A review on current epidemiology and herbal approach towards the management of diabetes mellitus in India

Roy S.¹, Biswas S.², Das S.³, Majumder S.⁴, Ghosh P.⁵, Choudhury S.⁶, Bose A.⁷, Mondal S.⁸*

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¹ Sukanta Roy, The Neotia University, Sarisha, West Bengal, India.
² Sudeepto Biswas, TAAB Biostudy services, Kolkata, West Bengal, India.
³ Sourav Das, TAAB Biostudy services, Kolkata, West Bengal, India.
⁴ Shramana Majumder, Covance India Pharmaceutical Services, Bengaluru, Karnataka, India.
⁵ Parag Ghosh, The Neotia University, Sarisha, West Bengal, India.
⁶ Sangeeta Choudhury, TAAB Biostudy services, Kolkata, West Bengal, India.
⁷ Anirbandeep Bose, TAAB Biostudy services, Kolkata, West Bengal, India.
⁸* Subhasish Mondal, The Neotia University, Sarisha, West Bengal, India.

The article here is about the disorder Diabetes Mellitus (DM) and the various treatments from the herbal background more specifically in India. It has been found that DM is a very common disorder affecting people mostly from the Asian subcontinent. The most common form of diabetes is Non-insulin dependent Diabetes Mellitus (NIDDM) or Type 2 DM (T2DM) and although a number of treatment approaches have been taken for this, herbal drugs never stand apart. Herbal medicines have been the backbone of the entire medicinal system in India and hence this paper will specifically look into all the original, novel, and ancient ways to treat the disorder. Several plants have been found to have anti-diabetic effects like catechu, basil, ginko biloba, fenugreek, and much more. Also, there have been many marketed herbal products too like Bitter gourd powder, episulin, Dia care, and much more which have been discussed in detail in the paper. Interestingly, all of these herbal products have some mechanism of action which are quite varied and have been discussed here. So, the main approach behind this paper is to re-establish herbal drugs as effective ways of medication against the disorder of Diabetes Mellitus.

Keywords: Diabetes Mellitus, Herbal drugs, Metabolic disorder, Traditional plants

Subhasish Mondal, , , The Neotia University, Sarisha, West Bengal, India.
Email: subhasish.mondal@iu.in

Introduction

Diabetes mellitus (DM) is considered one of the oldest metabolic disorders notorious to society. It was initially stated about 3000 years ago in an Egyptian manuscript [1]. In the year 1936, two types of diabetes were found which further stated type 1 DM and type 2 DM. Depending upon their biological appearance they simultaneously phrase at Insulin-dependent Diabetes mellitus (IDDM) and Non-Insulin-dependent Diabetes mellitus (NIDDM) [2]. Type 2 DM NIDDM is the most abundant form of DM which is associated with hyperglycemia, insulin resistance, and relative insulin deficiency [3]. Type 2 DM results from the collaboration of various factors like genetic, behavioral, and environmental risk factors [4,5].

Till now, Type 2 DM is considered to be the utmost form of DM, which occurs in 85 to 95% of the nations that are developed and with more incidence in the nations which are developing, as per the International Diabetes Federation. This disease generally takes years or even decades to mature. Diabetes starts off with pre-diabetes at first, in which the levels of glucose (blood sugar) are mostly within the normal range but not as much high as to be eligible for the diagnosis of diabetes. Normal but not high enough yet for a diagnosis of diabetes. People with prediabetes can often delay or prevent the escalation to type 2 diabetes by losing weight through improvements in exercise and diet, like the Diabetes Prevention Program.

The existing therapies against DM mainly mostly contain oral hypoglycemic or anti-hyperglycemic agents and insulin. The anti-DM drugs generally work by the mechanism of acting on a particular metabolic pathway to control hyperglycemia and are so associated with a number of side effects. The search for a better remedy starts with this realization that focuses on other metabolic pathways apart from just carbohydrate, protein, or fat metabolism.

The herbal drugs come into existence here, the preparations are made from more than 800 traditional plants and the active constituents are supposed to have antidiabetic activity as it is proved by the in-vivo and in-vitro studies. The extracts act at various levels like inhibition of glucose absorption from the intestines, increasing insulin secretion from the pancreas, increasing the glucose uptake through the adipose and muscle tissues, or inhibition of glucose formation from the hepatocytes. The best part about the herbal extracts is that along with their unique mechanism of action they have very less side effects as compared to synthetic drugs and are of natural origin. So, for the treatment of diabetes, the significance of herbal medicines can be considered well. The only challenge is there is very limited research on the therapeutic use of the extracts.

Epidemiology: Diabetes is about to become a pandemic in India with over 62 million diabetic patients currently identified with it [6, 7]. In the year 2000, India became the maximum number (31.7 million) of individuals with DM in the world. Meantime, China with 20.8 million and the United States with 17.7 million are gaining second and third place respectively [8]. By the year 2030, it is assumed that DM may affect up to 79.4 million people in India, whereas China with 42.3 million, and the United States with 30.3 million will also observe a noticeable increment in those affected by the disease [8, 9]. The causality of DM in India is involved several factors as well as it includes environmental influenced genetic factors like obesity associated with growing living standards, high rate of urban migration, and evolving lifestyle [10].

The diabetes prevalence in India can be drawn into a pattern that is related to the demographical distribution of DM countrywide. A rough estimation shows that the occurrence of DM in rustic populations is one-fourth that of the urban population of India including other Indian subcontinent countries like Bangladesh, Nepal, Bhutan, and Sri Lanka [8, 11].

A large community study led by the Indian Council of Medical Research (ICMR) from which the initial results revealed that a lesser percentage of the population is undertaken by diabetes in North Indian states like Chandigarh with 0.12 million, Jharkhand with 0.96 million as compared to Maharashtra with 9.2 million and Tamil Nadu with 4.8 million[11]. The National Urban Survey steered all the metropolitan cities of India which revealed a similar trend: 11.7% in Kolkata (East Indian), 6.1% in Kashmir Valley (North Indian), [12] 11.6% in New Delhi (North Indian), and 9.3 % in West Indian (Mumbai) compared with (13.5% in Chennai (South Indian), 16.6% in Hyderabad (south Indian), and 12.4% Bangalore (South Indian) [13].
In conclusion, the different states that the north Indians are migrated populations from throughout Asia and south Indians are termed as host populations [14].

Current western method of diabetes management and mechanism of action:
- T2DM or NIDDM is considered a chronic metabolic disorder. By DM millions of people are affected globally and are accompanied by several comorbidities and micro/macrovascular difficulties. DM management is a complex process and must be designed personalized to the individual. Physicians and paramedics like nurses, pharmacists, and dieticians are usually employed as a well-adjusted healthcare team in the management of a diabetic individual. The American Diabetes Association (ADA) encourages diabetes self-management education, an arrangement in which the patient associated with DM is fortified with enough knowledge and skills to afford self-care, manage emergency (severe hyperglycemic and hypoglycemic events), and introduce a healthy lifestyle [15, 16].
- Primarily non-pharmacological management of T2DM includes suitable diet and exercise. Diet should be maintained in such a way that does not involve in weight gain. Minimum30 minutes of moderate to intense physical activity can recover T2DM and weight supervision. Intense lifestyle modifications (LSMs) are the topmost choice of all disease management models and must be stimulated in both individuals who are at risk for developing DM (pre-diabetic) and individuals who are already associated with DM.
- For individuals necessitating medical assistance for T2DM, metformin, a biguanide, is cast off as a first-choice treatment for most patients who are not able to maintain their glycemic level within the desired limits with LSM. Metformin intensifies the glucose uptake by the skeletal muscles [17], constrains gluconeogenesis in hepatic cells [18], as well as facilitates insulin sensitivity towards its receptor [19] (summarized in Table1). Metformin is not only the first choice for the treatment of T2DM but also helps in the prevention of high-risk populations towards T2DM [20].
- Sulfonylureas are used as a second choice
- of Oral hyperglycemic agents which surges insulin discharge by coupling to K+/ATPase (potassium) channels in the β-cells present in Islets of Langerhans in the pancreas [21]. Second-generation sulfonylureas are extensively used because of their acute pharmacological action, lesser drug interactions, and lesser severe adverse drug reactions [22]. Insulin, which is more often stated as the last choice of therapy in the treatment of T2DM and is the compulsory treatment of Type 1 DM (T1DM, IDDM), is now considered an effective combination in association with metformin as a second choice of treatment instead of sulfonylureas [22,23]. Insulin is highly efficient in controlling blood glucose and glycosylated hemoglobin (HbA1C). Insulin routines are varying depend upon the individual patient and can be used in various combinations.
- Further, less corroborated classes of a hyperglycemic agents which are used along with metformin are thiazolidinediones (TZDs) and GLP-1 analogue (glucagon-likepeptide-1). TZDs (pioglitazone, rosiglitazone) control peroxisome proliferator-activated receptor γ (PPARγ), a nuclear receptor that modulates glucose and lipid metabolism up to a certain level. Stimulation of PPARγ directed to the primary enhancement of insulin sensitivity in adipose tissue and also imparts an effect on skeletal muscle and liver [24]. TZDs are found to be responsible for amplifying cardiovascular events due to a trial that confirmed the myocardial events with rosiglitazone [25]. GLP-1 analogues (exenatide, liraglutide) are peptides derivative that are incretin hormones released from the small intestines after meals [26]. It imparts the action by binding to the GLP-1 receptors which are situated in the pancreas and help to trigger the insulin release and deplete glucagon release. The meglitinides class (repaglinide, nateglinide) shows identical pharmacological activity to sulfonylureas [27] but coupled to the SUR-1 site on the K+/ATPase pump of the β-islet cells in the pancreas, which further trigger the insulin release. There is an improved risk of lower glycemic condition of hypoglycemia associated with the meglitinides.
- α-Glucosidase inhibitors (acarbose, miglitol) show pharmacological effects initially by constraining the effect of α-glucosidase
- enzymes on the intestinal brush border in the gut wall. α-Glucosidase is considered a key enzyme that leads to the breakdown of carbohydrates to lower molecular weight carbohydrates like starch, dextrin, and disaccharides for systemic absorption [28]. α-Glucosidase inhibitors could also have a synergistic effect to stimulate GLP-1 secretion. A protease enzyme called Dipeptidyl peptidase-4 (DPP-4) is accountable for the deactivation of hormones GLP-1 and GIP (gastric inhibitory peptide) [29].

**Table-1: Mechanism of action of western and herbal medicine mechanism upon different area in management of diabetes control (figure- 1)**

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<th>Drug used</th>
<th>Carbohydrate uptake inhibition (1)</th>
<th>Increment of Peripheral glucose uptake (2)</th>
<th>PPA R activation (3)</th>
<th>Modulation of insulin receptor activity (4)</th>
<th>Insulin receptor response improvement (5)</th>
<th>Reduction of endogenous incretins activities (6)</th>
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- DPP-4 inhibitors (sitagliptin, saxagliptin, linaglaptin) help to intensify the endogenous GLP-1 levels.

- An endogenous enzyme called amylin and its analogs (pramlintide) further facilitate endogenous amylin secretion along with insulin from pancreatic β-islet cells by binding to amylin receptors present in the brain as well as reducing gastric emptying, reducing post prandial glycemic levels [30,31].

- Table -1 contains the different mechanisms of action by western medicine as well as medicine used in Chinese and Indian traditional herbal systems to manage the diabetic condition.

**Herbal medications for treatment and prevention of diabetes in India and China:**

Around 800 plants are identified which have been found to possess a key role in the prevention and treatment of T2DM in the traditional Chinese and Indian herbal medicinal cultures. Ancient traditional herbal medicine provided the foundation for the prevention and treatment of numerous diseases. Out of them, several herbal preparations are present as a unit of herbal extract or in a mixture of herbal extract formula. Over 400 herbal extracts were found to be a positive effect in In-vitro or In-vivo while treating T2DM or NIDDM [32].

**Fig. no. 1:** Different mechanisms of action of herbal (1. Inhibition of carbohydrate absorption. 2. Insulin sensitivity improvement of insulin-resistant cells. 3. Rising glucose uptake by peripheral cells. 4. Modulating insulin release. 5. Improving endogenous incretins release. 6. Exercising antioxidant effects and constraining cell apoptosis. 7. Triggering the glycogenesis or suppressing hepatic glycogenolysis).

The medicinal activity of the herbal extract can be differentiated as (Figure1) [32-34].
1. Inhibition of carbohydrate absorption.
2. Insulin sensitivity improvement of insulin-resistant cells.
3. Rising glucose uptake by peripheral cells.
5. Improving endogenous incretins activities.
6. Exercising anti-oxidant effects and constraining cell apoptosis.
7. Triggering the glycogenesis or suppressing hepatic glycogenolysis.

**Gymnema sylvestre Schult** (synonym. Periploca sylvestris Retz, *Gurmar in Hindi*), belongs to the genus Gymnema and the family of Apocynaceae, mostly found in the tropical forests present beneath the equator as southeast Asian countries like the central portion of India, the southern part of China and Vietnam. It is also found in countries like Australia, and the African continent. In India and China as an herbal medicine practice the leaves of sylvestre are mostly used in several treatment regimens for conditions like diabetes, hypercholesterolemia, joint pain, and snake bites [35, 36]. The chemical constituents which are present in higher amounts within the leaves of G. sylvestre are gymnemic acids I-VII, conduritol IA, triterpenoid saponins (gymnemosides A-F and gymnemoside W1-2), and dihydroxy gymnemic triacetate. The active constituents that are pharmacologically active in the leaves are gymnemic acids, a class belonging to the oleanane-type triterpenoid saponins (gymnemosides A-F and gymnemoside W1-2), and dihydroxy gymnemic triacetate. The active constituents that are pharmacologically active in the leaves are gymnemic acids, a class belonging to the oleanane-type triterpenoid saponins (gymnemosides A-F and gymnemoside W1-2), and dihydroxy gymnemic triacetate. The active constituents that are pharmacologically active in the leaves are gymnemic acids, a class belonging to the oleanane-type triterpenoid saponins (gymnemosides A-F and gymnemoside W1-2), and dihydroxy gymnemic triacetate.

**Momordica charantia** (commonly called bitter melon or bitter gourd, *karela in hindi*, or balsam pear), is a creeper consisting of a tendril and comes under the family of Cucurbitaceae that is used in treating diabetes in China, India, South America, East Africa, and the Caribbean. The main constituents of charantia seeds are mostly eleostearic acid and stearic acid, which make up almost 45% of its entire weight. Apart from this, various glycosides, like charantin and vicine, have also been isolated from their stem and fruit. Polypeptide-p, lipids, triterpenoids, and alkaloids are also found in sufficient amounts in the plant. [32, 39]. T2DM patients have been found to be benefitted from the juice obtained freshly from its fruit, as it lowers the glucose. [40, 41], although the extract of the dried fruit is not so useful [42]. The ethyl acetate extract of M. charantia has shown activity in terms of stimulating peroxisome proliferator-activated receptors (PPAR α and γ) and also by regulating the countenance of the acyl CoA oxidase gene upon the H4IIEC3 hepatoma cells. The restriction of peroxidation and apoptosis causes the enhancements in the functioning of the β cell and also improvises the insulin release. In adipocyte cells, the glucose transporter-4 (GLUT4) triggered transport to the cell membrane and enhanced the action of adenosine monophosphate-activated protein kinase (AMPK), which also can increase the glucose uptake from the blood by momordicosides from M. charantia [43].

**Morus alba L.** (also known as the mulberry tree, *Shahtut in Hindi*) is found broadly in the Asian continent. With a wide variety of substituents for its leaves, Folium is more used clinically in Chinese ancient medicine as a hypoglycemic, hypotensive, and diuretic agent. Traditionally mori has been used to treat uncontrolled glucose levels in blood or hyperglycemic condition. The key pharmacologically active constituents are flavonoids, alkaloids (1 deoxynojirimycin), and polysaccharides [44, 45]. The extract of F. mori improved glucose uptake and consequently boost the translocation of GLUT-4. The possibilities of ameliorated adipocytokines extract in white adipose tissue is probably due to the constraining of oxidative stress. 1 deoxynorimycin, one of the alkaloidal...
contain has been found to be a powerful suppressor of α-glucosidase [46-49].

**Trigonella foenum-graecum L** (also known as fenugreek seeds, *Methi in hindi*), belongs to the family Fabaceae. Ancient Egyptians used the fenugreek seed as a traditional remedy and infiltrated it across Asian countries like India and China. These seeds contain a high amount of galactomannan, which is basically a polysaccharide and also known as a source of other chemical components like diosgenin, yamogenin, gitogenin, and tigogenin, which are basically saponins. It is also consisting of other pharmacologically active components like mucilage, volatile oils, alkaloids, and neotigogens [50-52]. An amino acid obtained, purified from fenugreek seeds known as 2S, 3R, 4S, and 4-hydroxy iso leucine, displayed positive feedback towards insulin release that enhanced the glucose uptake by peripheral organs in an In-vitro study [59–61]. A meta-analysis of foenum-graecum also revealed that the herb has the possibility to reduce HbA1C by 1.13% ($P = 0.03$) [67]. At the same time, it reduces the hepatic enzymatic activity (hexokinase, glucokinase, G6P, and fructose-1,6-bisphosphatase) and increases insulin activity which leads to a reduction in blood sugar levels [53-61].

**Radix rehmanniae** (Chinese medicine known as *Sheng Di huang*), is a root of the plant Rehmannia glutinosa Libosch, which belongs to the family Scrophulariaceae or It is used as a remedy for several diseases condition related to the blood, immune system, endocrine system, nervous system, and cardiovascular systems. Usually, it is prepared as a mixture of different herbs like R. ginseng, R. scutellariae, and R. astragali. These mixtures triggered the insulin release and β-cell rejuvenation by induction of insulin receptor substrate 2. The presumed mechanism of action are triggering insulin release, improving glucose metabolism, and constraining glycogen activity in hepatic cells [62-64].

**Stephania tetranda Moore** (Chinese medicine known as *Hang Fang Ji*), an herbaceous perennial creeper from the family of Menispermaceae, which is a very essential herb used in the Chinese herbal system for the purpose of decreasing inflammation and as a pain reliever (analgesic). The hypothesized anti-hyperglycemic action of tetrandra extract is the provocation of insulin secretion through β-cells in the pancreas [65, 66].

**Rhizoma coptidis** (Chinese name of *Huang Lian*), is a rhizomal part of Coptis chinensis Franch from the family known as Ranunculaceae. It is generally used in innumerable treatment counter to several clinical conditions like intestinal infections, diarrhea, swelling, hypertension, and hypoglycemia. It contains isoquinoline alkaloid and berberine. Berberine is considered for its antihyperglycemic effects. Berberine shows an anti-hyperglycemic effect by stimulating the AMPK pathway or inducing insulin receptor expression leads to enhancement of insulin sensitivity [67, 68].

**Radix astragali** (in Chinese *Huang Qi*), is a dehydrated root of a long-living herbs Astragalus membranaceus (Fisch.) Bunge and Astragalus mongholicus (Fabaceae) Bunge belongs to the family Leguminosae. The herb is usually found in northern parts of China. The main clinically active constituents in astragali are formononetin, calycosin, and ononin which are chemically classified under the categories of the isoflavones and isoflavonoids. It also contains saponins derivatives like stragaloside IV, astragaloside II, astragaloside I and acetylastragaloside. A saccharide known as astragaluspoly is involved in the improvement of the activity of insulin and diminishing the chances of fatty liver development [69, 70].

**Eriobotrya japonica Lindl** (Chinese name *Loquat*), belongs to the family Rosaceae. japonica dried leaves are also termed Folium eriobotryae. It is used for several disease management like chronic respiratory conditions like bronchitis, and dry cough. It was also found to be effective in the management of DM. The main chemical constituents identified are classified under a large variance of chemical entities like triterpenes, sesquiterpenes, and flavonoids. It also contains glycosides known as Megastigmmane and its derivative. Other polyphenolic derivatives like ursolic acid, oleanolic acid, cinchonain Ib, procyanidin...
- B-2, chlorogenic acid, and epicatechin are also identified. It generally works by stimulating insulin secretion [71-73].

- **Ginkgo biloba** (Chinese name *Maidenhair tree*), improved glucose metabolism by hepatic cells and peripheral muscle. It also plays a role in constraining the formation of atherogenic plaque, which further leads to atherogenesis, which is more often considered to be associated with comorbidities of patients with DM. An In-vitro assay concluded that the anti-hyperglycemic action of ginkgo is due to its suppressing effect upon activities of enzymes like α-glucosidase and amylase. Though in the case of T2DM individuals, oral administration of biloba extract displayed a significant reduction in insulin clearance which further helps the reduction of systemic insulin concentration to preserve the β-cells function and maintain peripheral insulin levels to control the high blood glucose. early use of G.biloba may facilitate endothelial activity in diabetic nephropathy without affecting blood glucose levels [74, 75].

- **Radix ginseng**, ginseng is often named depend up on its demographical occurrence like Asian ginseng, American ginseng, and Chinese ginseng. More than 700+ compounds are found in ginseng. Most of the active chemical constituents known are ginsenosides polysaccharides, peptides, and polyacetylenic alcohols [76]. Anti-hyperglycemic effects have been found more prominent in the case of lipophilic extracts than the aqueous R. ginseng extracts. The extract acted by triggering the insulin excretion from isolated cells of pancreatic islets. Vuksan al., have performed a series of human trials which provide confirmations of significant reduction of postprandial blood glucose (PPG), fasting blood glucose (FBG), and glycosylated hemoglobin (HbA1C) levels, which is an important parameter for the individual with DM and having a risk factor associated with renal impairment [77-79]. At the same time, it helped to reduce β-cell apoptosis by improving adipocytic PPAR-γ protein expression. It also reduces β-cell degeneration by upregulating adipocytic cellular gene known as PPAR-γ protein expression. R. ginseng improves glucose absorption by diminishing glucosidase activity [80,81]. Ginsenoside Rb1, one of the constituents has the ability to increase glucose transport by triggering the adipocyte differentiation by improving the PPAR-γ and C/EBP-α gene expression in adipocytic tissue. Ginsenoside Rb1 also possessed a synergistic affect along with modification in tissue-specific gene expression by increasing GLUT-4 movement to the cell wall which amplified glucose uptake from the systemic circulation by adipocytes [82, 23].

- **Fructus schisandrae**, in China it is well known as “five-flavor berry”. It is considered a rich source of lignans and gomisins. The lignans are such as schizandrins (schizandrin A) whereas gomisins are of three types gomisin A, J, and N. A subtype of gomisins called angeloymomisin H is also present as a chemical constituent. It also contains polysaccharides. It has been seen that the basal glucose metabolism by immortalize HepG2 cells obtained from hepatic carcinoma cells of a 15 year old Caucasian male is facilitated by gomisins N and schizandrin A [84]. Other schizandrin were also found which are also having the ability to avert β-cell degeneration and improve insulin sensitivity [85]. The main imagined mechanisms are (i) the triggering the insulin release, (ii) improved insulin sensitivity, (iii) reducing insulin resistance, (iv) improved PPAR-γ activity, and (v) inhibiting the enzyme called aldose reductase schisandrae can also improve glucose homeostasis [86].

- **Pueraria lobata** is also known as It is a dried root of Pueraria lobata (Willd.), Belonging to the family Leguminosae. The vine is frequently found in a native portion of Southeast Asia and is known by different names like yegen, kudzu root, etc. The main chemical constituent in P. lobata is puerarin which has the ability to increase the glucose uptake in a dose-dependent manner in a clinical trial with high glucose-treated preadipocytes [87]. A chemical constituent known as Puerarin facilitates insulin-induced preadipocyte differentiation. The purarin also caused increased mRNA expression upon the PPARY gene of adipocyte cells, which helps to control several mechanisms like g

- glucose homeostasis by uptaking glucose from the systemic circulation, adipocyte glucose intake, and lipid absorption [88].
Cornus officinalis, usually found in several parts of Asia like China, Japan, and Korea, belongs to the family Cornaceae. The main chemically active constituents are iridoid glycosides, morroniside, loganin, mevaloside, loganic acid, ursolic acid, oleanolic acid, 5-hydroxymethyl-2-furfural, and 7-O-galloyl-D-sedoheptulose. Fructus corni ethanolic extract stimulated the GLUT-4 transporter in the cell wall by triggering the regeneration of pancreatic islets cells which further leads to improved insulin excretion. Another active constituent known as ursolic acid signaled an inhibitory response toward protein tyrosine phosphatase (PTP) 1B, which improves the sensitivity of insulin towards cells. The stated mechanisms include several pathways like suppression of glucosidase enzyme, reducing the gene modulated hepatic gluconeogenesis, protecting the β-cells against toxicity, and improvement of insulin release [89,90].

Barringtonia racemose (in Hindi Hijjal), is an evergreen mangrove tree that grows in the delta region of Padma river in Bangladesh, the west and east coastal area especially the Bay of Bengal (Sundarban) of India, and Sri Lanka. Several di and tri-terpenoids are found in racemosa extract. The main chemical constituent was found to be a pentacyclic triterpenoid chemically known as bartogenic acid. The hexane and alcoholic extracts including pure bartogenic acid suppressed the intestinal α-glucosidase activity [91].

Syzygium cumini (L.) Skeels (Jamun in Hindi), is a tree found in the tropical region of India, China, and Indonesia. Depending upon demographical variances Skeels is also well known by different names like Eugenia jambolana, Jamun, Jambu, Black Plum, or Black Berry. In countries like India and Brazil, cumin is used very frequently as a common remedy in the management of T2DM. It showed significant depletion in glycemic levels especially PPG as well as LDL, and free fatty acids. The extracts of S. cumini exhibit the ability to inhibit α-glucosidase activities. On the other hand, significant reduction of enzymatic activities in the liver by glucokinase and phosphofructokinase, which have a major character in glucose digestion in cases of DM [92, 93].

Tinospora cordifolia (guduchi, giloy) falls under the family Menispermaceae. It is a juicy climbing plant. The abundance of this plant was found in tropical areas of Indian subcontinent countries like India, Bangladesh, Myanmar, and Srilanka. The primary bioactive constituents identified are alkaloidal derivatives like palmatine, jatrorrhizine, and magnoflorine. It also contains glycoside and its derivative including di-terpenoid lactones, sesquiterpenoid, steroids, phenolics, aliphatic compounds, and polysaccharides. cordifolias has been found to benefit diabetic neuropathy when taken at a dosage of 400 mg/kg body weight. The anti-hyperglycemic effect is often due to the reduction of the formation of thiobarbituric acid-reactive constituents to release oxidative stress. The extract of this plant also enhances the manifestation of thioredoxin and glutaredoxin. The extract of this plant also helps in the regulation of carbohydrate metabolism and decreases gluconeogenesis through the inhibition of G6P and fructose1, and 6-diphosphatase. There are other different ways that are found to increase insulin release and also blockα-glucosidase [94, 95].

Ocimum basilicum, (Tulsi in hindi) is commonly known as basil, or sweet basil is a herb used in cooking and falls under the family Lamiaceae (mints). The primary constituents of basil contain apigenin, linalool, and ursolic acid, that often showed various anti-viral actions. Basil improvised lipid metabolism. The ethanolic extract of basil decreased cholesterol production too. It is advised that basilicum can be used in the case of dietary therapy in minor to moderate T2DM [94, 96].

Berberis aristate, in India, is also known as Zarshik, Daruharidra. It belongs to the family Berberidaceae. It is also a traditional herb that has been used since ancient times in South Asia mostly in the form of herbal decoction to enhance the liver and heart functionalities. The prime ingredients from the root are found to be berberine, berbamine, and also palmatine. The root of aristateextract shows a good possibility to control glycemic homeostasis by reducing gluconeogenesis by hepatic cells and also by constraining oxidative stress. B. aristate plant helps to enhance the glucokinase activity which helps glucose break down to glucose-6P.
and reduced the Glucose 6-P dehydrogenase activity for further metabolism. B. aristate extract and S. marianum extract synergistic action in fatalities who have conditions like sub-optimal glycemic control, impaired basal insulin, high HbA1C, insulin resistance, uncontrolled amount of total and also low-density lipoprotein cholesterol, and triglycerides were prominently decreased after the 90-day treatment with [94, 97, 98].

Few other Indian herbs which are also used for the prevention and management of Diabetes Mellitus are discussed in Table- 2 along with their mechanism of action

Table-2 Other Indian herbs which show antidiabetic activities [99]

<table>
<thead>
<tr>
<th>Plant name</th>
<th>Common name</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annona squamosa</td>
<td>Sugar apple</td>
<td>Ethanol leaf extract of the leaves displays hypoglycemic and anti-hyperglycemic activities and Improves the plasma insulin level.</td>
</tr>
<tr>
<td>Areca catechu</td>
<td>Supari</td>
<td>Hypoglycemic effect</td>
</tr>
<tr>
<td>Boerhavia diffusa</td>
<td>Punarnava</td>
<td>Intensify the activity of hexokinase, constraining the activity of glucose-6- phosphatase and fructose bis-phosphatase, surge the plasma insulin concentration, and also impart an anti-oxidant activity.</td>
</tr>
<tr>
<td>Bombax ceiba</td>
<td>Semul</td>
<td>Glucose lowering effect</td>
</tr>
<tr>
<td>Butea monosperma</td>
<td>Palasa</td>
<td>Glucose lowering effect</td>
</tr>
<tr>
<td>Camellia sinensis</td>
<td>Tea</td>
<td>Glucose lowering activity imparts an anti-oxidant activity.</td>
</tr>
<tr>
<td>Emblica officinalis</td>
<td>Amla, Dhathriphala, “Triphala”</td>
<td>Diminishes peroxidation of lipid, acts as an anti-oxidant, blood glucose-lowering effect.</td>
</tr>
<tr>
<td>Ipomoea batatas</td>
<td>Sakkargand</td>
<td>Declines insulin resistance.</td>
</tr>
<tr>
<td>Musa sapientum</td>
<td>Banana</td>
<td>Anti-hyperglycemic, antioxidant effect.</td>
</tr>
<tr>
<td>Punica granatum</td>
<td>Anar</td>
<td>Antioxidant, anti-hyperglycemic effect.</td>
</tr>
<tr>
<td>Swertia chirayita</td>
<td>Chirata</td>
<td>Triggersinsulin secretion from the pancreas.</td>
</tr>
<tr>
<td>Terminalia belerica</td>
<td>Behada, a constituent of “Triphala”</td>
<td>Antibacterial, hypoglycemic</td>
</tr>
<tr>
<td>Withania somnifera</td>
<td>Ashwagandha or winter cherry</td>
<td>Glucose lowering effect, as an effective diuretic and constraining the high lipid concentration.</td>
</tr>
</tbody>
</table>

**Marketed diabetes formulation in India:**

There are several herbal formulations for diabetes management (refer to Table 2) that are already available in the Indian market. These herbal formulations are used more often by the individuals associated with DM as directed by physicians. Below is the table the components of each formulation are enlisted.

**Table-3: Marketed formulation of herbal mixture in India and their mechanism of action [99].**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Company</th>
<th>Composition</th>
<th>Mechanism of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic tonic 180 HP</td>
<td>Ayurvedic herbal supplement</td>
<td>Vijaysar (P. marsupium), Gurmar (G. sylvestre), Karela (M. charantia), Jamun (S. cumini), Methi(T. foenum graceum), Neem (A. indica), Gular (F. racemose), Bael (A. marmelos), Tjapata (C. tamala)</td>
<td>As a dietary supplement.</td>
</tr>
<tr>
<td>Ayurveda alternative herbal formula for Diabetes</td>
<td>Chakrapani Ayurveda</td>
<td>Gurmar, Karela, Pushkarmool (I. racemose) Jamun Gutli (S. cumini) Neem (A. indica) Methi (T. foenum gracecum), Guduchi (T. cordifolia)</td>
<td>Gurmar trigger insulin release and reduce blood sugar level. It possesses the ability to block the sweet taste buds if applied to the tongue in diabetic patients to avoid glycosuria. Act as a cardiotoxic. Act as a diuretic. Help to improve metabolic events that occur in hepatic cells, renal tissues, and skeletal muscles.</td>
</tr>
<tr>
<td>Bitter gourd Powder</td>
<td>Garry and Sun natural Remedies</td>
<td>Karela (M. charantia)</td>
<td>It lowers blood &amp; urine sugar levels. Anti-hemorrhoidal helped in protein precipitation (astringent), improved digestion, improve the sexual problem, improve hepatic activity, act as an anthelmintic, and also helped in blood purification.</td>
</tr>
<tr>
<td>Dia-care</td>
<td>Admark Herbs Limited</td>
<td>Sanjeevan Mool; a mixture of Kali harad (black Hime), Jamun beej, Kadu/chirota (A. Paniculate), Namejav, Neem chal powder (A. indica)</td>
<td>Lowering blood &amp; urine glycemic levels.</td>
</tr>
<tr>
<td>Diabetes Daily Care</td>
<td>Nature’s Health Supply</td>
<td>α-Lipoic Acid, 4% Cinnamon Extract, Chromium picolinate (chromax®), Vanadum, 50% Fenugreek seed extract, 25% alcoholic extract of Gymnema sylvestre, 7% alcoholic Momordica extract, 20% ethanolic extract of Licorice Root</td>
<td>Exhibited insulinotropic effects that enhanced the peripheral glucose uptake</td>
</tr>
<tr>
<td>Epinsulin</td>
<td>Swastik Formulations</td>
<td>Vijaysar (P. marsupium)</td>
<td>Mechanism not disclosed</td>
</tr>
<tr>
<td>Diabecure</td>
<td>Nature beauté santer</td>
<td>Common walnut (J. regia), Common berry (B. vulgaris), Common centaury (C. erytharea), Yarrow (Millefolium), Boudi/Baran (T. officinale)</td>
<td>It helps to provide comfort from the conditions like normal cold associated with weakness, leg pain, and lethargy. Also, help in the case of multi urination (polluna) and hypersensitivity reaction like pruritus.</td>
</tr>
</tbody>
</table>
In the current scenario, an urge to know about herbal treatments were engraved in their marks as one of the most accepted methods to manage and treat several physiological conditions including DM. In this current scenario, an urge to know about herbal treatments were engraved in their marks as one of the most accepted methods to manage and treat several physiological conditions including DM. As an anti-hyperglycemic agent, Act as potent immunomodulators, Imparts a lipid-lowering effect, is an anti-depressant, and possesses hepatoprotective activity. Help to improve the sensitivity of oral hypoglycemic agent while used as an adjuvant.

### Discussion and Conclusion

Herbal treatments were engraved in their marks as one of the most accepted methods to manage and treat several physiological conditions including DM. In the current scenario, an urge to know about herbal treatments were engraved in their marks as one of the most accepted methods to manage and treat several physiological conditions including DM.

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