

Comparative Evaluation of Fenugreek, Berberine, and Metformin in Type 2 Diabetes Mellitus: Implications for Glycemic Control and Diabetes Care in Pakistan

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ABSTRACT

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Type 2 diabetes is a growing health problem in Pakistan causing a big economic and healthcare burden. Conventional antidiabetic drugs such as metformin remain first-line therapy [1]; however, interest in traditional Unani and Ayurvedic medicinal plants including fenugreek (*Trigonella foenum-graecum*) and berberine-containing herbs has increased because of their affordability, cultural acceptance, and perceived safety [2]. This review compares fenugreek, berberine and metformin for controlling blood sugar levels, reducing HbA1c, risk of developing hypoglycemia, cost and how well patients follow treatment. Evidence suggests that metformin works best and consistently reduces HbA1c (1.0%-1.5%) . Fenugreek (0.5%-1.0%) and berberine (0.7%-1.2%) shows moderate reduction in HbA1c. Herbal treatments usually have a low risk of hypoglycemia and are less expensive but have issues with standardization, varying dosages, and limited long-term evidence. In Pakistan, socioeconomic factors, access to remedies and medicine affordability greatly affect how well patients follow their treatment. Combining medicine with regular diabetes care may improve access to treatment and patient care. Type 2 diabetes and diabetes management are major growing issues in Pakistan. Integration of evidence-based herbal medicine with conventional diabetes management may improve accessibility and patient-centered care.

KEYWORDS: Type 2 Diabetes Mellitus ,Metformin ,Fenugreek (*Trigonella foenum-graecum*) ,Berberine ,Glycemic Control ,Herbal Medicine

INTRODUCTION

Type 2 diabetes is a major health problem all around the world and especially in Pakistan. More and more people in Pakistan are getting Type 2 diabetes either because they are not being physically active or they are eating differently. While some genetic factors may also contribute to the multiple pathophysiological disturbances that are

responsible for impaired glucose homeostasis in T2DM [3]. Type 2 diabetes is closely linked to the epidemic of obesity [4]. Individuals with T2DM are at high risk for both microvascular and macrovascular complications that include retinopathy, nephropathy, neuropathy and some cardiovascular comorbidities [5]. Commonly prescribed medications include metformin, sulfonylureas, thiazolidinediones,

dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, sodium-glucose cotransporter-2 (SGLT2) inhibitors and insulin therapy [6-9]. These medications primarily aim to enhance insulin sensitivity, decrease hepatic glucose production, stimulate insulin secretion, or facilitate glucose uptake by peripheral tissues [10]. Doctors usually prescribe Metformin to people with type 2 diabetes because it works well and is not too expensive. Alternative to these synthetic agents, plants provide a potential source of hypoglycemic drugs and are widely used in several traditional systems of medicine to prevent diabetes. Several

Overview of Agents:

Fenugreek (*Trigonella foenum-graecum*):

Fenugreek (*Trigonella foenum-graecum* L.) is an annual herb belonging to family fabaceae and had been used widely for centuries in traditional medicinal systems, including Unani, Ayurvedic, Chinese, and Middle Eastern medicine [11]. The seeds and leaves of the plant are utilized commonly both as a culinary ingredient and as a medicinal remedy for various health conditions, including digestive disorders, inflammation, hyperlipidemia, and diabetes mellitus. Interest in fenugreek as a potential antidiabetic agent has increased substantially in recent decades due to the global rise in T2DM and the growing demand for affordable and culturally accepted therapeutic alternatives. Fenugreek seeds contain several bioactive compounds that contribute to their hypoglycemic effects, including soluble dietary fiber (galactomannan), alkaloids such as trigonelline, steroidal saponins, flavonoids, and the unique amino acid 4-hydroxyisoleucine. These phytochemicals exert multiple pharmacological actions that help in regulation of the glucose and

medicinal plants have been investigated for their beneficial use in different types of diabetes [2]. A lot of people in Pakistan like to use old home remedies like Unani and Ayurvedic medicine to help them feel better. Some plants like fenugreek and berberine are popular because they help lower blood sugar levels. The treatment must not only be effective and safe but also improve the quality of life. Several novel medications are in development, but the greatest need is for agents that enhance insulin sensitivity, halt the progressive pancreatic β -cell failure that is characteristic of T2DM and prevent or reverse the microvascular complications. insulin sensitivity. One of the main mechanisms responsible for the antidiabetic activity of fenugreek is its high soluble fiber content. Galactomannan delays gastric emptying and slows intestinal carbohydrate absorption, thereby reducing postprandial blood glucose excursions. Additionally, the amino acid 4-hydroxyisoleucine has been shown to stimulate glucose-dependent insulin secretion from pancreatic β -cells, and enhancing insulin availability without causing excessive hypoglycemia. Trigonelline and other polyphenolic compounds contribute to improve insulin sensitivity and reducing oxidative stress which is associated with chronic hyperglycemia. Experimental studies have demonstrated that fenugreek can improve glucose metabolism through several pathways, including enhanced peripheral glucose uptake, inhibition of digestive enzymes involved in carbohydrate breakdown, reduction of insulin resistance, and modulation of inflammatory processes. Animal studies have consistently shown reductions in fasting blood glucose levels, [12] improved insulin secretion, and protection against pancreatic β -cell dysfunction. These findings have provided a strong scientific basis for the traditional use of the fenugreek in diabetes management, reducing blood glucose levels and improving insulin sensitivity in

obese and overweight patients with T2DM. Fenugreek is generally well tolerated and has a favorable safety profile. The most commonly reported adverse effects are mild gastrointestinal symptoms such as bloating, diarrhea, abdominal discomfort, and a characteristic maple syrup-like odor in sweat and urine.

Berberine:

Berberine can be found as an active constituent in some medicinal plants. These plants include *Berberis aristata* (barberry), *Berberis vulgaris* (European barberry), *Coptis chinensis* (Chinese goldthread), and *Hydrastis Canadensis* (goldenseal). People have been using berberine for a time in traditional Chinese medicine, unani and ayurvedic medicine to help with problems like stomach infections, inflammation. Recently people have started to think that berberine might be the way to help people with T2DM. Berberine can affect different pathways in the body that are involved in glucose and lipid metabolism [13]. It does not work in one way like other several antidiabetic agents, rather it can affect different, molecular pathways at the same time. One of the ways that berberine works is by activating monophosphate-activated protein kinase [14], also called as AMPK which is like a switch that helps the body cells use energy. When AMPK is activated it helps the body cells take in the glucose, use fat for energy, reduce the amount of hepatic glucose, and helps the body in using the insulin better way. Berberine also causes reduction in insulin resistance. It also causes inhibition of the mitochondrial functions, regulation of islet function, modulation of gut microenvironment, and upregulation of insulin receptor expression. In general, BBR was safe and effective in the treatment of patients with T2DM [15]. Some people may get some side effects like constipation, diarrhea, stomach discomfort, nausea and gas. These side effects are usually not very

serious and do not last very long. The hypoglycemic effect of berberine was similar to that of metformin [13], but berberine is not very likely to cause hypoglycemia, because it works by helping the body use insulin better than, by making the body make too much insulin. Beneficial effects of berberine were also observed in combating diabetic complications. Diabetes related endothelial dysfunction, nephropathy, and neuropathy could be relieved after berberine administration.

Metformin:

Metformin is a medicine used widely in T2DM since 1950s. The glucose-lowering, insulin-sensitizing agent metformin works mainly by reducing gluconeogenesis and opposing glucagon-mediated signaling in the liver and, to a lesser extent, by increasing glucose uptake in skeletal muscle [16]. It is mostly used as initial therapy in T2DM [1]. Recent Developments have shown that this medication, besides its ability to lower glucose levels, could be promising for specifically addressing metabolic differences between normal and abnormal metabolic signaling. The core mechanism of metformin lies in changing the cell's energy metabolism. Metformin primarily lowers glucose levels by suppressing hepatic gluconeogenesis and counteracting glucagon's effects. Inhibiting mitochondrial complex I leads to impaired cAMP and protein kinase A signaling when glucagon is present. Activation of 5-AMP-activated protein kinase, while not essential for the glucose-lowering effect of metformin, enhances insulin sensitivity by regulating lipid metabolism [17]. Recent findings indicate that metformin may enhance obesity-related meta-inflammation through both direct and indirect impacts on immune cells located in metabolic tissues (such as adipose tissue, the gastrointestinal tract, and the liver). Additionally, the gastrointestinal system plays a significant role in

metformin's effects by influencing the glucose-reducing hormone glucagon-like peptide 1, the bile acid pool in the intestines, and changes in the composition of gut microbiota. Its preferred position stems from its effectiveness, affordability, and favorable safety records. Additional advantages have also been reported, such as enhancements in specific lipids, inflammatory indicators, and a decrease in cardiovascular incidents, seemingly unrelated to the medication's glucose lowering impact [18, 19].

METHODOLOGY

Literature Search Strategy:

The objective of this narrative review is to provide a critical comparison between the effectiveness and clinical usefulness of herbal therapies (fenugreek, berberine) and conventional therapy (metformin) in the treatment of type 2 Diabetes Mellitus (T2DM). This review will specifically focus on the reduction of HbA1c levels, the risk of developing hypoglycemia, cost-effectiveness, compliance, and the applicability of these agents in the healthcare system of Pakistan. A thorough literature search was done through major databases such as PubMed, Google Scholar, ScienceDirect, Scopus, and WHO publications. The

Relevant articles published from 1996 to 2025 were considered. Further articles were sourced manually from the selected articles.

Study Selection and Inclusion Criteria:

The studies chosen were pertinent to the objectives of the review and are added to the understanding of the comparative efficacy of herbs and standard medicine for T2DM. Articles included were randomized controlled trials, systematic reviews, meta-analyses, observational studies, and comparative clinical studies related to fenugreek, berberine, or metformin. Articles that discussed the influence of HbA1c levels, fasting blood glucose levels, post-meal blood glucose, instances of hypoglycemia, compliance with treatment, and safety issues were chosen. Articles not included in the review were those not in English, related to Type 1 Diabetes Mellitus, focused on gestational diabetes, purely experimental studies utilizing animals with no clinical significance, conference abstracts that lack sufficient data, and duplicate publications. Chosen articles were examined and compiled to compare the effectiveness, safety, cost, and usability of fenugreek, berberine, and metformin in Pakistan.

Result Table; Herbal Agents Vs Conventional Drug:

Parameter	Fenugreek	Berberine	Metformin
HbA1c Reduction	Mild to moderate reduction (0.5-1.0%)	Moderate reduction (0.7-1.2%). Improved results when given with metformin [20]	Significant reduction (1.0-1.5%) [21]
Effect on Hypoglycemia Risk	Very low risk when used alone; may reduce glucose fluctuations	Low risk; generally does not cause severe hypoglycemia alone	Low risk as monotherapy; risk increases in combination therapy [22]
Cost	Low cost; widely available as dietary supplement /food [23]	Moderate cost depending on formulation and purity	Low to moderate cost; widely accessible globally
Patient Adherence	Moderate; influenced by taste, odor and large doses	Moderate; gastrointestinal intolerance may affect	High; once established, generally long term adherence

	required	compliance	
Common Adverse Effects	Bloating, diarrhea, flatulence, mild gastrointestinal discomfort	Constipation, abdominal pain, nausea, diarrhea	Diarrhea, nausea, abdominal discomfort, metallic taste [21]
Serious/Rare Adverse Effects	Allergic reactions, possible herb-drug reactions	Drug interactions, rare hepatotoxicity or hypotension	Rare lactic acidosis, Vit B12 deficiency
Overall Safety Profile	Generally Safe with mild adverse effects	Relatively safe but requires monitoring for interactions [24]	Well-established safety profile with extensive clinical evidence
Evidence Strength	Limited to moderate clinical evidence	Moderate and growing evidence	Strong evidence from large clinical trials and guidelines
Clinical role in T2DM	Adjunctive complementary therapy	Potential alternative/adjunct therapy	Standard first line pharmacological therapy [1]

DISCUSSION

The present review compared fenugreek, berberine, and metformin in the management of T2DM, mainly focusing on HbA1c reduction, cost-effectiveness, safety profile, risk of hypoglycemia, patient's compliance, and their applicability within the healthcare system of Pakistan. The findings indicate that all three agents possess glucose lowering properties, but significant differences exist

in the strength of evidence, magnitude of the HbA1c reduction, safety profiles, and their clinical applicability. Among the evaluated therapies, the most consistent and clinically significant glycemic benefits are demonstrated by metformin. Extensive evidence from RCTs, meta-analysis, and international treatment guidelines supports its use as the first line pharmacological treatment for T2DM. Metformin achieves HbA1c reductions of approximately 1.0-1.5% [21], primarily through the

suppression of hepatic gluconeogenesis and peripheral insulin sensitivity enhancement. Berberine on the other hand emerged as the most promising herbal intervention among the reviewed agents. Several clinical studies showed reduction in fasting blood glucose and HbA1c that approach those achieved with the conventional oral antidiabetic medications. The mechanism of antidiabetic action of berberine resembles closely to that of the metformin [13], which may explain the similarities in glycemic outcomes that are reported in certain studies. However, despite the encouraging findings, use of the berberine remains limited by variabilities in product quality, differences in the dosage formulations, and insufficient long term clinical data. Therefore although berberine might act as a useful adjunctive therapy [24], current evidence does not support its replacement of established pharmacological treatment. Fenugreek demonstrated relatively modest but relevant antidiabetic effects clinically. Studies generally show HbA1c reductions ranging from 0.5% to 1.0% , making fenugreek comparatively less potent than both the berberine and metformin. However, fenugreek offers multiple practical advantages, including low cost, widespread availability, and a favourable safety profile. Its high fiber content (galactomannan) may also contribute in improving the postprandial glucose control and lipid metabolism [25]. All these characteristics make fenugreek more attractive in low resource settings where the access to the healthcare services and medications may be limited. The risk of hypoglycemia represents a significant consideration when selecting anti-diabetic therapies. All three reviewed interventions exhibited relatively low risks of hypoglycemia, especially when used as monotherapy. Metformin is known for lowering blood glucose without stimulating the insulin secretion directly, therefore it minimizes the likelihood of

severe episode of hypoglycemia, when used alone [26]. Similarly, fenugreek and berberine promote glucose regulation mainly through enhancement of insulin sensitivity, delaying the carbohydrate absorption, and modulating glucose metabolism instead of causing excessive insulin release [2]. Consequently, the herbal therapies thought to provide a safer alternative for patients who are particularly concerned about the risk of hypoglycemia or who have experienced any adverse event with other glucose-lowering agents. Cost-effectiveness is a main consideration in developing countries such as Pakistan, where healthcare expenditure is often borne directly by the patients and access to long-term treatment may be constrained by the financial limitations. Fenugreek is inexpensive, cultivated widely, and readily available in the local markets, making it an economically more attractive option for many individuals among others. Berberine is generally more affordable than several other newer antidiabetic medications but it may vary in price depending on the formulation and the product quality. However, Metformin remains one of the most cost-effective conventional antidiabetic agents and is widely available through both public and private healthcare sectors. Therefore, all three interventions may contribute to accessible diabetes management from an economic perspective, although metformin continues to provide the greatest balance between the cost and proven clinical effectiveness. Another critical determinant of therapeutic success is patient adherence. Sustained compliance with medication regimens, lifestyle modifications, and regular monitoring is required for the long term management of the diabetes. Generally, metformin demonstrates high adherence rates because of the established efficacy, availability, and the acceptance by the physician. However, gastrointestinal adverse effects may reduce

compliance in some patients. Fenugreek adherence may be influenced by the taste, odor, preparation requirements, and relatively, the larger quantities are required for therapeutic benefit. Berberine may also cause gastrointestinal discomfort, which can

The findings of this review also highlight the growing importance of integrating the evidence-based traditional medicine in modern healthcare systems. In Pakistan, the use of Unani and Ayurvedic remedies, due to cultural beliefs, accessibility, and lower costs, remains widespread. Many patients utilize herbal products alongside the prescribed medications, and that too often without informing the healthcare providers. This practice underscores the need for healthcare professionals to understand the efficacy, safety, and potential interactions of common herbal therapies. Appropriate integration of the validated herbal interventions into conventional diabetes care may improve the patient engagement, adherence, and overall treatment satisfaction while maintaining evidence-based standards of practice. Despite the observed promising results of fenugreek and berberine, several challenges still exist. One of the most significant challenge is the lack of standardization of herbal preparations [2]. Variations in plant species, cultivation conditions, extraction methods, and concentrations of active constituents can result in inconsistent therapeutic outcomes. Furthermore, many clinical studies that are available, involve relatively small sample sizes,

negatively affect adherence. Nevertheless, the cultural familiarity with herbal remedies may enhance acceptance and willingness to use fenugreek or berberine as part of diabetes management strategies in Pakistan.

short follow-up periods, and heterogeneous study designs. These limitations reduce the ability to draw definitive conclusions regarding long-term efficacy and safety. In contrast, metformin has been evaluated extensively in clinical trials on large scale and possesses a well-established evidences supporting its long-term use.

Overall, the evidence reviewed suggests that the metformin remains the most effective and scientifically validated option for the glycemic control in T2DM. While berberine and fenugreek demonstrate modest antidiabetic activity and may offer several advantages related to affordability, cultural acceptance, and low hypoglycemia risk. But the current evidence supports their use mainly as adjunctive rather than replacement therapies. Future large-scale, well-designed RCTs are needed to establish standardized dosing protocols, evaluate long-term safety, and clarify the role of herbal therapies in comprehensive diabetes management. Such research may be particularly valuable in Pakistan, where integrating affordable and culturally accepted interventions could contribute to improved diabetes outcomes and reduced healthcare burden.

CONCLUSION

The comparative evaluation of Fenugreek, Berberine, and Metformin demonstrated that, although, Unani and Ayurvedic medicinal plants possess promising and modest antidiabetic potential, but yet they cannot be considered superior to conventional pharmacotherapy (metformin) for

the management Type 2 Diabetes Mellitus (T2DM). Among herbal agents, berberine showed glycemic efficacy that is almost same as shown by the metformin in several clinical studies, particularly in lowering HbA1c and improving insulin sensitivity. While fenugreek showed moderate glucose-lowering activity with a favorable safety profile. Overall, fewer severe adverse effects are

associated with herbal therapies and a lower risk of hypoglycemia, making them more attractive as complementary or adjunctive options [2]. Their natural origin, lower cost, and cultural acceptability contribute to better patient preference in some populations. However, despite all these advantages, the evidence supporting herbal medicines remains limited due to smaller sample sizes, short study durations, lack of standardization of herbal preparations, and insufficient long-term safety data. Metformin, on the other hand, continues to demonstrate the strongest clinical evidence with predictable pharmacological actions, established dosing protocols, and long-term cardiovascular and metabolic benefits that are supported by internal treatment guidelines and randomized clinical trials

on large-scale. In moderate-to-severe diabetes, conventional medicine also provides more reliable glycemic control than the herbal therapies. Therefore, current evidence indicates that Unani and Ayurvedic plants should not replace conventional antidiabetic therapy, particularly in uncontrolled or advanced T2DM. Rather, they may serve as effective complementary agents or adjunctive therapies that can enhance glycemic management, reduce treatment burden, and improve patient-centered care when used under appropriate clinical supervision. Future large-scale, well-standardized clinical trials are necessary before recommending the herbal therapies as standalone alternatives to conventional drugs in T2DM management.

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