydrocarbons.[17] Fenugreek seeds mainly contain fiber, glycolipids, phospholipids, linolenic acid, oleic acid, choline, trigonelline, linoleic acid, vitamins A, thiamin, riboflavin, ascorbic acid, nicotinic acid, niacin, and polysaccharides in form of mannose and galactose.[15,18,19] The bioactive compound N55 extracted from the seeds is the main principle behind enhancing the activity of Glucagon-like peptide-1, that is known to control type 2 diabetes.[20]

The fenugreek seed also contain saponin, and HPLC-DAD-MS and GC-MS hydrolysis yields high amount of sapogenins and low amount of tocopherol and phytosterols.[21] The seed oil mainly contains linoleic, linolenic, and oleic acid.[22] Under elevated CO_2 hypocholesterolaemic potentiality increases resulting enhancement in antioxidant, antibacterial and anti-lipid peroxidation activities.[23] The bioactive principal of the plant seeds are diosgenin, trigonelline, galactomannan, 4-hydroxyisoleucine, and quercetin.[24] The silver nanoparticles (Ag-NPs) biosynthesis of seeds resulted enhancement in the yield of diosgenin, increasing root length, shoot length, leaf number, and wet weight of the plant.[25]

4. Pharmacological Activities

The pharmacological studies of various plants have been conducted in the past to enhance their medicinal uses and pharmacological applications.[26,27] The newly pandemic Covid19 has become a matter of global concern and a major challenge for medics and pharmacist to discover relevant drugs or plant derived product to counter the corona virus.[28]

4.1 Anti-Corona virus activities

The in-silico studies reveals that Trigoneoside IB present in Fenugreek, has potentiality in controlling the amino acid residue existing in active sites of Covid-19 proteins with binding affinity -7.6 for SARS-CoV nucleocapsid protein (PDB ID: 1SSK), and -8.5 kcal/mol for SARS-CoV spike glycoprotein (PDB ID: 6ACD) respectively, and found significant against standard drug Remdesivir.[29]

4.2 Antioxidant and Anti-Inflammatory

The hydroethanolic extract of seeds has a significant antioxidant activities showing low IC_{50} value inhibiting both ABTS (2,2′-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid) and DPPH (2,2-diphenyl-1-picrylhydrazyl). The extract was reported to be non-toxic against human murine macrophage RAW 264.7 cells and RBC. Further, the extract reduces intrlukin-6 (IL-6), the lipopolysaccharide (LPS)-induced tumor necrosis factor alpha (TNF-α), nitric oxide (NO) and prostaglandin E2 (PGE2), in RAW 264.7 cells.[30] The aqueous extract of seeds shows an immense potentiality against ethanol induced gastric peptic ulcer in Wistar rats, with an increase in antioxidant enzymatic activities of catalase, superoxide dismutase, and glutathione peroxidase and a reduction in non-enzymatic antioxidants.[31] The ethanol seed extract shows a significant anti-inflammatory activity inhibiting the lipid peroxidation and DPPH in rat liver homogenate.[32] The methanolic extract of the plant also exhibit a significant anti-inflammatory activity in inhibition of edema.[33] An experimental study reported that trigonelline, an important constituent of seed extract shows a very minute impact on drug metabolizing isozymes CYP3A4 and CYP2D6 and thus safely consumed for proper liver functioning.[34]

4.3 Anti-obesity activities

The plant seed containing a non-protein amino acid 4-Hydroxyisoleucine (4-OHIle), possess insulin resistance property assessing proper regulation of blood glucose, total cholesterol, plasma triglycerides, free fatty acid levels, and liver functioning, and thus can be used in obesity related disorders.[35] The aqueous extract of the seeds plays a significant role in dyslipidemia and atherosclerosis as tested in animal model. It causes reduction in triglycerides (TGs), serum total cholesterol (TC), aspartate amino transferase (AST), lactate dehydrogenase (LDH), hepatic, alanine amino transferase (ALT), and cardiac lipid peroxides (MDA) and elevation in serum high density lipoprotein cholesterol (HDL-C), cardiac and hepatic, along with antioxidant enzymes like superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH) levels.[36] The high dose seed extract possess hypocholesterolemic properties reducing triglycerides, total cholesterol, glycated hemoglobin, and higher-density-lipoprotein-cholesterol as experimented in animal model.[37]

4.4 Anti-diabetic activities

The high dose seed extract exhibit hypoglycemic properties lowering body and kidney weight, blood lipid levels, blood glucose, and improves hemorheological levels in experimental diabetic animal models.[37] The plant seeds exhibits significant glycemic control properties with improvement in fasting blood glucose, postload glucose, and HbA1c level in animal model.[38]

The experimental testing of seed powder in type II diabetes rats shows improvement in fasting blood glucose levels, increase in thiobarbituric acid reactive substances (TBARS), with antioxidants potential minimizing liver and pancreas damage.[39] The aqueous and ethyl acetate seed extracts possess a significant property in inhibiting α-glucosidase and α-amylase activities, justifying antidiabetic potentiality.[40] The seed powder solution shows contrasting effects in improving lipid profile lowering total cholesterol, triglyceride, and low-density lipoprotein cholesterol level, in type II diabetic patients and found competitive with standard drug.[41] The administration of 2 gm seeds per day for twelve weeks shows a significant glycemic control and improvement in lipid profile in type II diabetes patients.[42]

4.5 Anti-arthritis activities

The experimental studies on menopause induced hyperlipidemia animal model reveals that dietary seed extract, a rich constituent of phytoestrogens improves trabecular and cortical bone structure and functioning, flexor load, and tibia dry weight, caused due to menopausal osteoporosis.[43] The plant mucilage is a good anti- arthritis agent showing edema inhibition, reducing cyclooxygenase-2, myeloperoxidase, and thiobarbituric acid reactive substance (TBARS) activities, along with increasing vitamin C, antioxidants enzymes and glutathione level. Further, reduction in RBC count and hemoglobin, increase in ESR and total WBC, and modifications in C-reactive protein (CRP) levels get restored in experimentally tested animal model.[44]

4.6 Anti-cancer activities

The seed extract possess a significant anti-cancer activities reducing papillomas and minimizing the rate of tumor incidence, improving hepatic antioxidant defense system to counter tumorigenesis in animal model.[45] The diosgenin present in leaves and seeds helps in inhibiting human telomerase reverse transcriptase gene (hTERT) expression and can be used as anti-lung cancer agent.[46] The compound also possess anti-prostate cancer activity controlling the expression of protein 4 (NEDD4), a ligase produced in prostate cancer cells.[47] The methanolic extracts of the seeds and sprouts with chief constituents as glycosides (vicenin-2, apigenin, vitexin, orientin, and luteolin) and isoflavones (formononetin and daidzein) shows a significant anti-proliferative activities reducing the viability of MCF-7 breast cancer cells without cytotoxic effects.[48]

5 CONCLUSIONS

The Fenugreek has been used as fodder, leafy vegetable and seed spices in various part of the world. The plant has nutritive value, medicinal benefits with less or negligible side effects. The therapeutic potentials of plant in neurological disorders and covid-19 makes it an important phyto-candidate and requires detailed research on phytochemical compounds to make valid its pharmaceutical significance.

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