Review article

Phytotherapeutics in Diabetes Management: Exploring Herbal Alternatives

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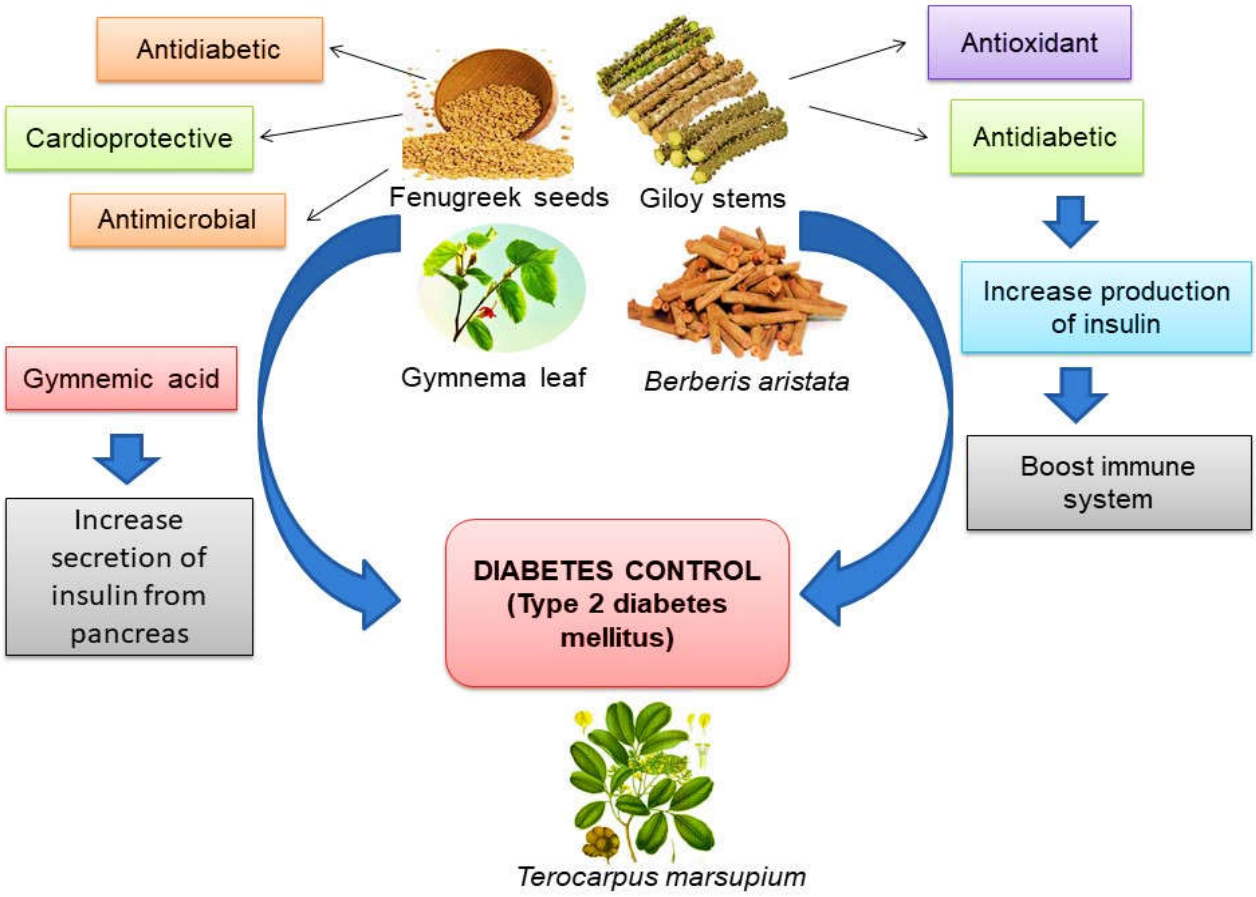
ABSTRACT

Diabetes mellitus presents a global health challenge, necessitating effective management strategies to mitigate its complications. While conventional medications play a pivotal role, concerns over long-term side effects have spurred interest in herbal alternatives or phytotherapeutics. This paper provides a concise overview of the potential of phytotherapeutics in diabetes management. Numerous herbal remedies, such as, Trigonella foenum graceum (fenugreek), Tinospora cardifolia (giloy), Terocarpus marsupium (Bijasal), Berberis aristata (daruhaldi) and Gymnema sylvestre (gudmar) have undergone extensive preclinical and clinical evaluation for their efficacy in glycemic control and insulin sensitivity improvement. These

botanical agents not only show promising results in regulating blood glucose levels but also offer additional health benefits, including antioxidant and anti-inflammatory properties, which are advantageous in mitigating diabetes-related complications. Despite their potential, challenges exist in integrating phytotherapeutics into mainstream diabetes care. Variability in product composition, lack of standardization, and potential herb-drug interactions hinder widespread adoption. Additionally, cultural perceptions, accessibility issues, and regulatory frameworks influence acceptance and utilization. Future research endeavors should prioritize elucidating the mechanisms of action, conducting robust clinical trials, and establishing standardized formulations to ensure consistency and quality. Collaboration among traditional healers, healthcare providers, researchers, and regulatory bodies is vital to facilitate the effective integration of herbal alternatives into diabetes management protocols.

Keywords: *Diabetes management, Phytotherapeutics, Herbal alternatives, Medicinal plants, Diabetes complications, Glycemic control*

Graphical Abstract



1. INTRODUCTION

Diabetes mellitus is a systemic metabolic disorder characterized by elevated blood sugar, elevated lipid levels, elevated amino acid levels, and low insulin levels. Insulin secretion and action are reduced as a result. Insulin and a number of oral antidiabetic medications, such as glinides, biguanides, sulfonylureas, and glucosease inhibitors, are currently the available treatments for diabetes management [1]. Because insulin is a key anabolic hormone, there are anomalies in the metabolism of proteins, carbohydrates and fats. Insulin resistance of target tissues, mainly skeletal muscles, adipose tissue , and to a lesser extent, the liver, is the cause of theses metabolic abnormalities . insulin receptors the signal transduction system effector enzymes, or genes all play a role in insulin resistance[2]. Diabetes mellitus, one of the earliest

known human illnesses, was first mentioned in an Egyptian text around 3,000 years ago. The distinction between type 1 and type 2 diabetes was made in 1936, and in 1988, type 2 diabetes was recognized as part of the metabolic syndrome. Type 2 diabetes, also known as non-insulin dependent diabetes mellitus, is the most common form, characterized by high blood sugar levels, insulin resistance, and a relative lack of insulin. It is a prevalent metabolic disorder affecting 2.8% of the global population, a figure projected to rise to 4.4% by 2030. The epidemic has already reached an unparalleled level. Even though diabetes is not a communicable disease, it is regarded as one of the top five morbidities globally. Diabetes frequency and categorization varies according to how severe the symptoms are. During the initial phases of their illness, some diabetics, particularly those with type 2 diabetes, may not exhibit any symptoms. While others exhibit obvious hyperglycemia. Diabetes that is not under control or managed might result in coma, stupor, or even death [4]. Recent surveys indicate that the prevalence of diabetes among adults is expected to increase from 4% in 1995 to 6.4% by 2025. Projections suggest a rapid escalation, with numbers climbing from 84 million to 228 million in developing nations and a 42% increase in wealthy countries from 51 million to 72 million. By 2025, the United States, China, and India are anticipated to be the most heavily impacted nations by diabetes. A concerning aspect is that nearly half of the patients, approximately 50%, remain undiagnosed. [5]. Despite of this, post-diagnosis complications particularly chronic ones are common everywhere. In the world consequently, diabetes continues to be a major contributor to cardiovascular ailment, lower extremity amputation, end-stage kidney disease and blindness. In recent decades, the number of cases of type 2 diabetes mellitus has more than doubled, and rising obesity rates are thought to be a major contributing factor to the increased global burden of type 2 diabetes mellitus. The terms "diabesity" and type 2 diabetes mellitus (T2D) have often been used interchangeably [6]. India is additionally known as the global center for diabetes, The prevalence is notably higher among urban populations, approximately six times greater than in rural areas. Major factors contributing to diabetes mellitus over the past two decades include reduced physical activity, weight gain, stress, dietary changes, malnutrition, alcohol intake, and viral infections. [7]. Undoubtedly, a fresh and efficient strategy to Diabetes mellitus therapy is required due to the disease's increasing prevalence. A new development in genomics, molecular biology, and genetics has increased our knowledge of the genetic foundation of all types of diabetes. Several studies have connected the pathophysiology of diabetes mellitus, including type

2 diabetes, to mutations in certain genes. Through various ways, these genes cause Type 2 diabetes mellitus in addition to environmental stimuli. According to scientific consensus, personalized approaches are necessary for the efficient treatment or management of diabetes mellitus (DM). This involves treating different forms of the disease according to the genes and mechanisms that cause them [8].

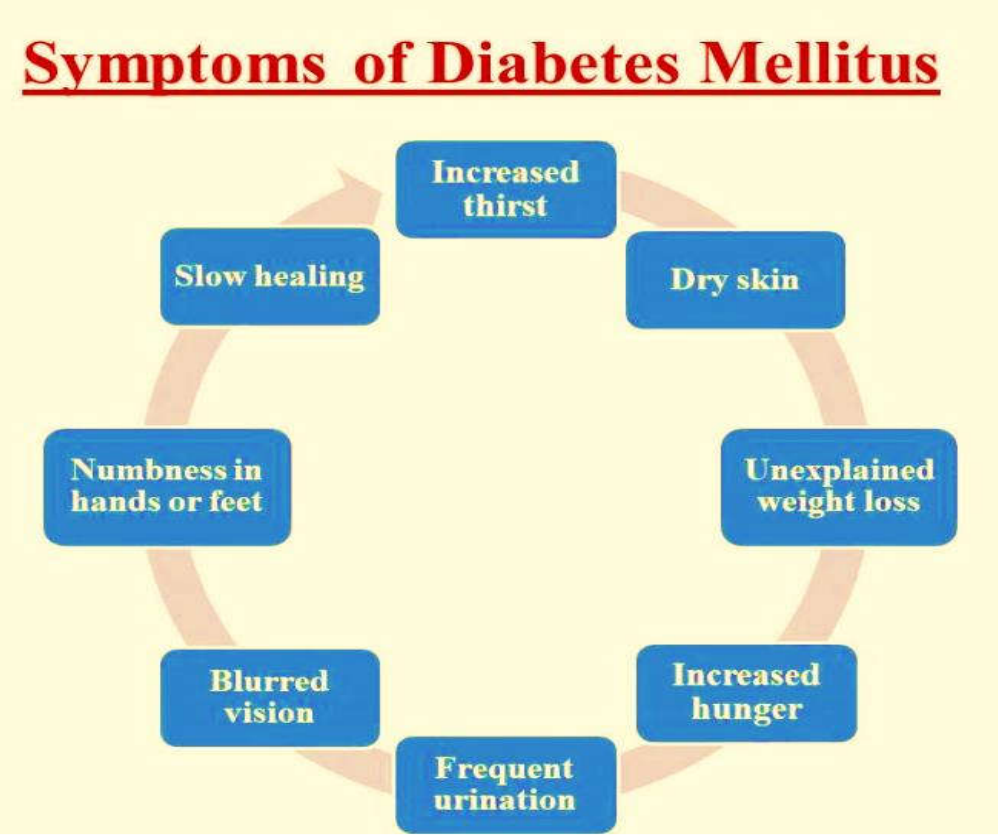


Fig. (1) Symptoms of Diabetes Mellitus

2. TYPES OF DIABETES MELLITUS

While understanding the type of diabetes is crucial and influences treatment approaches, it can be complex. Some patients, especially younger individuals, don't neatly fit into a single classification, and around 10% of those initially categorized may require reclassification. The traditional categorization of diabetes, endorsed by the American Diabetes Association (ADA) in 1997, encompasses type 1, type 2, other forms, and gestational diabetes mellitus (GDM). This

classification remains the most commonly employed framework. The factors present at the time of diagnosis are sometimes crucial in determining the type of diabetes a person has, and many diabetics are hard to classify into a single group. For example, if a person with gestational diabetes mellitus (GDM) has hyperglycemia after delivering birth, they may acquire type 2 diabetes. However, in the event that if high doses of exogenous steroids are stopped, a person who developed diabetes given that they might become the norm for glucose. But following repeated bouts of pancreatitis, they might have diabetes for a long time. An individual receiving thiazides and developing diabetes years later would be another example. Since thiazides rarely result in significant hyperglycemia, these individuals most likely have type 2 diabetes, which is exacerbated by medication. Therefore, knowing the specific kind of diabetes and how to manage it effectively are more important to the patient and the doctor than identifying the disease [9]. Diabetes is one of the main causes of morbidity and mortality worldwide, and it is rightly acknowledged as a rising global epidemic. Because of its insidious and relentless character, hyperglycemia is a prevalent characteristic of both type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM), posing the risk of significant complications. The goal of this special issue is to publish both original research and reviews that highlight recent, important developments in our knowledge of the problems associated with diabetes. The underlying biological mechanisms, newly developed technologies that aid in early detection and novel therapeutic options for these problems have all received significant attention. These topics are categorized by the papers.

- Pathogenesis of Diabetic Complications
- Diabetic Neuropathy
- Diabetic Nephropathy
- Diabetic Retinopathy
- Macrovascular Complications [10].

Although the two main etiopathogenetic groups account for the majority of diabetes cases. In some individuals this rigid classification is not applicable. The classification often depends on the clinical presentation at diagnosis and it is common clinical practice to classify individuals based on the following variables:

1. Age at onset of diabetes
2. The abruptness of hyperglycemia
3. Presence of ketosis at presentation
4. Degree of obesity
5. Need for insulin at diagnosis [11].

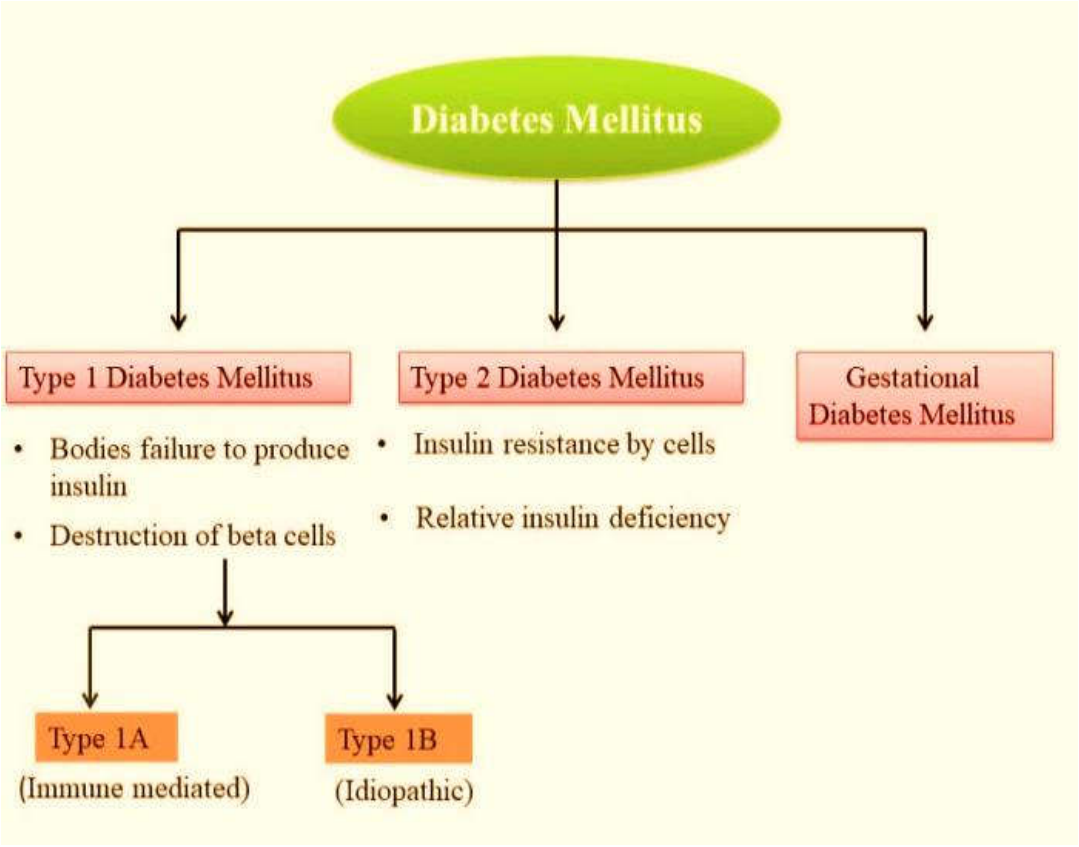


Fig. (2) Classification of Diabetes Mellitus

2.1 TYPE 1 DIABETES MELLITUS

Type 1 diabetes mellitus (T1DM) is one common subtype of diabetes, which is characterized by an insulin shortage and is typically identified in childhood. Type 1 diabetes mellitus constitutes a significant subtype of diabetes, accounting for approximately 5% of all cases of the condition. Insulin shortage is the primary characteristic of type1diabetes (T1DM), and Individuals with this condition require treatment with various types of exogenous insulin, including rapid short-, intermediate-, and long-acting insulin. Hence, insulin-dependent diabetes mellitus is another term for Type 1 diabetes [12]. Type 1 Diabetes Mellitus is distinguished by the autoimmune

destruction of pancreatic beta cells., leaving patients dependent on life-sustaining exogenous insulin injections. The blood sugar levels of a healthy individual are tightly controlled and typically fall between 70 and 110 mg/dl. However, T1DM patients' blood glucose levels remain abnormally high because the body generates so little insulin [13]. Multiple organ involvement is a common feature of T1DM, and the primary target organ's damage usually determines the disease's clinical presentation. As opposed to the overall population, patients with DM-1 have an approximately twofold increased incidence of depression and mental symptoms are common in both diabetes mellitus and other autoimmune disease patients. More than 30 million individuals worldwide are afflicted with type 1 diabetes mellitus [14]. Major depressive disorder (MDD) is notably common among young individuals and teenagers diagnosed with type 1 diabetes mellitus. The background rate of MDD reported for non-diabetic kids (5–8%) is at least two to three times less common than the occurrence of MDD among children with type 1 diabetes (20–27%). When combined with diabetes, The third most typical chronic condition in children, 54 early-onset MDD is severe and linked to Early-onset Major Depressive Disorder (MDD) is severe and correlates with poorer diabetes control, heightened diabetes-related complications, increased frequency of emergency department visits and hospitalizations, greater functional impairment, elevated risk of suicidal ideation, and higher healthcare costs. [15]. Type 1 diabetes are older and in danger of fractures arising from osteoporosis. To minimize The National Osteoporosis Foundation guidelines propose treating the morbidity and mortality related to fractures screening for osteoporosis in the general public for females in the age ≥ 65 years and men aged ≥ 70 years [16]. The American Diabetes Association (ADA) defines low-carbohydrate diets as those containing no more than 130 grams of carbohydrates per day or 26 percent of total energy intake (TEI) from carbohydrates. Before insulin was discovered, the treatment of diabetes was commonly achieved with stringent low carb diets that required extreme carbohydrate restriction (~10 g/day) or water fasting until glycosuria was resolved. More recently, a significant observational study involving 1020 type 1 diabetic outpatients in Europe found a correlation between lower HbA1c levels and a lower total carbohydrate intake [17].

2.2 TYPE 2 DIABETES MELLITUS

Globally, diabetes mellitus (DM) impacts roughly 400 million individuals and is a significant public health concern. Life-threatening chronic microvascular, macrovascular, and neuropathic

consequences are gradually brought on by this metabolic condition. Diabetes mellitus (DM) can be caused by impaired insulin secretion, injury to the pancreatic β cell, or insulin resistance stemming from insufficient insulin usage. The increasing prevalence of sedentary lifestyles is believed to be the primary cause of the global rise in diabetic cases, projected to reach 366 million by 2030 among the elderly population (>65 years old) [18]. Urinary tract infections (UTIs) in diabetic individuals can stem from various factors including immune system deficiencies, inadequate metabolic regulation of diabetes, and impaired bladder emptying due to autonomic neuropathy. Age, metabolic control, and long-term complications such as diabetic nephropathy and cystopathy have all been found to elevate the incidence of UTIs in diabetics [19]. Type 2 diabetes mellitus (T2DM) is a progressive condition characterized by insulin resistance and dysfunction of beta cells. Despite this, there is now ample proof that maintaining strict blood glucose control greatly lowers the chance of developing diabetic complications. Before 2000, there was a limited range of pharmacological treatments, especially oral drugs, available for the management of type 2 diabetes. Notwithstanding these disadvantages, sulfonylureas and metformin are still commonly used in clinical practice Also; their prices are fair [20]. The treatment of cardiovascular risk and the epidemiology of diabetes complications have been highlighted in relation to individuals with diabetes. It is crucial to reduce cardiovascular risk and may be more economical and successful to treat hypertension or use lipid-lowering medications than to treat hyperglycemia. The primary focus of this paper is the evidence backing the utilization of lipid-lowering medications in type 2 diabetes. Individuals with diabetes commonly exhibit low levels of high-density lipoprotein (HDL) cholesterol, elevated triglyceride levels, and average levels of low-density lipoprotein (LDL) cholesterol; LDL cholesterol particles in diabetics are typically denser, smaller, and potentially more atherogenic [21]. Sarcopenia can additionally arise from damaged muscle mass and function caused by advanced glycation end-products (AGEs) and diabetic vasculopathy. Particularly in older adults, the latter has been has been connected to a 1.5–2 fold higher risk of fractures and falls. Thus, it is possible that sarcopenia also Contributes to the elevated fracture risk linked to diabetes [22].

3. Herbal Remedy

Any plant utilized as therapeutic qualities is considered a herb. Many nations, like the United States and the United Kingdom, where a sizable section of the population uses herbal treatments [23]. Herbal remedies are typically sold as over-the-counter (OTC) supplements that can be purchased ready-made or customized for a person after consulting with a herbal practitioner. These supplements are not subject to such regulations and may "contain potent bioactive substances [24]. A different study found that 16% of those who took prescription medications also took vitamin and/or herbal supplements. The most popular herbs were ginkgo (2.2%) and ginseng (3.3%), both of which might be capable of interact with 86 some prescription medications [25]. Herbal medications are completed and labeled pharmaceutical products that include active substances, aerial or subterranean plant parts, or another type of plant material or mixtures, according to the World Health Organization (WHO). The quality control problem has been investigated consideration in practically all ancient medical systems, starting with self-inspection by Rishis, Vaidyas, and Hakims. On the other hand, contemporary concepts necessitate alterations in their methodology; However, in contrast, contemporary concepts necessitate alterations in their methodology, resulting in the creation of concrete quality control techniques in terms of contemporary approaches [26]. According to a 2007 National Health Interview Survey, the use of complementary and alternative medicine (CAM) by 38% of adults and 12% of children resulted in around $33.9 billion in out-of-pocket expenses. Despite the fact that there is mounting evidence of these treatments' safety and efficacy, practitioners should be mindful of the limits of the evidence base and take them into account along with everything other relevant considerations when making clinical decisions [27]. Therapies known as complementary and alternative medicine (CAM) aim to address a wide range of conditions and fall into two main categories: Because they are "natural" or are grounded in a spiritual, philosophical, or deeply felt concept of "wellness" and health, Exogenous substances such as vitamins, herbal supplements, or plant extracts, along with natural or self-therapies (NST) methods such as hypnosis, meditation, prayer, relaxation, biofeedback, or physical strengthening, are believed to be more effective and safer than conventional medical care. Herbal medicine treatments focus on restoring or enhancing the body's inherent healing abilities. Because complementary and alternative medicine (CAM) practices are "natural" or stem from a deeply held religious,

philosophical, or emotional understanding of "wellness" and health, they are thought to be safer and superior to mainstream medical therapy [28].

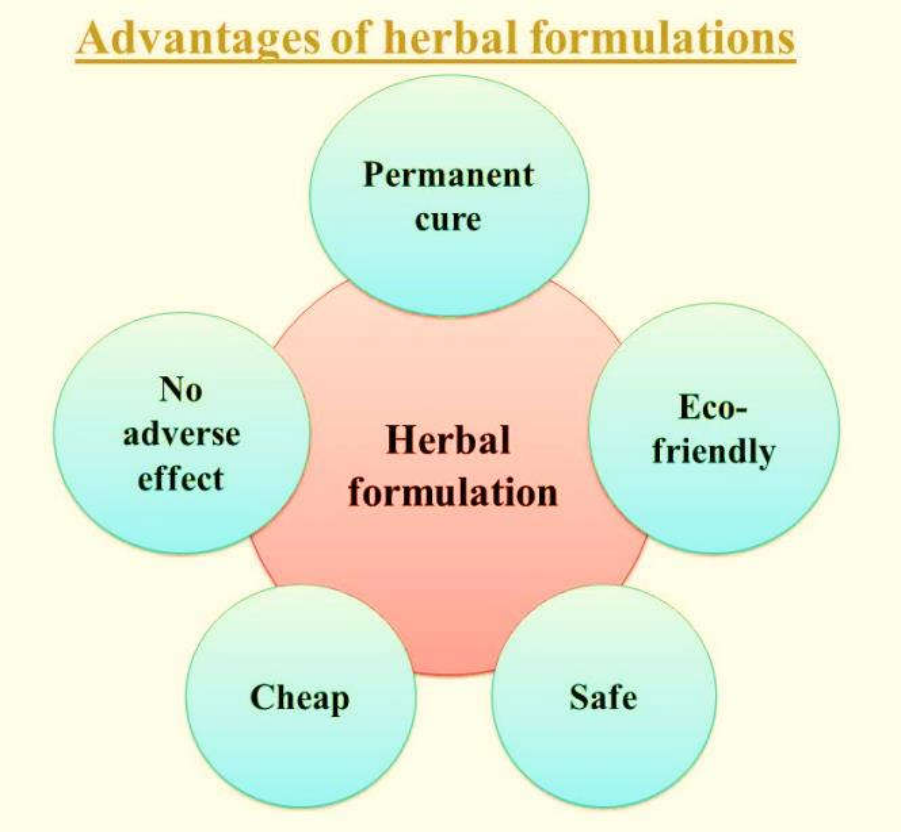


Fig. (3) Advantages of herbal formulation

4. OVERVIEW OF HERBAL PLANTS USED FOR TREATMENT OF DIABETES MELLITUS

4.1 TRIGONELLA FOENUM GRAECUM

Fenugreek (*Trigonella foenum graecum*) is a seasonal relates to the family Leguminosae is the well-known spice used in human food. As has long been done in human history, fenugreek seeds and green leaves are utilized in food furthermore medicine. This has been applied to improve the Taste and color of food ingredients additionally changes their texture. Fenugreek seed numerous medicinal applications, such as g lowering cholesterol, helping with lactation, fighting bacteria, stimulating the stomach, treating anorexia, acting as an antidiabetic, galactogogue, hepatoprotective, and having anticancer effects [29]. Trigonella foenum-graecum thrives in

regions with moderate to light rainfall. It features auxiliary white to yellowish flowers, compound pinnate trifoliate leaves, and slender, pointed beaked pods measuring 3–15 cm in length, containing 10–20 oblong, greenish-brown seeds. This erect plant can grow to heights ranging from 3 to 60 cm. Its seeds are widely used as spices across the globe, while its leaves are consumed as green leafy vegetables [30]. The bitter-tasting seeds of *Trigonella foenum-graecum* have been renowned for their medicinal properties for a long time. Oral consumption of the seeds of *Trigonella foenum-graceum* L. (Leguminosae) has been documented as having hypoglycemic effects. Trigonella seeds and their main alkaloids, trigonelline, have a hypoglycemic effect that was initially reported by Fournier (1948) and Nadakarnis (1954). Patients with non-insulin dependent diabetic mellitus are strongly advised to use the seeds [31]. Leucine, lysine, and the entirety of aromatic amino acids are important amino acids that are abundant in 79 75 10 fenugreek seed. The seed has recently been revealed to contain 6%–8% oil, 45%–50% dietary fibre, 20%–25% protein, and 2%–5% steroidal saponin. The seed is widely prized in culinary applications as a food spice in the nations where it is grown because of its characteristic strong aroma, which affects the flavour, colour, and aroma of dishes. Fenugreek has garnered attention as a functional food due to advancements in neutraceuticals and the growing demand for such meals. An increase in the demand for food means that more edible oil alternatives must be produced [32]. Rich in vitamins and minerals, fenugreek is not only a seed but also a legume, making it high in protein. It is also a significant source of diosgenin [33]. Fenugreek leaves have been found to contain 19 mg of 14 β-carotene and 220.97 mg of ascorbic acid per 100 g of leaves [34]. It also has a high concentration of calcium, zinc, and iron along with IbGr. Fenugreek was historically advised to boost milk supply in nursing mothers. Interestingly, Moroccan Saharawi women also used fenugreek to increase their appetite and physical beauty [35].

Table 1 Botanical classification of *Trigonella foeum graceum*

S.NO.	Domain	Eukarya
1.	Kingdom	Plantae
2.	Division	Magnoliphyta
3.	Class	Magnoliopsida
4.	Order	Febales or Leguminales
5.	Family	Fabaceae

6.	Sub family	Trifoliae
7.	Genus	Trigonella
8.	Sub genus	Foenum graceum
9.	Species	*Trigonella foenum graceum*
10.	Source	Extract of Fenugreek Seeds Could Reduce the Blood Glucose Level
11.	Common name	Fenugreek, Methi

4.1.1 Materials and Method

(A) Plant material

Trigonella foenum graceum (fenugreek) seed is collected the local market, gopalganj, of Dr. Harisingh Gour Vishvavidyalya Sagar Madhya Pradesh.

(B) Extraction of fenugreek seeds with ethanol

We bought *Trigonella foenum graecum* (fenugreek) seeds from the neighbourhood store. To get coarse powder, the seeds are rinsed with water, dried, ground, and sieved through a 40 mesh screen. Using a Soxhlet extractor, g of 100g powdered fenugreek seeds were extracted over the course of 10 hours using 500ml of 95% ethanol. Following the extraction time, a rotary vacuum evaporator was used to filter and concentrate the solutions. To find different phytoconstituents, the extract was put through a series of chemical assays [36].

(c) Extraction of aqueous plant material

Twenty-five grams of powdered Trigonella foenum-graecum, or fenugreek, were extracted in 500 milliliters of boiling distilled water for a duration of five minutes. Subsequently, the decoction was cooled at room temperature for thirty minutes after heating. Following two filtration processes, the obtained filtrate underwent lyophilization and was preserved in a cold environment. The leftover material after lyophilization amounted to 0.589 g, resulting in a yield of 2.36%.

(D) Extraction of methanolic plant material

For six days, 250 grammes of *powdered Trigonella foenum-graecum,* also known as fenugreek, were immersed in 500 millilitres of methanol. The decoction was thrice filtered after six days. The filtrate was refrigerated after being concentrated using a rotary evaporator. The yield (w/v) was (3.3 %**)** [37].

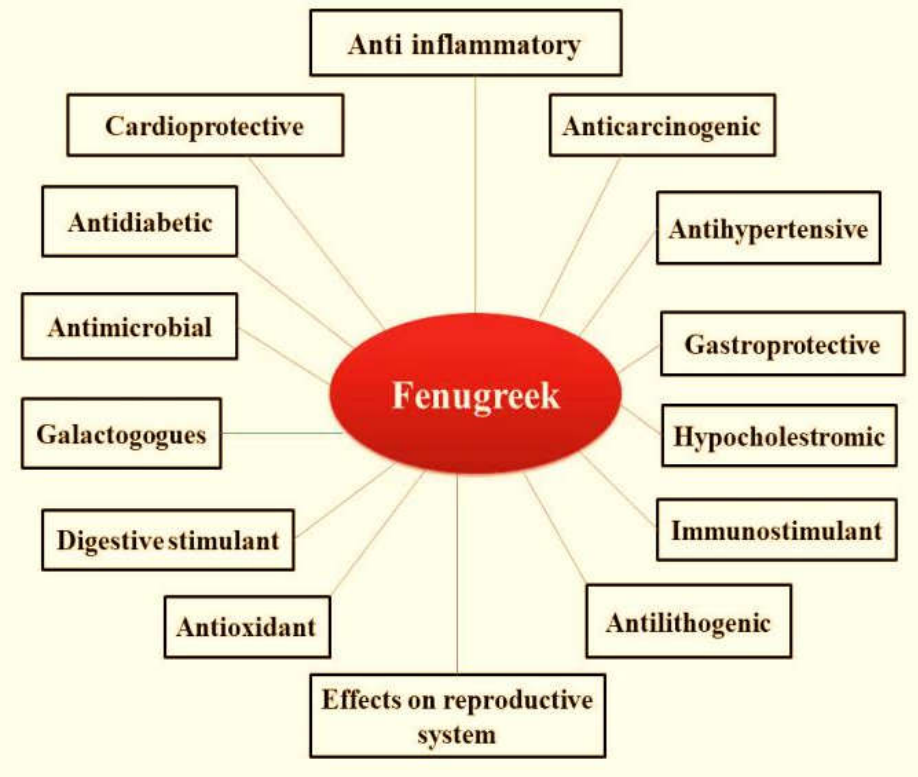


Fig. (4) Therapeutic uses of *Trigonella Foenum Graceum*

Diabetes mellitus (DM) is marked by increased blood sugar levels and abnormal glucose metabolism. The elevated blood glucose levels are linked to either insufficient or resistant insulin, which leads to reduced utilization of glucose in insulin-dependent organs including the liver or muscles that depend on insulin for glucose absorption. Both human diabetic patients and experimental animals showed a noteworthy decline in blood glucose levels when administered with trigonella. Among the many therapeutic benefits of trigonella, its hypoglycemic or antihyperglycemic impact has received the greatest research attention and is also used by individuals with diabetes [38]. Several studies have demonstrated that treating fenugreek seed

decoction can improve diabetes, decrease glycosuria in mild cases of the disease, and ameliorate severe cases of the disease. Fenugreek comprises 51.7% fiber, consisting of 19.2% mucilaginous fiber and 32.5% neutral fiber. Additionally, it contains trigonelline, an alkaloid recognized for its impact on glycosuria. [39].

4.2 TINOSPORA CORDIFOLIA

Tinospora cordifolia is a glabrous succulent shrub that climbs and is typically found in hedges. It is indigenous to India and grows readily in tropical climates. In Indian Ayurvedic medicine, it is extensively utilised. as a tonic, vitalizer and as a remedy for diabetes and metabolic disorders [40]. Since ancient times, *tinospora cordifolia* has been a vital component of Indian medicinal traditions. This well-known bitter from India is given for fevers, diabetes, dyspepsia, jaundice, skin conditions, urinary issues, and persistent diarrhoea and dysentery. Additionally, it has shown promise in the treatment of leprosy, helmenthiasis, and cardiac disease. The highly nutritious and digestible starch derived from the stem is employed in various illnesses [41]. Tinospora cordifolia (TC), belonging to the family Menispermaceae, is referred to as Gulancha in English, Guduchi in Sanskrit, and Giloya in Hindi. It has been extensively documented in Ayurvedic literature, the traditional medical system of India also practiced as an alternative medicine elsewhere, for its tonic and vitalizing properties. Additionally, it is recognized as a remedy for diabetes and various other metabolic disorders [42]. T. cordifolia has anti-diabetic, anti-tumor, immune stimulating, diabetic cataract preventing, cholesterol-lowering, hepatoprotective effects and promising activity in healing diabetic foot ulcers [43].

Table 2 Botanical classification of *Tinospora cardifolia*

S.NO.	Kingdom	Plantae
1.	Subkingdom	Tracheophyta
2.	Division	Mangliophyta
3.	Class	Mangoliopsida
4.	Subclass	Polypetalae
5.	Order	Renale

6.	Family	Menispermaceae
7.	Genus	Tinospora
8.	Species	Cardiflolia
9	Source	Stem , leaves or whole plants

4.2.1 Methods and material

(A) Plant material

Tinospora cordifolia stems were obtained from the Dr. Harisingh Gour University Botany Department in the Sagar, Madhya Pradesh and subsequently confirmed by the Botany Department. It is kept in the department's herbarium beside the specimen.

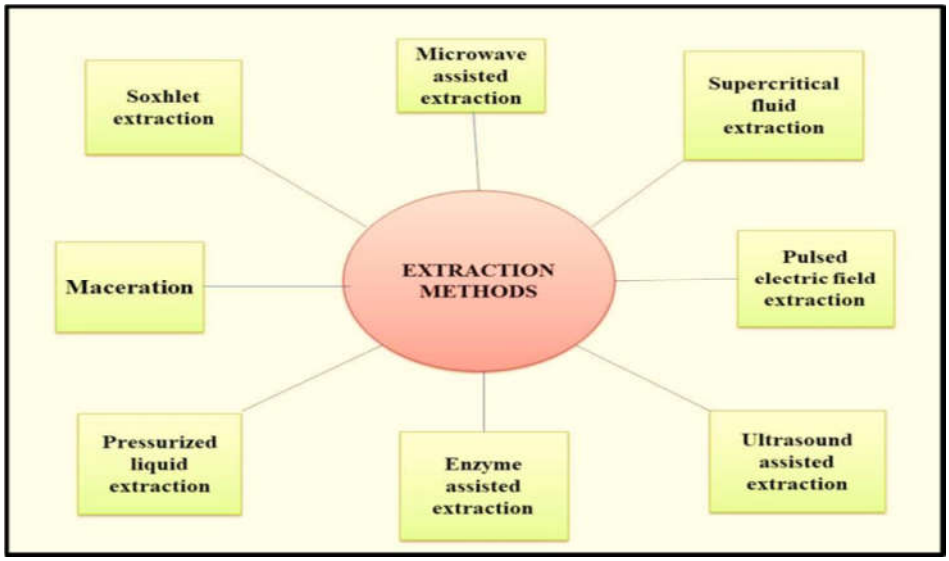


Fig. (5) Different extraction methods of herbal plants

(b) Extraction by Soxhlet apparatus

A 20 gram sample was extracted in two steps, progressively increasing in polarity from non-polar to polar solvent. The several extracts that were obtained in that order were made using petroleum ether, distilled water, ethyl acetate, chloroform, and acetone, in that order. To carry

out the extractions, Soxhlet equipment was used. Every extraction was conducted for a fixed duration of 0 hours, meaning that the temperature was kept between 10 and 20 degrees Celsius below the melting point of the solvents utilised. The resulting extracts were then filtered, boiled to concentrate to a volume of 5 ml, and refrigerated until needed again [44].

(c)Extraction with hexane

The stems that had been shade-dried were broken into tiny bits and ground into a fine powder. At room temperature, 20 grammes of plant material were soaked in 100 millilitres of hexane while being periodically shaken. The substance soluble in hexane was filtered off after 15 hours. Using a rotary evaporator, the filtrate was concentrated to dryness under vacuum at a low temperature (408 C). Similarly, extracts of dichloro methane, ethyl acetate, and chloroform were prepared and utilised in the investigation [45].

4.3 TEROCARPUS MARSUPIUM

*Pterocarpus marsupiu*m Roxb. (Fabaceae), also referred to as the Malabar Kino Tree and the Indian Kino Tree. Native to Sri Lanka, Nepal, and India, Kino is known locally as "Bija" and is found in several areas of the Western Ghats. This tree species has been added to the red data book because its population in the wild is decreasing. Its bark is used medicinally, and its timber is exploited [46].The plant is frequently referred to as Honne (Kannada), Red Kino tree (English), and Asanahm bijakah (Sanskrit). The leaves are excellent for external applications for boils, ulcers, and skin conditions. The gum that is extracted from the stem is used as an astringent, for toothaches, diarrhoea, and other conditions. The gum is administered locally for leucorrhea and passive haemorrhage, and the blossoms are used for fever. The plant's heart wood yielded the flavonoid components marsupin, pterosupin, and liquiritigenin [47]. Marshupin and pterostilbene are the two main phytoconstituents of Pterocarpus marsupium. These include 7, 4'-dihydroxyflavone, propterol, marsupol, carsupin, pterosupin, 17 liquidrtigenin, isoliquirtigenin, p-hydroxybenzaldehyde, and so on [48].The World Health Organisation (WHO) estimates that over 80% of 200 of the 9,600 plant species that are known to have medicinal qualities in Indonesia have been utilised as raw materials by the pharmaceutical industry to prepare traditional medicine [49].

Table 3 Botanical classification of *Terocarpus Marsupium*

S. No.	Domain	Eukaryota
1.	Kingdom	Plantae
2.	Subkingdom	Viridaeplantae
3.	Class	Magnoliopsida
4.	Order	Fabales
5.	Family	Fabaceae
6.	Genus	Terocarpus
7.	Species	Marsupium
8.	Common name	Bijsar, indian kino tree, malbar kino tree, vijaysar, Bibla

4.3.1 Phytochemistry and Therapeutic Values of *Pterocarpus marsupium*

Active Constituents

A significant number of crucial phytochemicals, including glucosides, sesquiterpene, and vijayoside, have been isolated from the aqueous extract of the heartwood of Pterocarpus marsupium. Specifically, the heartwood extract comprises pterostilbene, liquiritigenin, and epicatechin. The bark extract is rich in various esteemed phytochemicals such as 3-o-methyl-D-glucose, n-hexadecanoic acid, 1,2-benzenedicarboxylic acid, tetradecanoic acid, 9,12-octadecadienoic and lupeol. Notably, eleven bioactive compounds, including pterocarposide, 2,6-dihydroxyphenyl glucopyranoside, pteroside, vijayoside, pterosupol, marsuposide, epicatechin, quercetin, vanillic acid, formononetin, and naringenin, have been effectively removed from heartwood of *Pterocarpus marsupium* [50]

Table no. 4. List of medicinal plants having antidiabetic effect

Plants name	Common name	family	Parts of plants used	Antidiabetic and other beneficial effects in traditional medicine	Active constituents	References
Artemisia vulgaris L	Ajenjo	Asteraceae	Leaf	Acupuncture therapy utilizes analgesics for pain relief. Neonatal jaundice treatment often incorporates analgesics. Analgesics are employed in managing gastric ulcers. Hepatitis treatment may involve the use of analgesics. Analgesics are utilized to alleviate convulsive crises.	Artemisinin camphor, camphene,	51
Artemisia pallens	Davana	Asteraceae	Aerial parts	It lowers blood sugar levels by enhancing peripheral glucose utilization or impeding glucose reabsorption. Its mechanism involves reducing blood glucose levels by increasing	terpenes, p-cymene, and 1,8-cineole	52

				peripheral glucose utilization or blocking glucose reabsorption.		
Areca catechu	Supari	Arecaceae	fruit	Hypoglycemic	arecoline, arecaidine, guvacine, and guvacoline	52
Aloe barbadensis Mill.	Sabila	Liliaceae	Juice of the leaves	anti-diabetic, anti-oxidant, anti-inflammatory as well as immunostimulatory and immunomodulatory properties	anthraquinones,	53
Allium sativum	Touma	Liliaceae	Garlic bulb	It impedes and eradicates bacteria, fungi, and parasites while also reducing blood pressure, cholesterol, and sugar levels. Additionally, it prevents blood clotting and safeguards the liver.	Allyl propyl disulfide, allicin, cysteine sulfoxide, and S-allyl cysteine sulfoxide, alliin	53
Beta vulgaris	Betabel	Chenopodiceae	Juice of the leaves	antihypertensive, hypoglycemic, antioxidant, anti-inflammatory, and hepatoprotective activities	betacyanins and betaxanthins	54
Coccinia indica	Bimb Kanturi	Cucurbitaceae	juice of the roots and leaves	Hypoglycemic	Saponins, flavonoids, sterols and alkaloids	54

Catharanthus roseus	Vicaria	Apocinaceae	Root	antimicrobial, antioxidant, anthelmintic, antifeedant, antisterility, antidiarrheal, antidiabetic effect	vinblastin, vincristine tetrahydroalstonin, prinin, vindolin, catharanthin, vindolinin, ajmalicin, vincoside	55
Emblica officinalis	Amla, Dhatriphala	Phyllanthaceae	fruits	Decreases lipid peroxidation, antioxidant, hypoglycemic	quercetin, kaempferol, and routine	55
Ficus bengalenesis	Bur	Moraceae	Bark	Hypoglycemic, antioxidant	flavonoids, phenols, terpenoids, and terpenes	55
Gymnema Sylvestre	Gudmar Gurmar	Apocynaceae	Leaf	hypoglucemic	Gymnemic acids	55
Hemidesmus indicus	Anantamul	Apocynaceae	Root	Anti-snake venom activity, anti-inflammatory	hexatriacontane, lupeol, its octacosanoate, α-amyrin, β-amyrin, its acetate and sitosterol	56
Ipomoea batatas	Sakkargand	Convolvulaceae	Leaf extract	Reduces insulin resistance	anthocyanins and phenolic acids	56
Momordica charantia L.	Cundeamor,	Cucurbitaceae	Leaves	It demonstrates therapeutic properties against diabetes, cancer, inflammation, viral	Charantin, sterol	56

				infections, and high cholesterol levels.		
Mangifera indica	Mango	Anacardiacea e	Leaves extract	It possesses antioxidant, cardioprotective, immunomodulatory, hypotensive, wound-healing, and antidiabetic properties.	Beta carotene Alpha carotene	56
Momordica cymbalaria	Kadavanch i	Cucurbitacea e	fruits	Hypoglycemic, hypolipidemic		57
Momordica chirata	Bitter gourd	Cucurbitacea e	Fresh green leaves	It stimulates PPARs α and γ, resulting in decreased plasma levels of ApoB-100 in mice subjected to a high-fat diet.	Charantin, sterol	57
Musa sapientum	Banana	Musaceae	Flower	Antihyperglycemic, antioxidant	alkaloids, flavanoids, steroids, glycosides and saponins	57
Punica granatum	Anar	Lythraceae	flower	Antioxidant, anti-hyperglycemic effect		57
Syzygium jambolana		Myrtaceae	Fruit	Diabetic rabbits	Ellagic acid, isoquercetin, kaemferol and myrecetin.	57
Terminalia belerica	Behada	Combretacea e	Fruit	Antibacterial, hypoglycemic	galliacid, ellagic acid, chebulanic acid	56,57

Trigonella foenum graceum	Methi	Fabaceae	seed	Stimulate the secretion of insulin , reduce insulin resistance	Trigonelline	55,58
Tinosprora cardifolia	Giloy Guduchi	Menispermaceae	stem	anti-spasmodic anti-microbial anti-osteoporotic anti-inflammatory anti-arthritic anti-allergic anti-diabetic	Giloin, Tinosporan acetate	58
Terminalia chebula	Hirda	Combretaceae	Fruits	Antibacterial, hypoglycemic	Chebulagic acid and chebulinic acid	58
Vinca rosea	Sadabahar	Apocynaceae	Leaf and flower	Anti-hyperglycemic	Catharanthin vincristine vinblastine	58
Withania somnifera	Ashvagandha,winter cherry	Solanaceae	leaves, roots, flowers, bark, and stem	Hypoglycemic, diuretic and hypocholesterolemic	Withanolides withanine	58
Zingiber officinalis	Sunth	Zingiberaceae	Rhizome	Increases insulin level	Gingerol, shogaol	58

4.4 RUBIA CORDIFOLIA

Rubia cordifolia Linn is an important crude drug commonly utilised in the traditional medical system for the treatment of rheumatoid arthritis, inflammation and fever. This herb is not only mentioned in Ayurveda but is also among the major ingredients of many marketed products.[59] *Rubia cordifolia*, often known as Common Madder or Indian Madder, a member of the flowering plant species in the coffee family, Rubiaceae, has been historically cultivated for its red pigment

derived from its roots. The genus Rubia comprises approximately 70 species distributed worldwide, with a total of 36 species and 2 varieties reported in China. The extracts and phytochemicals obtained from Rubia plants have garnered significant attention due to their potent bioactivities. In Ayurvedic materia medica, Manjistha is cited as a detoxifying herb capable of removing toxins from the blood. The term "Rubia" signifies "red," reflecting the plant's ability to impart a reddish hue to breast milk and urine upon internal use. The roots of this plant are highly valued as a medicinal herb and are officially recognized for their therapeutic properties [61].

Table 5 botanical classification of Rubia cardifolia

S .No.	Kingdom	Plantae
1.	Division	Magnoliophyta
2.	Class	Dicotyledons
3.	Order	Rubiales
4.	Family	Rubiaceae
5.	Genus	Rubia
7.	Species	Cardifolia
8.	Source	Root
9.	Common name	Manjishtha, Indian madder, Chay root or Chay-aver

Rubia cordifolia has been observed to exhibit wound healing activity in mice. Wounds represent physical injuries that cause a breach or disruption of the skin. The effective healing of wounds is crucial for restoring the interrupted anatomical continuity and compromised functional status of the skin. The process of healing is intricate and multifaceted, triggered in response to an injury, aiming to restore the function and integrity of damaged tissues. Wound healing entails ongoing interactions between cells and between cells and the extracellular matrix, facilitating progress through three overlapping phases [62].

Madder has been used in many Asian countries as a dye, for imparting shades of red, scarlet, brown and mauve to cotton and woolen fabrics. In India and neighboring countries, madder also

has a long history in skin care and treatment and it has been used internally in disorders of the urinary tract [63]. The plant *Rubia cordifolia* has been reported for anti-inflammatory, immunomodulatory, anticonvulsant and anxiolytic and anti-tumor activities. In the ethnobotanical claims, that has been raised up., the roots are employed in the management of jaundice by the folk tribes of west Bengal and Uttaranchal, but to the best of our understanding there is no scientific report on the hepatoprotective activity of Rubia cordifolia [64].

4.4.1 Material and methods

(A) Plant material

The roots of Rubia cordifolia were obtained from the botany garden and were taxonomically authenticated by Dr. Pradeep Tiwar, Department of botany, Dr. Hari Singh. Gour University, Sagar-470 003 (MP), India.

(B) Extraction

The authenticated roots of *Rubia cardifolia* were harvested and shade dried. After reducing them to a coarse powder, they were sieved to achieve uniform particle size. This powdered root material was then subjected to extraction with ethanol and water using a Soxhlet apparatus. Following extraction, the root extracts were filtered, collected, and concentrated using a Rotatory Flash Evaporator. These concentrated extracts were then utilized for subsequent experimental models [65, 66].

4.4.2 Pharmacological actions

1. Anti-inflammatory Effect
2. Wound Healing Activity
3. Diuretic
4. Antimicrobial
5. Radioprotective
6. Anti-Adipogenic
7. Gastro-protective
8. Anti-convulsant
9. Immunity enhancing activity

10. Antioxidant
11. Anti-acne
12. Anti-cancerous
13. Anti-diabetic activity
14. Anti-proliferative activity
15. Nephroprotective Activity
16. Cardioprotective [67].

4.4.3 Traditional Therapeutic Uses:

- It is highly valuable plant in Ayurvedic system of medicine used for treatment.
- For the internal therapy of spleen disorders and skin problems, powdered dried fruits and roots are ingested.
- It is applied to treat severe burns, ulcers, and fractures of the bones.
- It is useful for persistent mild fevers and is thought to be tonic and antitussive.
- Internal usage of the roots is used to treat a variety of conditions, including rheumatism, pneumonia, internal and external haemorrhage, kidney, bladder, and gallstones, dysentery, and so on. Blood problems are treated using this herb.
- Alterative, anodyne, antiphlogistic, astringent, diuretic, expectorant, styptic, and vulnerary are the properties of the roots. [60]

4.4.4 Anti-diabetic activity

In an experimental study, an alcoholic extract derived from the roots of *Rubia cardifolia* exhibited promising antidiabetic properties in an animal model. The extract was administered to normal rats, rats with induced hyperglycemia through glucose feeding, and rats with alloxan-induced diabetes. It resulted in a significant decrease in blood glucose levels across all groups, including a reduction in blood sugar levels in the alloxan-treated diabetic rats, suggesting an extra-pancreatic effect of the extract. Moreover, when rats were treated with the aqueous extract of *Rubia cordifolia*, they showed improved oral glucose tolerance compared to glucose-fed animals. Additionally, when insulin was administered along with the drug extract, there was a potentiation of the hypoglycemic effect compared to insulin treatment alone. Furthermore, the leaf extract of Rubia cordifolia demonstrated a decrease in blood glucose levels compared to

glibenclamide in both normal fasted rats and alloxan-induced diabetic rats. Additionally, the extract exhibited a favorable effect on glucose disposition in glucose-fed hyperglycemic rats. Notably, the extract also led to a reduction in serum cholesterol and triglyceride levels while increasing serum high-density lipoprotein and protein levels in diabetic rats [68].

4.5 GYMNEMA SYLVESTRE

Gymnema sylvestre (Asclepiadaceae), popularly known as “gurmar” due to its unique ability to breakdown sugar. Triterpene saponins referred to as gymnemic acids and gymnemasaponins, as well as the polypeptide gurmarin, are the phytoconstituents that exhibit sweet suppression activity. The plant is used to treat a variety of conditions, including arthritis, diuretics, anaemia, osteoporosis, hypercholesterolemia, cardiopathy, asthma, constipation, microbiological infections, indigestion, and inflammation. It also shows promise as a natural cure for diabetes [69]. Indian climbing shrub Gymnema sylvestre R.Br. is known in ancient writings as Gurmar, or the sugar killer. In Ayurvedic medicine, this plant's leaves are taken orally to cure diabetes. It is also known to reduce blood cholesterol and triglycerides. Similar to sulfonylureas, an extract from the plant called gymnemic acid decreases blood sugar by inducing the release of endogenous insulin storage. Additionally, the small intestine's glucose receptors are blocked by gymnemic acid. The roots and leaves are used as a cure for snakebite and a paste made from the leaves is helpful for eye problems and toe mycosis [70]. G. sylvestre is a woody, slow-growing perennial climber that can reach a height of 600 meters and is found across India's arid woods. It is mostly found in Central and Southern India's tropical forests. Additionally, it can be found in the Deccan, Banda, Konkan, Western Ghats, and areas of northern and western India. The plant is a big woody climber that is rather hairy. The opposite leaves are typically oval or elliptic, measuring 1.25 to 2.0 inches by 0.5 to 1.25 inches. Little yellow flowers grow in axillary and lateral umbels in cymes [71].

Table 6 Botanical classification of *gymnema sylvestre*

S. No.	Kingdom	Plantae
1.	Division	Magnoliophyta
2.	Class	Magnoliopsida
3.	Order	Gentianales
4.	Family	Apocynaceae
5.	Sub family	Asclepiadoidceae
6.	Genus	*Gymnema*
7.	Species	*Sylvestre*
8.	Source	Leaves
9.	Common name	Gurmar, Australian cow plant, chigeng teng, buti, kober,

Based on recent research, formulations containing gymnemic acid have also been demonstrated to be effective against obesity. This is explained by gymnemic acids' capacity to postpone the blood's absorption of glucose. Gymnemic acid molecules have an atomic configuration with glucose molecules. By blocking the receptors on the taste buds from being activated by sugar molecules found in food, these chemicals reduce the craving for sugary foods. In a similar vein, gymnemic acid molecules bind to receptor sites in the absorptive outer layers of the intestine, hindering the absorption of sugar molecules and thereby reducing blood sugar levels [72].

4.5.1 Mechanism of Action of Gymnemic Acids

These molecules, known as gymnemic acid, attach to the receptor on the tongue's taste buds, blocking sugar molecules from activating them and inhibiting the absorption of sugar Comparably, gurmarin, a peptide that was extracted from G. sylvestre leaves, also has the similar effect of blocking the consumption of meals high in sugar. The pancreas secreting more insulin, encouraging the regeneration of islet cells, and boosting glucose utilisation by increasing enzyme

activity—an insulin-dependent pathway—are some potential mechanisms for the hypoglycemic effects of gymnemic acids from G. sylvestre leaves. Moreover, gymnemic acid molecules have the ability to attach to the intestinal Na+-glucose transporter receptors, blocking the absorption of glucose[73]

Table 7 List of Marketed herbal products for type 2 diabetes mellitus

Drug	Company name	Ingredients
Dia-care	Admark Herbals Limited	Sanjeevan Mool; Himej, Jambu beej, Kadu, Namejav, Neem chal
Diabecon	Himalaya	*Gymnema sylvestre , Pterocarpus marsupium, Glycyrrhiza glabra, Casearia esculenta, Syzygium cumini, Asparagus racemosus, Boerhavia diffusa, Tinospora cordifolia, Tribulus terrestris, , Gossypium herbaceum, Berberis aristata, Commiphora wightii, shilajeet, Momordica charantia, Piper nigrum, Ocimum sanctum, Abutilon indicum, Curcuma longa, Rumex maritimus Sphaeranthus indicus, , Gmelina arborea, Swertia chirata, Phyllanthus amarus, Aloe vera, Triphala,*
Gurmar powder	Garry and Sun natural Remedies	Gurmar (*Gymnema sylvestre)*
Bitter gourd powder	Garry and Sun natural Remedies	Bitter gourd (*Momordica charantia)*
Diabetes-Daily Care	Nature's Health Supply	Alpha Lipoic Acid, Cinnamon 4% Extract, Chromax, Vanadium, Fenugreek 50% extract, Gymnema sylvestre 25% extract Momordica 7% extract, Licorice Root 20% extract

Diabeta	Ayurvedic cure Ayurvedic Herbal Health Products	*Gymnema sylvestre, Curcuma longa* (Turmeric), *Pterocarpus marsupium* (Kino Tree), , *Syzygium cumini* (Black Plum), *Acacia arabica* (Black Babhul), *Tinospora cordifolia , Zingiber officinale* (Ginger), *Azadirachta indica* (Neem), *Momordica charantia* (Bitter Gourd), *Vinca rosea* (Periwinkle)
Syndrex	Plethico Laboratories	Germinated Fenugreek seed extract
Diabecure	Nature beaute sante	*Juglans regia, Berberis vulgaris, Erytherea centaurium, Millefolium Taraxacum*
Pancreatic tonic 180 cp	Ayurvedic herbal supplement	*Pterocarpus marsupium, Ficus racemosa Momordica charantia, , , Aegle marmelos, Cinnamomum tamala Syzygium cumini, Gymnema sylvestre, Azadirachta indica, Trigonella foenum graceum,*
Ayurveda alternative herbal formula to Diabetes:	Chakrapani Ayurveda	Karela *(Momordica charantia*) Pushkarmool (Inula racemosa) Jamun Gutli (*Syzygium cumini*) Gurmar *(Gymnema sylvestre*) Neem (*Azadirachta indica*) Guduchi *(Tinospora cordifolia*) Methika *(Trigonella foenum gracecum)*
NBRMAP-DB	CSIR CIMAP	*Trigonella foenum graceum* *Gymnema sylvestre, Tinospora cardifolia* *Rubia cardifolia, Berberis aristata*

CONCLUSION

The exploration of phytotherapeutics in diabetes management through herbal alternatives underscores a promising avenue for enhancing treatment strategies. The research reviewed suggests that certain herbs and botanicals possess potential in regulating blood sugar levels and improving overall glycemic control. Research suggests that certain herbs and botanicals have demonstrated potential in managing diabetes by helping to regulate blood sugar levels. These include herbs, *trigonella foenum graeum* (methi), *gymnema sylvestre* (gudmar or gurmar) *tinospora cardifolia* (giloy), *terocarpus marsupium* among others. However, while findings are encouraging, caution should be exercised in integrating herbal alternatives into diabetes management protocols. Further robust clinical trials are warranted to elucidate their efficacy, safety profile, and optimal dosage regimens. Collaboration between healthcare professionals and patients is essential to ensure informed decision-making and appropriate monitoring. Overall, while herbal alternatives offer promise, continued research and careful implementation are necessary to maximize their potential benefits in diabetes management.

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