Novel Herbal–Chemical Combination Tablet of Fenugreek, Jamun and Metformin for Antidiabetic Therapy

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Abstract

Fenugreek (Trigonella foenum-graecum) is a commonly cultivated medicinal herb throughout Asia, and its seeds have long been used in traditional medicine to manage several ailments, particularly diabetes. Both the seeds and leaves contain numerous bioactive compounds that contribute to their blood glucose–lowering properties. However, a comprehensive and systematic review summarizing its antidiabetic mechanisms and isolated bioactive components has not yet been available.The present review aims to consolidate preclinical and clinical findings on the antidiabetic potential of fenugreek and its active constituents, emphasizing their molecular mechanisms of action. Relevant studies were collected from PubMed, Google Scholar, Science Direct, and Scopus databases up to June 2024.

Preclinical research revealed that fenugreek's antihyperglycemic activity is primarily linked to enhanced glucose transporter type 4 (GLUT4) translocation and increased hexokinase activity, alongside reduced activities of glucose-6-phosphatase and fructose-1,6-bisphosphatase. Additionally, fenugreek inhibits α-amylase and maltase enzymes, preserves pancreatic β-cell function, and promotes insulin secretion. Some studies also suggest that it may act as a modulator of glucagon-like peptide-1 (GLP-1), an activator of 5′-AMP-activated protein kinase (AMPK), and an inhibitor of dipeptidyl peptidase-IV (DPP-IV).Clinical evidence further indicates that fenugreek seed supplementation improves blood glucose control, reduces insulin resistance, enhances insulin sensitivity, and positively affects lipid metabolism.

Keywords: Metformin, Fenugreek (Trigonella foenum-graecum), Jamun (Syzygium cumini), Herbal–synthetic combination therapy, Antidiabetic agents, Polyherbal formulations

Introduction

Diabetes mellitus type 2 (T2DM) remains a major global health challenge, characterised by chronic hyperglycaemia due to insulin resistance and impaired pancreatic β-cell function. Given the limitations of existing monotherapies — such as reduced efficacy over time, adverse side effects, and patient compliance issues — there is increasing interest in combination therapies that integrate synthetic antidiabetic drugs with herbal phytoconstituents.

Among synthetic agents, Metformin is widely accepted as first-line therapy due to its ability to decrease hepatic gluconeogenesis, enhance peripheral glucose uptake, and improve insulin sensitivity. However, metformin can be associated with gastrointestinal side effects and in rare situations lactic acidosis, thereby encouraging exploration of adjunctive therapies to enhance benefit and reduce dose. Herbal medicines have long been used in traditional systems and increasingly studied for their antidiabetic potential. For example, Trigonella foenum-graecum (fenugreek) seeds contain bioactive saponins, alkaloids and soluble fibres which have shown significant reductions in fasting plasma glucose and HbA_1c levels in clinical trials. A recent meta-analysis concluded that fenugreek improved glycaemic parameters and lipid profiles safely in T2DM patients. Similarly, Syzygium cumini (Jamun) seeds have demonstrated antihyperglycaemic and insulin-sensitising effects in preclinical models and add-on therapy studies, making them promising candidates in combination formulations.

Review Of Previous Literature

Several clinical and preclinical reports suggest that adding fenugreek to metformin therapy can produce additive or synergistic benefits — for example, larger improvements in lipid profile and sometimes better glycaemic markers

compared to metformin alone. One clinical add-on study showed significant lipid improvements when fenugreek was given with metformin versus metformin alone. At the same time, review papers on herb–drug interactions urge caution: herb addition can alter pharmacodynamics (additive glycaemic lowering) and, less commonly, pharmacokinetics (altered absorption or clearance). Thus, while the combination holds promise for greater therapeutic benefit and possibly lower metformin dose requirements, it also requires careful standardization of herbal extracts and monitoring for unexpected interactions.

Mechanism of Action and Synergistic Effect

Metformin:

Drug Profile:

- Chemical Name: 1,1-dimethylbiguanide
- Molecular Formula: C4H11N5
- Molecular weight :129.16 g/mol
- Use: Type 2 diabetes management

Metformin is the most commonly used oral antidiabetic drug for Type 2 Diabetes Mellitus (T2DM). It primarily acts by reducing hepatic glucose production (gluconeogenesis) and increasing peripheral glucose uptake in skeletal muscles. It activates an enzyme called AMP-activated protein kinase (AMPK), which plays a key role in regulating energy balance and glucose metabolism. AMPK activation decreases glucose synthesis in the liver, enhances insulin sensitivity, and promotes glucose utilization by cells. Metformin also delays intestinal glucose absorption, which helps lower postprandial blood sugar levels. However, long-term metformin use may cause gastrointestinal side effects like nausea, diarrhea, or metallic taste.

Fenugreek (Trigonella foenum-graecum):

Pharmacognostic Profile:

- Botanical Name: Trigonella foenum-graecum
- Family: Fabaceae
- Synonyms:Methi (Hindi) Greek Hay Fenugrec (French)
- Key Constituents: Alkaloids (trigonelline), saponins (diosgenin), flavonoids (apigenin, quercetin), mucilage, vitamins (A, B, C).
- Uses:Diabetes management,Lactation support,Digestive health,Anti-inflammatory

Fenugreek seeds are rich in soluble fibers (galactomannans), saponins, and the unique amino acid 4-hydroxyisoleucine, which enhances insulin secretion from pancreatic β-cells.The soluble fiber forms a viscous gel in the intestine, slowing carbohydrate digestion and glucose absorption. Trigonelline and diosgenin (bioactive compounds in fenugreek) improve insulin receptor sensitivity, increase glycogen storage, and reduce lipid accumulation in the liver. Fenugreek also exhibits antioxidant and anti-inflammatory properties that protect pancreatic β-cells from oxidative stress, thereby preserving insulin function.

Jamun (Syzygium cumini):

Pharmacognostic Profile:

- Botanical Name : Syzygium cumini
- Family: Myrtaceae
- Synonyms: Indian Blackberry, Java Plum
- Key Constituents: Alkaloids (jamboline), tannins, anthocyanins, flavonoids, saponins, vitamin C.
- Uses:Diabetes management,Digestive health,Antioxidant, Skin health

Jamun seeds contain alkaloids (jambosine, jamboline), flavonoids, tannins, and anthocyanins with strong antidiabetic and antioxidant properties. These compounds inhibit carbohydrate-hydrolyzing enzymes like α-amylase and α-

glucosidase, leading to slower glucose release into the bloodstream. Jamun also helps enhance insulin secretion, regenerate β-cells, and protect against oxidative stress in pancreatic tissues. Animal studies show that Jamun extracts significantly reduce fasting glucose and improve glucose tolerance.

Synergistic Effect of Metformin with Fenugreek and Jamun

Combining Metformin with Fenugreek and Jamun offers a multi-targeted antidiabetic action: Drug/Herb Main Mechanism Complementary Role in Combination metformin activates AMPK → ↓ Glucose production, ↑ insulin sensitivity provides base control of blood glucose Fenugreek ↑ Insulin secretion, ↓ Glucose absorption, ↑ Glycogen storage enhances insulin effect, reduces lipid levels Jamun Inhibits α-amylase/α-glucosidase, ↑ β-cell protection Slows glucose release, adds antioxidant protection.

Method of Preparation:

1. Raw Material Selection:

- Fenugreek powder (Trigonella foenum-graecum)
- Jamun powder (Syzygium cumini)
- Metformin hydrochloride (standardized form)

2. Powder Preparation: Dry and finely grind Fenugreek seeds and Jamun fruits separately to obtain fine powders. Ensure that the Metformin is in the appropriate pharmaceutical grade (typically microcrystalline or granulated form).

3. Mixing: Blend the Fenugreek powder, Jamun powder, and Metformin in a suitable blender or mixer to achieve a uniform mixture.

4. Excipients Addition: Add excipients like binders (e.g., PVP or HPMC), disintegrants (e.g., starch), and lubricants (e.g., magnesium stearate) to the mixture. Lubricants help in smooth tablet compression, while binders ensure that the tablet holds together.

5. Granulation (Optional for better flow properties): Perform wet granulation if required, adding a suitable granulating agent (e.g., water or alcohol), rthen dry the granules to a free-flowing consistency.

6. Tablet Compression: Compress the homogeneous mixture into tablets using a tablet compression machine with the desired weight and size.

7. Coating (Optional): Apply a coating (e.g., film coating) if necessary to mask any unpleasant taste or enhance stability.

8. Quality Control: Perform standard quality control tests for the tablets, including hardness, dissolution, content uniformity, and tablet friability.

Conclusion

The combination of Fenugreek, Jamun, and Metformin offers a promising and scientific approach for effective management of Type 2 Diabetes Mellitus. Each component contributes through different mechanisms — Metformin lowers hepatic glucose production, Fenugreek enhances insulin secretion and reduces glucose absorption, while Jamun provides antioxidant protection and slows carbohydrate digestion. Together, they show a synergistic effect, improving glycaemic control more effectively than single therapy and potentially reducing Metformin-related side effects.

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