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HERBAL APPROACHES TO GLYCEMIC CONTROL: AN IN-DEPTH REVIEW OF MEDICINAL PLANTS AND THEIR BIOACTIVE COMPONENTS - ROLE OF MEDICINAL PLANTS AND THEIR ACTIVE COMPOUNDS ON GLYCEMIC CONTROL

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Abstract

Diabetes mellitus is a chronic metabolic disorder characterized by insulin deficiency and resistance. The two main types are Type-1 and Type-2 diabetes. According to the International Diabetes Federation (IDF), over 90% of diabetes cases globally are Type-2, projected to rise from 6.4% to 7.7% of the population by 2030. Diabetes is managed using both pharmacological and non-pharmacological treatments, with genetic and environmental factors being the primary causes of Type-2 diabetes. Herbal medicines are often recommended due to their affordability and minimal side effects. However, integrating herbal medicine into modern medical practices is challenging due to insufficient clinical data on their safety, efficacy, and drug interactions. This review concludes that most anti-diabetic medicinal plants lower blood glucose levels by stimulating insulin secretion from pancreatic beta-cells, altering specific hepatic enzymes involved in glucose metabolism, and/or reducing intestinal glucose absorption. The review includes information on readily available and easy-to-prepare herbal remedies. These herbal treatments have shown significant anti-diabetic effects with minimal side effects, making them a preferable alternative to synthetic drugs to avoid severe and adverse effects.

Keywords: Diabetes, Herbal Drugs, Medicinal Plant, Antidiabetic Drug, Polyherbal, Traditional Medicine.

1. INTRODUCTION

An irregular breakdown of carbohydrates leads to a long-term metabolic disorder known as diabetes mellitus., which is exacerbated by variables like insulin insufficiency and/or insulin resistance (1). In general, there are 2 primary forms of diabetes: T1D (Type-1 Diabetes), often named as insulin-dependent DM (Diabetes Mellitus), and T2D (Type-2 Diabetes), also named as non-insulin-dependent diabetic mellitus. Individuals diagnosed with T1D have a substantial impairment in islet β-cell activity, leading to an insulin shortage, whereas insufficient insulin production and insulin resistance together characterize T2D (2). Nephropathy, retinopathy, dyslipidemia, and cardiovascular disorders are among the most prevalent complications that both forms of diabetes eventually trigger in the body (2,3). Nonpharmacological and pharmacological therapies are the two main techniques used to treat diabetes mellitus. Diet therapy, exercise, acupuncture, hydrotherapy, and mineral supplements are examples of nonpharmacological interventions (4,5). Diabetes mellitus is traditionally controlled with insulin treatment and oral glucose-lowering agents, including meglitinides, thiazolidinediones, alpha-glucosidase inhibitors, biguanides, and

sulfonylurea (6–11). Another strategy that was considered is the use of immunosuppressive drugs to prevent autoimmune attacks (12,13). It was also attempted to transplant tissue preparations from islets of the pancreas (14). The use of synthetic medications to treat diabetes was linked to many adverse consequences, including nausea, vomiting, diarrhea, alcohol flush, headaches, edema, malignant anemia, and dizziness. Herbal medications are a better option because they have fewer negative effects and side effects than synthetic treatments. These medications are also employed in cases where chemical medications fail to treat a patient's illness. Natural herbs and fruit and vegetable extracts are included in herbal formulations, which help treat a variety of illnesses without having any negative side effects. Chemical medications, on the other hand, are made artificially and also have negative effects. These are safe, natural medications. Numerous clinical investigations have verified that extracts from medicinal plants exhibit anti-diabetic properties and restore the function of pancreatic β-cells (15).

2. PATHOPHYSIOLOGY OF TYPE 2 DIABETES MELLITUS [Fig. (1)]

DM is a chronic metabolic illness that has life-threatening impacts. The IDF (International Diabetes Federation) assesses that 285 million individuals worldwide, or 6.4% of the total population, had diabetes in 2010, and by 2030, that number is projected to increase to 439 million people worldwide, or 7.7% of the total population (16). Type 2 diabetes (T2D) affects more than 90% of diabetic people (17,18). Despite significant advances in scientific analysis of T2D as well as research and development of anti-diabetic medications, the cause of T2D remains unknown.

Epidemiological research reveals that environmental and genetic factors are the main causes of T2D. Impaired insulin production, insulin action, or both result from these two causes of insulin resistance as well as cell function decline. One of T2D's main pathogenic features is hyperglycemia, which is caused by this deficiency (19). This type of hyperglycemia is harmful to peripheral and cell tissues, a condition known as glucotoxicity, and it is clinically significant as a cause of diabetes-related problems like peripheral gangrene, neuropathy, retinal blindness, nephropathy and CVD (Cardiovascular Disease) (20). Therefore, the most popular therapeutic goal for individuals with type 2 diabetes is preserving glucose homeostasis. Proteins called hormones, such as insulin, regulate how the body breaks down proteins, fats, and carbohydrates (21). Pancreatic cells are the only known endocrine cells capable of producing insulin. When insulin resistance and increasing hyperglycemia coexist, T2D results in a decline in cellular function. This impairment may start early in the disease and intensify as T2D progresses due to compensatory overwork (22) . The condition recognized as insulin resistance appears when the body's cells become less receptive to insulin effects. Due to the combination of hereditary and environmental factors, insulin resistance usually appears years before type 2 diabetes (22). The following factors contribute to insulin resistance: excess food, adipose hypoxia, Oxidative stress/ER stress, systemic free fatty acids, adipose inflammation, and metabolic hormones (such as glucagon, adiponectin, and leptin) (23).

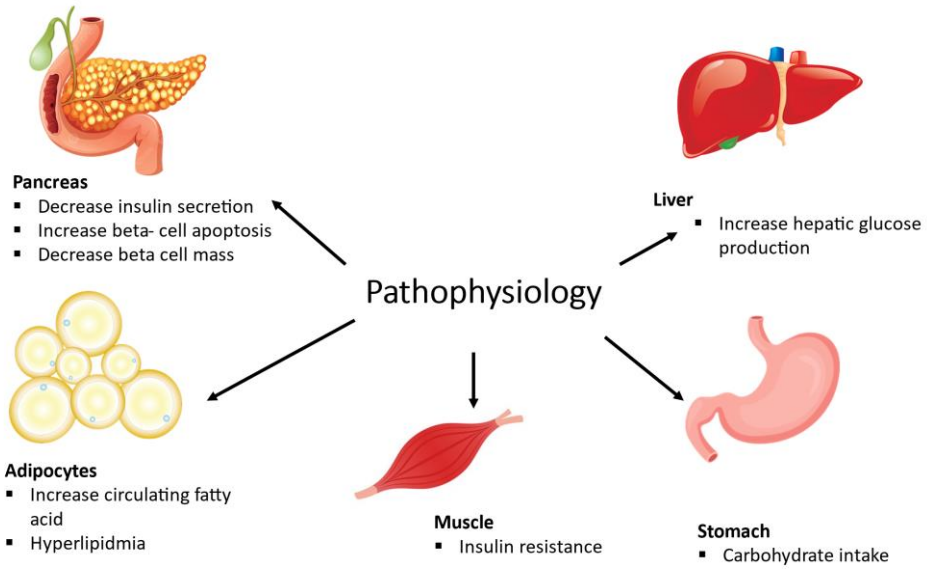

Fig (1): Pathophysiology of type-2 diabetes

3. PHARMACOTHERAPIES FOR DIABETES MELLITUS AND THE RELATED CHALLENGES

A malfunction in insulin action, secretion, or both causes type 2 diabetes. Consequently, T2D treatment has changed from monotherapy with insulin secretagogues, sensitizers, or insulin to combination therapy, which now includes sensitizers, incretin-based medications, insulin, and/or insulin secretagogues. These treatments' methods of action include GLP-1 secretion, insulin synthesis, and/or sensitization of the insulin receptor pathway (21).

Several medicines for T2D, such as OAAs (oral antidiabetic agents), insulin, as well as incretin-based therapies, were produced in the past to control blood homeostasis sugar by several methods (24). Sulfonylurea-type OAA medications, such as glimepiride and glibenclamide, are examples of insulin releasers that can directly stimulate pancreatic cells to generate insulin. Blood glucose levels drop as a result. On the other hand, these secretagogues cannot stop cell atrophy. On the other hand, biguanides like metformin and TZDs like rosiglitazone and pioglitazone are insulin sensitizers that can directly reduce blood glucose and insulin resistance.

One potential substitute strategy for reducing blood glucose levels is glucose reabsorption. The activity of glucosidases and sodium-glucose co-transporter-2 is decreased by Sglt 2 inhibitors, empagliflozin, dapagliflozin, and -glucosidase inhibitor, acarbose, respectively. This reduces the gut's and renal tubules' ability to absorb glucose reabsorption (25,26). Another cutting-edge class of diabetic treatments includes DPP-4 inhibitors (like sitagliptin, vildagliptin, linagliptin, and saxagliptin) and GLP-1 analogs (exenatide and liraglutide) (27).

In addition to these drugs, food, and lifestyle modifications are crucial for both preventing and treating T2D. However, existing diabetes medications are ineffective and have unwanted side effects (28). Insulin secretagogues, for example, are usually associated with hypoglycemia, weight gain, as well as the inability to protect cells from death (24,29). Weight gain and renal damage are side effects of TZDs and biguanides, respectively. Acarbose typically causes stomach distress. Diarrhea and farts are two

examples. In addition, a clinical study due to safety issues, Sglt 2, recently failed (25). Despite the many benefits of incretin-based medications, certain serious stomach problems such as indigestion, diarrhea, vomiting, nausea, belching, and sour stomach are still associated with these treatments, as depicted in Table 1 (26,30).

Table 1: Examples of synthetic medications for type 2 diabetes and their adverse effects. (30)

Serial Number	Synthetic drug	Action	Side effect
1	Metformin	Reduced hepatic glucose synthesis increases insulin sensitivity in the body.	Nausea, bloating, and abdominal pain.
2	Sulfonylureas	encourage the body to release more insulin.	Low blood sugar level, nausea, and weight gain.
3	Glinides (Biguanide)	Stimulate the pancreas to secrete more insulin.	Low blood sugar, kidney toxicity, and an increase in body weight.
4	Thiazolidinediones (Glitanide)	make the body's tissues more insulin-sensitive	Risk of CHF, bladder cancer, bone fracture, cholesterol.
5	DPP 4 inhibitors	Help to reduce sugar levels.	Risk of pancreatitis and joint pain.
6	SGLT 2 inhibitors	Inhibit the return of glucose is excreted in the urine.	Risk of amputation, bone fracture, vaginal yeast function, high cholesterol and urinary tract infection

4. HERBAL THERAPY FOR T2D

Medicinal plants were used long before modern Western medicine to cure a wide range of disease types (31). Modern Western medicine's focus on scientism as well as other complex factors has led to its dominance over "traditional" medical practices, such as herbal medicine systems.

Though herbal medical systems are sometimes misunderstood as unscientific and outdated, their extensive history demonstrates that they can compete with Western pharmaceuticals on some level. Medicinal herbs are still widely used in human healthcare and have never gone out of style. It has been stated that more than 1200 plants can treat diabetes (32,33).

More than 400 plants, 700 recipes, and chemicals were scientifically studied for the treatment of T2D (34). The present review centers on the scientific investigations of specific herbs and phytocompounds that lower blood sugar levels and their potential to address glucose reabsorption, incretin-related pathways, cell function, and insulin resistance.

Potential modes of action, phytochemistry, and antidiabetic bioactivities. The chosen compounds' and plants' modes of action are examined.

5. HERBS FOR DIABETES

Herbal remedies provide a long-term cure for patients' conditions, offering fewer side effects compared to synthetic drugs. The advantages of herbal remedies for diabetes mellitus have been schematically represented in Fig. (2).

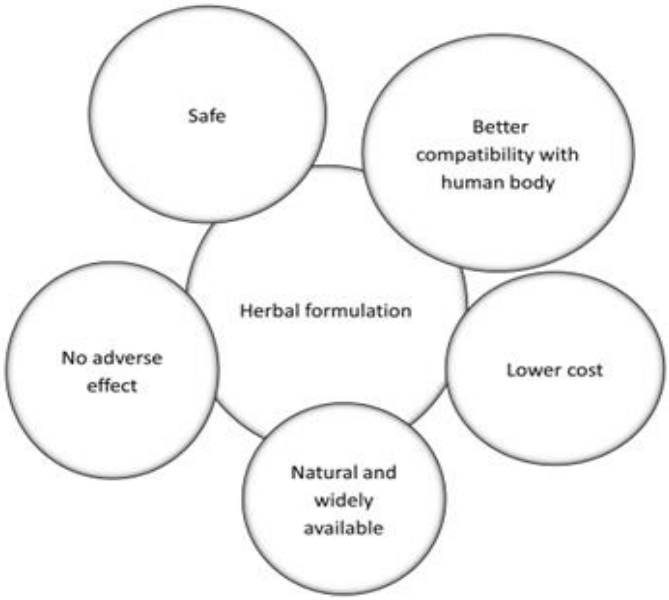

Fig (2): Advantages of utilizing herbal remedies

6. BENEFICIAL EFFECTS OF INDIAN MEDICINAL PLANTS AND THEIR PHYTOCHEMICALS WITH ANTIDIABETIC EFFECTS

The beneficial effects of the various Indian medicinal plants used for their antidiabetic effects have been described below (Table 2):

6.1 Amorfrutins and Licorice

Commonly employed in herbal treatment to treat a range of conditions, licorice is the common term for plants in the genus Glycyrrhiza. *G. uralensis* ethanol extract has been shown to reduce blood pressure, fat mass, and blood glucose in mice models (35). Additionally, there is PPAR activity in this extract. Moreover, it was shown that amorfrutins isolated from G. foetida bind to and activate the "peroxide proliferator-activated receptor" (PPAR), a critical participant in glucose as well as lipid metabolism. These compounds demonstrated the anti-diabetic effects of licorice and its active amorfrutins via the PPAR pathway by lowering fat weight, dyslipidemia, and blood glucose.

6.2 Dioscorea Polysaccharides and Dioscorea

Dioscorea extract has been shown in numerous trials to increase insulin sensitivity and glycemic control in diabetic animal models (36–39). The mechanism of action of Dioscorea extract against diabetes involves lowering insulin resistance through decreased phosphorylation of pS6K and ERK and increased phosphorylation of Akt and Glut4 (Glucose Transporter 4). In rats given a high-fat diet, Dioscorea extract lowered blood sugar levels.

6.3 Blueberries and Anthocyanins

It has been shown that blueberries (*Vaccinium* spp.) reduce diastolic and systolic blood pressure, and lipid oxidation as well as enhance insulin resistance, digestion, diabetes, and diabetic complications (36,37,39). Anthocyanins and phenolics were suggested as potential active ingredients for treating insulin resistance and diabetes. In one clinical investigation, Insulin resistance decreased more in T2D or obese people

who took 22.5 g of blueberries 2 times a day for six weeks than in those who received a placebo. The evidence supports blueberries' beneficial effects on metabolic syndrome (38).

6.4 *Acacia arabica* (Babhul)

It is mostly observed in India's natural environments. The extract from the plant works as an insulin secretagogue to prevent diabetes. In rats that have not been alloxanized, hypoglycemia is the outcome. Giving 2, 3, and 4 g/kg of powdered *Acacia arabica* seeds to normal rabbits caused a hypoglycemic effect because the pancreatic beta cells released insulin (40).

6.5 Aloe vera (*Aloe barbadensis*)

Popular indoor plant aloe has long been used as a multipurpose traditional medicine. The plant can be divided into two main categories: latex and gel. Aloe latex, commonly called "aloe juice", is a bitter-yellow liquid that appears just below the outer layer of leaves on pericyclic tubules. Mucilage, or leaf pulp, is what makes aloe vera gel. Aloe gum extracts significantly improve glucose tolerance in rats with normal and diabetes glucose tolerance (41). Rats with alloxanized diabetes demonstrated a hypoglycemic response when chronically treated with Aloe barbadensis leaf exudates, as opposed to a single dosage. A single and repeated administration of the bitter component of the same plant caused a hypoglycemic effect in diabetic rats. Stimulating the release and/or production of insulin from pancreatic beta cells is the bitter principle of aloe vera (42). Additionally, this herb enhances wound healing in diabetic rats and exhibits dose-dependent anti-inflammatory properties (43).

6.6 *Caesalpinia bonducella*

Caesalpinia bonducella is applied by the Indian tribal people to control their blood sugar levels. Ethanolic and aqueous extracts demonstrated substantial hypoglycemic activity in chronic type II diabetic rats. Additionally, the amount of glycogen in the liver increased as a result of these extracts' enhanced glycogenesis (44). Isolated islets' ability to produce insulin may be improved by 2 fractions: BM 170 B and BM 169. The aqueous along with 50% ethanolic extracts of Caesalpinia bonducella seeds demonstrated hypolipidemic and antihyperglycemic effects in rats with diabetes treated with STZ (Streptozotocin). The antihyperglycemic effects could be due to the suppression of glucose absorption (45).

6.7 *Capparis decidua*

It is widespread throughout India, particularly in dry areas. Alloxanized rats displayed hypoglycemia effects after three weeks of feeding 30 percent extracts of *C. decidua* (*Capparis decidua*) fruit powder. Furthermore, the lipid peroxidation that alloxan caused in the kidney, heart, and erythrocytes was substantially decreased by this extract. The levels of the enzymes catalase and superoxide dismutase were also found to be altered by *C. decidua*, reducing oxidative stress (46). *C. decidua* also showed hypolipidemic activity (47).

6.8 *Eugenia jambolana* (Indian gooseberry, Jamun)

In India, eugenia jambolana kernel decoction is a well-liked home treatment for diabetes. Blood glucose levels are lowered by the antihyperglycemic effects of lyophilized powder, and alcoholic and aqueous extracts. The degree of diabetes affects this differently. It shows a 73.51% drop in mild diabetes (plasma sugar greater

than 180 mg/dl), while it is decreased in intermediate diabetes (plasma sugar greater than 280 mg/dl) as well as severe diabetes (plasma sugar greater than 400 mg/dl) to 55.62 & 17.72% correspondingly (48). The jamun pulp extract indicated hypoglycemic effects in streptozotocin-induced diabetic mice within 30 minutes of injection; however, the jamun seed took 24 hours to reveal similar effects. Oral administration of the extract increased blood insulin levels in diabetic rats. Insulin production was observed to increase when plant extract was incubated with isolated Langerhans islets from both normal and diabetic mice. The extracts reduced the insulin activity in the liver and kidney (49).

6.9 Cinnamon

Both *Cassia* (*C. aromaticum*) and common cinnamon (*C. zeylanicum* and *Cinnamomum verum*) have a long history of use as flavorings in foods, beverages, and medications (50). In the past, people have used cinnamon to treat colds, headaches, diarrhea, wounds, and rheumatism (51). Numerous research have recently been conducted on the impacts of cinnamon on diabetes and metabolic syndrome (50). Studies have indicated that cinnamon decreases blood sugar levels by decreasing insulin resistance and enhancing hepatic glycogenesis. The phenolic components in cinnamon were suggested to be active agents in regulating insulin signaling. Researchers are studying this element of cinnamon extract as a potential antidiabetic medication. Regrettably, the specific molecular target of cinnamon as well as cinnamaldehyde remains unidentified.

6.10 Serotonin Derivatives and Safflower

In Korea and other Asian nations, safflower (*Carthamus tinctorius*) seeds are utilized as an herbal remedy for diaphoresis, constipation, trauma, and menstruation pain (52). In rats with alloxan-induced diabetes, safflower hydroalcoholic extract improved insulin production, demonstrating antidiabetic effects (53). It was demonstrated that two serotonin derivatives extracted from safflower seeds significantly reduced the activity of α-glucosidase in comparison to the positive control, acarbose (52).

6.11 Berberine

An isoquinoline alkaloid called berberine was initially discovered in Berberis vulgaris. This substance performs a variety of tasks, including suppressing cancer and reducing metabolic syndrome (54–56). In a mouse model of T2D, this drug reduced lipid peroxidation, enhanced insulin resistance, reduced hyperglycemia, and encouraged pancreatic beta-cell regeneration (57,58). As a result, it might be helpful for the T2D treatment as well as other kinds of diabetes. Berberine used in combination with other OAAs showed improved glycemic control compared to either therapy used alone. Notably, those who took berberine saw a moderate antidyslipidemic benefit (59).

6.12 *Coccinia indica*

For six weeks, diabetic patients received dried extracts of *C. indica* (*Coccinia indica*) at a dose of 500 mg per kg body weight. These extracts enhanced the activity of the enzymes glucose-6-phosphatase, LPL (lipoprotein lipase), as well as lactate dehydrogenase, all of which were decreased in untreated diabetics (47). Significant hypoglycemia was seen in alloxanized diabetic dogs after receiving 500 mg/kg of *C. indica* leaves orally, and both normal and diabetic dogs had higher glucose tolerance.

6.13 *Trigonella foenum-graecum* (Fenugreek)

In addition to being used as a dietary supplement, fenugreek seeds have a long history of usage in traditional medicine to induce labor, aid in digestion, boost metabolism, and improve overall health (31). A fenugreek seed extract has been shown to lower blood sugar levels in animal studies (60,61) . This plant's glucose-lowering actions lead to a decrease in insulin resistance. The key anti-diabetic ingredients in fenugreek are galactomannan, diosgenin, trigoneosides, as well as 4-hydroxyisoleucine. The processes of these chemicals are, however, poorly understood (62). One of these, diosgenin, was found to decrease adipocyte differentiation as well as inflammation, suggesting that it also reduced insulin resistance (63). As per clinical analysis, fenugreek increases insulin sensitivity, which regulates blood sugar (64).

6.14 *Ocimum sanctum* (Holy Basil)

It is frequently referred to as Tulsi. This herb has long been valued for its medicinal qualities. When an extract of *Ocimum sanctum* leaves was given in water, the blood glucose levels of both normal and alloxan-induced diabetic rats significantly decreased (65). Tulasi demonstrated notable hypolipidemic and hypoglycemic impacts in diabetic rats by decreasing total lipid levels, triglycerides, total cholesterol, total amino acids, uronic acid, and fasting blood glucose (66). Oral administration of plant extract (200 mg per kg) on days 15 and 30 of the study resulted in a drop in plasma glucose levels by about 9.06 and 26.4%, respectively, after 30 days. Additionally, this herb exhibited antistress, antibacterial, antifungal, antiviral, anticancer, and stomach antiulcer properties.

6.15 *Litchi chinensis* (Lychee)

An evergreen fruit tree. Chinese herbal medicine uses its seeds to treat a variety of illnesses, including pain and gastrointestinal problems. Lychee seed has recently been linked to anti-diabetic effects in both rats (67) and people (68). Inhibiting insulin resistance is how lychee seed extract works (69). Additionally, in T2D animal models, oligonol from lychee fruit demonstrated anti-oxidative action and hence safeguarded the kidney and liver (70,71).

6.16 *Carica papaya* and *Pandanus amaryllifolius*

In mice treated with streptozotocin (STZ), “the ethanol extracts of *C. papaya* and *P. amaryllifolius* decreased hyperglycemia (72). The histological staining data indicated that these extracts considerably promoted cell regeneration, as shown by reduced blood glucose levels. There are no known active components as of yet. However, it has been suggested that both plants' flavonoids, alkaloids, saponin, and tannin are phytochemicals with biological activity (72)

6.17 *Tinospora cordifolia* (Guduchi)

It is a large, deciduous shrub that is classified under the Menispermaceae family. It is smooth. Guduchi is widely available in India. Administering Tinospora cordifolia root extract orally to alloxan-induced diabetic rats for six weeks substantially lowered blood and urine glucose levels, and serum and tissue lipid levels. A drop in body weight was also stopped by the extract (73). For the treatment of diabetes mellitus, *T. cordifolia* is frequently used in Indian Ayurvedic medicine. When oral *T. cordifolia* root extract (aqueous) was administered to Alloxan induced diabetic rats, there was a significant decrease in blood glucose and brain lipids levels. When administered at a dose of 400

mg/kg, the aqueous extract significantly reduced hyperglycemia in several animal models. This impact, however, was equal to one insulin unit per kilogram. Rats given frequent doses of *T. cordifolia* alcoholic or aqueous extract indicated reduced blood glucose levels and enhanced glucose tolerance (54).

6.18 *Phyllanthus amarus* (Bhuiawala)

This herb belongs to the Euphorbiaceae family and can reach a height of 60 cm. It is frequently recognized as Bhuiawala. It is spread widely in India's arid regions, mainly the Deccan, Konkan, and southern Indian states. It is commonly used in the treatment of diabetes. The methanolic extract of Phyllanthus amarus exhibited strong antioxidant activity. This extract also decreased blood sugar levels in rats" with diabetes who had been treated with alloxan (74). The herb also has anti-inflammatory, anti-carcinogenic, anti-mutagenic, as well as anti-diarrheal effects.

6.19 Capsaicin and Chili Pepper

Chili peppers are a type of fruit produced by Capsicum plants, and they are frequently consumed and used medicinally. Affecting beta cells, chili pepper extract has an insulinotropic effect (75). In 3T3-L1 preadipocytes, capsaicin, a hot pepper component, activates AMPK (76). According to the study, chili peppers and the chemicals in them stop type 2 diabetes by controlling insulin resistance and maybe beta cells. The application of capsaicin to T2D treatment, however, remains controversial. The reduction of insulin secretion may be how capsaicin causes T2D (77). Therefore, caution should be exercised when using capsaicin for T2D treatment.

6.20 *Gymnema sylvestre*

For decades, *G. sylvestre*, a medicinal herb of India, was applied to cure diabetes. It has been demonstrated that *G. sylvestre* extract lowers blood sugar. In rodents, it acts through insulin secretion and the regeneration of pancreatic β cells (78,79). In T2D patients, *G. sylvestre* reduced blood glucose concentrations and improved plasma insulin and C-peptide levels (80) . By regulating β-cell activity, this plant shows its antidiabetic action.

6.21 *Allium cepa* (Onion)

Dried onion powder contains specific ether-soluble and insoluble components that exhibit anti-hyperglycemic properties in diabetic rabbits. SMCS (S-methyl cysteine sulphoxide) at a dose of 200 mg per kg for 45 days, a sulfur-comprising amino acid obtained from Allium cepa, was given to alloxan-induced diabetic rats. This led to notable regulation of serum and tissue lipid levels, along with the normalization of glucose 6-phosphatase, liver hexokinase, as well as HMG Co-A reductase activities (81,82). Levels of post-prandial glucose were dramatically lowered in diabetic patients when they received a single oral dosage of 50 g of onion juice (83).

Table 2: Some plant-derived products for diabetes mellitus

Scientific Name	Common Name	Active Compound	Mechanisms Of Actions	References
AEGLE MARMELOS	Bael	Marmelosin	Enhance the functional state of pancreatic β- β-cells	(84)
ALLIUM CEPA	Onion	Dipropyl disulphide oxide	Stimulating the impacts on glucose utilization and antioxidant enzyme	(85)

ANDROGRAPHIS PANICULATA	Kalmegh	Kalmeghin	Increases glucose utilization and lower plasma glucose	(86)
ANNONA SQUAMOSA	Sharifa	Liriodenin, moupinamide	Improve glucose tolerance	(87)
BRASSICA JUNCEA	Mustard	Sulforaphane	Increase activity of glycogen synthetase	(88)
CAJANUS CAJAN	Arhar	2'-2'methylcajanone, isoflavones, cajanin cahanones	Significant reduction in serum glucose level	(89)
CATHARANTHUS ROSEUS	Vinca	Catharanthaine, vincristine, vinblastine	Lowering of glycemia	(87)
CURCUMA LONGA	Turmeric	α-phellantrene, tripinolene	Reduces blood sugar levels, enhances glucose metabolism, and boosts insulin effectiveness.	(90)
FICUS BENGALENSIS	Bargad	Leucodelphinidin	Promotes insulin secretion from β-cells.	(91)
MANGIFERA INDICA	Mango	β-carotene, α-carotene	Decrease in the absorption of glucose in the intestines	(92)
MUSA PARADISIACAL	Banana	β-Sitosterol, Leucocyanidin, Syringin	Lower blood glucose as well as glycosylated hemoglobin levels while increasing total hemoglobin.	(89)
PUNICA GRANTUM	Pomegranate	Punicalagin, punicalin	Decrease of glycemia	(93)
SWERTIA CHIRATA	Chirata	Methyl swertianin	Decrease blood glucose levels	(94)
TERMINELIA ARJUNA	Arjuna	Arjunic acid, arjunolic acid	Lower blood glucose levels and reduce G6P activity.	(95)
TINOSPORA CARDIFOLIA	Gulvel	Tinosporone, tinosporic acid	Reduction in blood sugar levels and brain lipids	(90)
TRIGONELLA FOENUM	Methi	4- hydroxy isoleucine	Enhance insulin production, lower insulin resistance, and reduce blood sugar levels.	(95)
ZINGIBER OFFICINALIS	Sunth	Gingerol, shogaol	Increases insulin level	(96)
HIBISCUS ROSA-SINESIS	Gudhal	Gossypetin, hibiscetin,	Stimulates the secretion of insulin from pancreatic beta cells	(97)

7. HERBAL MARKETED FORMULATIONS OF DIABETES MELLITUS

Presently, the Indian market offers a wide range of polyherbal formulations that are utilized in various forms to treat diabetes, including Vati, Churna, Arkh, and Quath. These combinations may involve powders or aqueous extracts of different plant parts that are used to treat diabetes.

As recommended by their doctors, diabetic individuals make use of the several formulations available on the market. Himalaya's Diabecon is said to boost hepatic and muscle glucagon contents, boost c peptide levels, support B cell regeneration and

repair, and improve peripheral glucose utilization. It guards B cells from oxidative stress and has antioxidant qualities. Reducing glycated hemoglobin levels, bringing microalbuminuria back to normal, and adjusting lipid profiles are how it mimics the effects of insulin. Diabetic problems in the long run are reduced.

The active component in Epinsulin, a product sold by Swastik Formulations, is epicatechin, a benzopyran molecule. Epicatechin raises the cAMP level of the islet, leading to an increase in insulin release. It enhances the action of cathepsin, facilitating the conversion of proinsulin to insulin. It treats neuropathy, retinopathy, and problems with the metabolism of fats and carbohydrates. It preserves the integrity of every organ system impacted by the illness.

Powdered bitter gourd sold by Sun and Garry. It brings down urine and blood sugar levels. It also cleanses the blood as well as strengthens the body's defenses against illnesses. The bitter gourd has several beneficial therapeutic properties. In addition to being laxative, it has antidotal, antipyretic, tonic, stomachic, and antibilious properties. Native African and Asian medicines also make use of the bitter gourd. Bitter gourd is specifically utilized in conventional medicine for the treatment of diabetes. The substance contains p-insulin, sterols, polypeptides, free acids, oils, phenolics, alkaloids, saponins, bitter glycosides, and 17 amino acids, such as methionine. Some of its purported advantages include blood purifier, anthelmintic, emmenagogue, stomachic, astringent antihaemorrhoidal properties, and hypoglycemic effect. (98)

Extracts of fenugreek seeds that have germinated are included in Plethico Laboratory's Syndrex product. For more than a millennium, fenugreek has been a part of conventional recipes. In addition to numerous other advantages, it exhibits antidiabetic activity. DIABETA is known for its powerful immunomodulator, antihyperlipidemic, anti-stress, and plant-based hepatoprotective properties. DIABETA is an Ayurvedic Cure formulation that is available in capsule form. It prevents diabetes. The formulation of Diabeta is derived from traditional Ayurvedic references and has been corroborated by contemporary research and clinical testing. Diabetes effectively regulates the variables and processes involved in diabetes mellitus through many mechanisms at different sites. It discusses the various factors that lead to diabetes and resolves the deteriorating effects caused by the illness.

Nature's Health Supply's Diabetes-Daily Care is a special all-natural formula that efficiently and safely enhances sugar metabolism. Type 2 diabetics were the target audience for the formulation of Diabetes Daily CareTM, which includes all-natural components. (99)

8. SAFETY OF HERBAL MEDICINES

Herbal items are generally thought to be extremely safe to eat. The majority of earlier trials did not track side effects, which explains this. We are aware of the nephropathy caused by Aristolochia in Chinese herbs used to treat obesity. Ginseng is one antidiabetic that can raise blood pressure, induce anxiety, and induce insomnia. It can cause vaginal bleeding and breast pain because of its estrogenic properties. A coumarin-like substance found in garlic, fenugreek, cinnamon, and ginger may enhance the tendency to bleed. Also, aloe can extend the bleeding period (100). Therefore, if the patient is on anticoagulants or is scheduled for surgery, these products need to be discontinued. In addition to these, fenugreek might result in itchiness and puffiness on the face. It may interfere with the absorption of other

medications due to its mucilage content. It is not recommended to consume bitter melon or fenugreek when pregnant (101). Neem products, on the other hand, have contraceptive properties (102). Herbal goods are derived from nature, in contrast to allopathic medications. For biological standardization and toxicological evaluation, bioassays must be created. Heavy metal levels in a variety of ayurvedic items are frequently detected to be well beyond allowable limits (103). Before utilizing them, all of these must be taken into account.

9. CHALLENGES OF HERBAL MEDICINES IN INDIA

Although herbs have therapeutic value, there are some arguments made against them. These include the need for consistency, the fact that patients are not prescribed a specific amount of medication, the fact that doses are not given strictly on time, the fact that the manufacturing process is not standardized, and the presence of variable amounts of the active ingredients. The issue at hand is how to prepare these herbal drugs to overcome the criticisms mentioned above and compete with pharmaceutical medicines. It will require extensive research that separates and classifies the active ingredients found in therapeutic plants; It is necessary to look for alternative medicinal approaches by studying the plant kingdom and evaluating their potential through related studies (104,105).

10. FUTURE ASPECTS OF HERBAL REMEDIES FOR DIABETES MELLITUS

Herbal drugs are increasingly used in healthcare, particularly in developing countries, where 80% of rural populations rely on conventional remedies. However, there is a growing interest in herbal drugs in developed countries, particularly for self-medication. New active medicines extracted from plants have shown more effectiveness in treating diabetes compared to oral hypoglycemic agents. The discovery of plants that may be beneficial to humans and have anti-diabetic properties has gained attention in recent years. Additionally, it could offer proof that a novel oral medication for the management of diabetes mellitus is getting better(106).

11. CONCLUSION

In today's world, diabetes mellitus is a major problem. Daily conditions and lifestyle choices largely cause these kinds of critical issues. Based on the available data, a significant number of individuals have type 2 diabetes mellitus. Because of this, treatments created using the tenets of allopathic Western medicine have excellent clinical and pharmacological activity in diabetic patients but also show little efficacy, a greater risk of side effects, and are excessively expensive. Thus, it is necessary to inform those who suffer from type 2 diabetes mellitus about the use of herbal preparations that have antidiabetic properties to treat this condition. The patient should frequently use herbal medicines because of their low cost and low side effects. This study research concludes that the majority of anti-diabetic medicinal plants function by either enhancing insulin secretion from pancreatic beta-cells, altering certain hepatic enzymes related to glucose metabolism, or decreasing intestinal glucose absorption to reduce blood glucose levels. This review paper contains information on herbal preparations that are readily available and easy to make. The herbal medications and their preparation covered in this review have demonstrated strong anti-diabetic effects with few side effects. Therefore, Herbal medications are preferred over synthetic drugs to avoid significant side effects and adverse effects.

List of Abbreviations

DM : Diabetes Mellitus

OAAS : Oral Antidiabetic Agents

CVD : Cardiovascular Disease

GLP-1 : Glucagon-like Peptide-1

DPP-4 : Dipeptidyl Peptidase-4

T1D : Type-1 Diabetes

T2D : Type-2 Diabetes

Consent For Publication

Not applicable. The study does not contain data from any person.

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References

1) Ozkol H, Tuluce Y, Dilsiz N, Koyuncu I. Therapeutic potential of some plant extracts used in Turkish traditional medicine on streptozocin-induced type 1 diabetes mellitus in rats. J Membr Biol. 2013;246:47–55.

2) Deshpande AD, Harris-Hayes M, Schootman M. Epidemiology of diabetes and diabetes-related complications. Phys Ther. 2008;88(11):1254–64.

3) Ghorbani A, Varedi M, Hadjzadeh MAR, Omrani GH. Type-1 diabetes induces depot-specific alterations in adipocyte diameter and mass of adipose tissues in the rat. Exp Clin Endocrinol diabetes. 2010;442–8.

4) Schlichtmann J, Graber MA. Hematologic, electrolyte, and metabolic disorders. Fam Pract Handbook 3rd ed St Louis, Missouri Mosby-yearb Inc. 1997;192–251.

5) Hooper PL. Hot-tub therapy for type 2 diabetes mellitus-Reply. N Engl J Med. 2000;342(3):218–9.

6) Bastaki S. Diabetes mellitus and its treatment. Int J Diabetes Metab. 2005;13(3):111–34.

7) Garg MK. Current perspective in insulin therapy in the management of diabetes mellitus. J Indian Med Assoc. 2002;100(3):194–5.

8) Rang HP, Dale MM, Ritter JM, Moore PK. The endocrine pancreas and the control of blood glucose. Pharmacology. 1991;4.

9) DeFronzo RA. Pharmacologic therapy for type 2 diabetes mellitus. Ann Intern Med. 1999;131(4):281–303.

10) Fuhlendorff J, Rorsman P, Kofod H, Brand CL, Rolin B, MacKay P, et al. Stimulation of insulin release by repaglinide and glibenclamide involves both common and distinct processes. Diabetes. 1998;47(3):345–51.

11) Kelley DE. Effects of weight loss on glucose homeostasis in NIDDM. Diabetes Rev. 1995;3(3):366–77.

12) Wright DC, Deol HS, Tuch BE. A comparison of the sensitivity of pig and human peripheral blood mononuclear cells to the antiproliferative effects of traditional and newer immunosuppressive agents. Transpl Immunol. 1999;7(3):141–7.

13) Knip M, Åkerblom HK. Environmental factors in the pathogenesis of type 1 diabetes mellitus. Exp Clin Endocrinol diabetes. 1999;107(S 03):S93–100.

14) Sutherland DER, Goetz FC, Sibley RK. Recurrence of disease in pancreas transplants. Diabetes. 1989;38(Supplement_1):85–7.

15) Gupta R, Bajpai KG, Johri S, Saxena AM. An overview of Indian novel traditional medicinal plants with anti-diabetic potentials. African J Tradit Complement Altern Med. 2008;5(1):1.

16) Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract. 2010;87(1):4–14.

17) Boyle JP, Engelgau MM, Thompson TJ, Goldschmid MG, Beckles GL, Timberlake DS, et al. Estimating prevalence of type 1 and type 2 diabetes in a population of African Americans with diabetes mellitus. Am J Epidemiol. 1999;149(1):55–63.

18) Attele AS, Zhou YP, Xie JT, Wu JA, Zhang L, Dey L, et al. Antidiabetic effects of Panax ginseng berry extract and the identification of an effective component. Diabetes. 2002;51(6):1851–8.

19) Laakso M. Insulin resistance and its impact on the approach to therapy of type 2 diabetes. Int J Clin Pract Suppl. 2001;(121):8–12.

20) Clements Jr RS, Bell DSH. Complications of diabetes: prevalence, detection, current treatment, and prognosis. Am J Med. 1985;79(5):2–7.

21) Leahy JL, Hirsch IB, Peterson KA, Schneider D. Targeting β-cell function early in the course of therapy for type 2 diabetes mellitus. J Clin Endocrinol Metab. 2010;95(9):4206–16.

22) Gianani R. Beta cell regeneration in human pancreas. In: Seminars in immunopathology. Springer; 2011. p. 23–7.

23) DeFronzo RA. From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus. Diabetes. 2009;58(4):773–95.

24) Krentz AJ, Bailey CJ. Oral antidiabetic agents: current role in type 2 diabetes mellitus. Drugs. 2005;65:385–411.

25) Jones D. Diabetes field cautiously upbeat despite possible setback for leading SGLT2 inhibitor. Nat Rev Drug Discov. 2011;10(9):645.

26) Egan JM, Bulotta A, Hui H, Perfetti R. GLP-1 receptor agonists are growth and differentiation factors for pancreatic islet beta cells. Diabetes Metab Res Rev. 2003;19(2):115–23.

27) Parkes DG, Mace KF, Trautmann ME. Discovery and development of exenatide: the first antidiabetic agent to leverage the multiple benefits of the incretin hormone, GLP-1. Expert Opin Drug Discov. 2013;8(2):219–44.

28) Howlett DHCS, Bailey CJ. A risk-benefit assessment of metformin in type 2 diabetes mellitus. Drug Saf. 1999;20:489–503.

29) Purnell JQ, Weyer C. Weight effect of current and experimental drugs for diabetes mellitus: from promotion to alleviation of obesity. Treat Endocrinol. 2003;2:33–47.

30) Adedapo AA, Ogunmiluyi IO. The use of natural products in the management of diabetes: The current trends. J Drug Deliv Ther. 2020;10(1):153–62.

31) Smith M. Therapeutic applications of fenugreek. Altern Med Rev. 2003;8(1):20–7.

32) Marles RJ, Farnsworth NR. Antidiabetic plants and their active constituents. Phytomedicine. 1995;2(2):137–89.

33) Habeck M. Diabetes treatments get sweet help from nature. Nat Med. 2003;9(10):1228–9.

34) Singh J, Cumming E, Manoharan G, Kalasz H, Adeghate E. Suppl 2: Medicinal chemistry of the anti-diabetic effects of Momordica charantia: active constituents and modes of actions. Open Med Chem J. 2011;5:70.

35) Mae T, Kitahara M, Nishiyama T, Tsukagawa M, Konishi E, Kishida H, et al. A licorice ethanolic extract with peroxisome proliferator-activated receptor-γ ligand-binding activity affects diabetes in KK-Ay mice, abdominal obesity in diet-induced obese C57BL mice and hypertension in spontaneously hypertensive rats. J Nutr. 2003;133(11):3369–77.

36) Grace MH, Ribnicky DM, Kuhn P, Poulev A, Logendra S, Yousef GG, et al. Hypoglycemic activity of a novel anthocyanin-rich formulation from lowbush blueberry, Vaccinium angustifolium Aiton. Phytomedicine. 2009;16(5):406–15.

37) Vuong T, Benhaddou-Andaloussi A, Brault A, Harbilas D, Martineau LC, Vallerand D, et al. Antiobesity and antidiabetic effects of biotransformed blueberry juice in KKAy mice. Int J Obes. 2009;33(10):1166–73.

38) Stull AJ, Cash KC, Johnson WD, Champagne CM, Cefalu WT. Bioactives in blueberries improve insulin sensitivity in obese, insulin-resistant men and women. J Nutr. 2010;140(10):1764–8.

39) Basu A, Lyons TJ. Strawberries, blueberries, and cranberries in the metabolic syndrome: clinical perspectives. J Agric Food Chem. 2012;60(23):5687–92.

40) Walia S, Dua JS, Prasad DN. Herbal Drugs with Anti-Diabetic Potential. J Drug Deliv Ther. 2021;11(6):248–56.

41) Al-Awadi FM, Gumaa KA. Studies on the activity of individual plants of an antidiabetic plant mixture. J Ethnopharmacol. 1988;22(3):315.

42) Ajabnoor MA. Effect of aloes on blood glucose levels in normal and alloxan diabetic mice. J Ethnopharmacol. 1990;28(2):215–20.

43) Davis RH, Maro NP. Aloe vera and gibberellin. Anti-inflammatory activity in diabetes. J Am Podiatr Med Assoc. 1989;79(1):24–6.

44) Chakrabarti S, Biswas TK, Rokeya B, Ali L, Mosihuzzaman M, Nahar N, et al. Advanced studies on the hypoglycemic effect of Caesalpinia bonducella F. in type 1 and 2 diabetes in Long Evans rats. J Ethnopharmacol. 2003;84(1):41–6.

45) Sharma SR, Dwivedi SK, Swarup D. Hypoglycaemic, antihyperglycaemic and hypolipidemic activities of Caesalpinia bonducella seeds in rats. J Ethnopharmacol. 1997;58(1):39–44.

46) Yadav P, Sarkar S, Bhatnagar D. Lipid peroxidation and antioxidant enzymes in erythrocytes and tissues in aged diabetic rats. Indian J Exp Biol. 1997;35(4):389–92.

47) Kamble SM, Kamlakar PL, Vaidya S, Bambole VD. Influence of Coccinia indica on certain enzymes in glycolytic and lipolytic pathway in human diabetes. Indian J Med Sci. 1998;52(4):143–6.

48) Sheela CG, Augusti KT. Antidiabetic effects of S-allyl cysteine sulphoxide isolated from garlic Allium sativum Linn. Indian J Exp Biol. 1992;30(6):523–6.

49) Achrekar S, Kaklij GS, Pote MS, Kelkar SM. Hypoglycemic activity of Eugenia jambolana and Ficus bengalensis: mechanism of action. In Vivo. 1991;5(2):143–7.

50) Qin B, Panickar KS, Anderson RA. Cinnamon: potential role in the prevention of insulin resistance, metabolic syndrome, and type 2 diabetes. J Diabetes Sci Technol. 2010;4(3):685–93.

51) Rafehi H, Ververis K, Karagiannis TC. Controversies surrounding the clinical potential of cinnamon for the management of diabetes. Diabetes, Obes Metab. 2012;14(6):493–9.

52) Takahashi T, Miyazawa M. Potent α-glucosidase inhibitors from safflower (Carthamus tinctorius L.) seed. Phyther Res. 2012;26(5):722–6.

53) Asgary S, Rahimi P, Mahzouni P, Madani H. Antidiabetic effect of hydroalcoholic extract of Carthamus tinctorius L. in alloxan-induced diabetic rats. J Res Med Sci Off J Isfahan Univ Med Sci. 2012;17(4):386.

54) Han J, Lin H, Huang W. Modulating gut microbiota as an anti-diabetic mechanism of berberine. Med Sci Monit Int Med J Exp Clin Res. 2011;17(7):RA164.

55) Vuddanda PR, Chakraborty S, Singh S. Berberine: a potential phytochemical with multispectrum therapeutic activities. Expert Opin Investig Drugs. 2010;19(10):1297–307.

56) Lau C, Yao X, Chen Z, Ko W, Huang Y. Cardiovascular actions of berberine. Cardiovasc Drug Rev. 2001;19(3):234–44.

57) Chen C, Zhang Y, Huang C. Berberine inhibits PTP1B activity and mimics insulin action. Biochem Biophys Res Commun. 2010;397(3):543–7.

58) Lee YS, Kim WS, Kim KH, Yoon MJ, Cho HJ, Shen Y, et al. Berberine, a natural plant product, activates AMP-activated protein kinase with beneficial metabolic effects in diabetic and insulin-resistant states. Diabetes. 2006;55(8):2256–64.

59) Dong H, Wang N, Zhao L, Lu F. Berberine in the treatment of type 2 diabetes mellitus: a systemic review and meta-analysis. Evidence-based Complement Altern Med. 2012;2012.

60) Pavithran K. Fenugreek in diabetes mellitus. J Assoc Physicians India. 1994;42(7):584.

61) Valette G, Sauvaire Y, Baccou JC, Ribes G. Hypocholesterolemic effect of fenugreek seeds in dogs. Atherosclerosis. 1984;50(1):105–11.

62) Puri D, Prabhu KM, Murthy PS. Mechanism of action of a hypoglycemic principle isolated from fenugreek seeds. Indian J Physiol Pharmacol. 2002;46(4):457–62.

63) Uemura T, Hirai S, Mizoguchi N, Goto T, Lee J, Taketani K, et al. Diosgenin present in fenugreek improves glucose metabolism by promoting adipocyte differentiation and inhibiting inflammation in adipose tissues. Mol Nutr Food Res. 2010;54(11):1596–608.

64) Gupta A, Gupta R, Lal B. Effect of Trigonella foenum-graecum (Fenugreek) seeds on glycaemic control and insulin resistance in type 2 diabetes. J Assoc Physicians India. 2001;49:1057–61.

65) Vats V, Grover JK, Rathi SS. Evaluation of anti-hyperglycemic and hypoglycemic effect of Trigonella foenum-graecum Linn, Ocimum sanctum Linn and Pterocarpus marsupium Linn in normal and alloxanized diabetic rats. J Ethnopharmacol. 2002;79(1):95–100.

66) Rai V al, Iyer U, Mani U V. Effect of Tulasi (Ocimum sanctum) leaf powder supplementation on blood sugar levels, serum lipids and tissues lipids in diabetic rats. Plant foods Hum Nutr. 1997;50:9–16.

67) Guo J, Li L, Pan J, Qiu G, Li A, Huang G, et al. Pharmacological mechanism of Semen Litchi on antagonizing insulin resistance in rats with type 2 diabetes. Zhong yao cai= Zhongyaocai= J Chinese Med Mater. 2004;27(6):435–8.

68) Zhang H, Teng Y. Effect of li ren (semen litchi) anti-diabetes pills in 45 cases of diabetes mellitus. J Tradit Chinese Med Chung i tsa chih ying wen pan. 1986;6(4):277–8.

69) Babu PS, Prabuseenivasan S, Ignacimuthu S. Cinnamaldehyde—a potential antidiabetic agent. Phytomedicine. 2007;14(1):15–22.

70) Noh JS, Park CH, Yokozawa T. Treatment with oligonol, a low-molecular polyphenol derived from lychee fruit, attenuates diabetes-induced hepatic damage through regulation of oxidative stress and lipid metabolism. Br J Nutr. 2011;106(7):1013–22.

71) Noh JS, Kim HY, Park CH, Fujii H, Yokozawa T. Hypolipidaemic and antioxidative effects of oligonol, a low-molecular-weight polyphenol derived from lychee fruit, on renal damage in type 2 diabetic mice. Br J Nutr. 2010;104(8):1120–8.

72) Sasidharan S, Sumathi V, Jegathambigai NR, Latha LY. Antihyperglycaemic effects of ethanol extracts of Carica papaya and Pandanus amaryfollius leaf in streptozotocin-induced diabetic mice. Nat Prod Res. 2011;25(20):1982–7.

73) Prince PSM, Menon VP. Hypoglycaemic and Hypolipidaemic Action of Alcoholic Extract of Tinospora cordifolia Roots in Chemical Induced Diabetes in Rats. Phyther Res. 2003;17(4):410–3.

74) Raphael KR, Sabu MC, Kuttan R. Hypoglycemic effect of methanol extract of Phyllanthus amarus Schum & Thonn on alloxan induced diabetes mellitus in rats and its relation with antioxidant potential. 2002;

75) Islam MS, Choi H. Dietary red chilli (Capsicum frutescens L.) is insulinotropic rather than hypoglycemic in type 2 diabetes model of rats. Phyther Res. 2008;22(8):1025–9.

76) Hwang JT, Park IJ, Shin JI, Lee YK, Lee SK, Baik HW, et al. Genistein, EGCG, and capsaicin inhibit adipocyte differentiation process via activating AMP-activated protein kinase. Biochem Biophys Res Commun. 2005;338(2):694–9.

77) Gram DX, Ahrén B, Nagy I, Olsen UB, Brand CL, Sundler F, et al. Capsaicin-sensitive sensory fibers in the islets of Langerhans contribute to defective insulin secretion in Zucker diabetic rat, an animal model for some aspects of human type 2 diabetes. Eur J Neurosci. 2007;25(1):213–23.

78) Ramkumar KM, Lee AS, Krishnamurthi K, Devi SS, Chakrabarti T, Kang KP, et al. Gymnema montanum H. protects against alloxan-induced oxidative stress and apoptosis in pancreatic β-cells. Cell Physiol Biochem. 2009;24(5–6):429–40.

79) Al-Romaiyan A, King AJ, Persaud SJ, Jones PM. A novel extract of Gymnema sylvestre improves glucose tolerance in vivo and stimulates insulin secretion and synthesis in vitro. Phyther Res. 2013;27(7):1006–11.

80) Al-Romaiyan A, Liu B, Asare-Anane H, Maity CR, Chatterjee SK, Koley N, et al. A novel Gymnema sylvestre extract stimulates insulin secretion from human islets in vivo and in vitro. Phyther Res. 2010;24(9):1370–6.

81) Roman-Ramos R, Flores-Saenz JL, Alarcon-Aguilar FJ. Anti-hyperglycemic effect of some edible plants. J Ethnopharmacol. 1995;48(1):25–32.

82) Kumari K, Mathew BC, Augusti KT. Antidiabetic and hypolipidemic effects of S-methyl cysteine sulfoxide isolated from Allium cepa Linn. Indian J Biochem Biophys. 1995;32(1):49–54.

83) Mathew PT, Augusti KT. Hypoglycaemic effects of onion, Allium cepa Linn. on diabetes mellitus-a preliminary report. Indian J Physiol Pharmacol. 1975;19(4):213–7.

84) Rakhi Mishra RM, Mohd Shuaib MS, Shravan S, Mishra PS. A review on herbal antidiabetic drugs. 2011;

85) Aggarwal N. Shishu. A Rev Recent Investig Med Herbs Possess Antidiabetic Prop Nutr Disord Ther.

86) Ravi K, Ramachandran B, Subramanian S. Protective effect of Eugenia jambolana seed kernel on tissue antioxidants in streptozotocin-induced diabetic rats. Biol Pharm Bull. 2004;27(8):1212–7.

87) Arumugam G, Manjula P, Paari N. A review: Anti-diabetic medicinal plants used for diabetes mellitus. J Acute Dis. 2013;2(3):196–200.

88) Ghosh R, Sharatchandra KH, Rita S, Thokchom IS. Hypoglycemic activity of Ficus hispida (bark) in normal and diabetic albino rats. Indian J Pharmacol. 2004;36(4):222–5.

89) Özkum D, Akı Ö, Toklu HZ. Herbal medicine use among diabetes mellitus patients in Northern Cyprus. Age (Omaha). 2013;18(25):0.

90) Sievenpiper JL, Arnason JT, Leiter LA, Vuksan V. Null and opposing effects of Asian ginseng (Panax ginseng CA Meyer) on acute glycemia: results of two acute dose escalation studies. J Am Coll Nutr. 2003;22(6):524–32.

91) Fareed M, Chaudhary AA. Herbal medicines for diabetes: Insights and recent advancement. In: Herbal Medicines. Elsevier; 2022. p. 207–22.

92) Bordoloi R, Dutta KN. A review on herbs used in the treatment of diabetes mellitus. J Pharm Chem Biol Sci. 2014;2(2):86–92.

93) Ghorbani A. Best herbs for managing diabetes: a review of clinical studies. Brazilian J Pharm Sci. 2013;49:413–22.

94) Dwivedi C, Daspaul S. Antidiabetic herbal drugs and polyherbal formulation used for diabetes: A review. J Phytopharm. 2013;2(3):44–51.

95) Giovannini P, Howes MJR, Edwards SE. Medicinal plants used in the traditional management of diabetes and its sequelae in Central America: A review. J Ethnopharmacol. 2016;184:58–71.

96) Wannes WA, Marzouk B. Research progress of Tunisian medicinal plants used for acute diabetes. J Acute Dis. 2016;5(5):357–63.

97) Sachdewa A, Khemani LD. A preliminary investigation of the possible hypoglycemic activity of Hibiscus rosa-sinensis. Biomed Environ Sci BES. 1999;12(3):222–6.

98) Gawade M, Adlinge A, Lipane V. Formulation & Evaluation of Polyherbal Antidiabetic Powder. 2023;1(1):1–6.

99) Panda C, Sharma P, Dixit US, Pandey LM. Potential and Prospective of Traditional Indian Medicinal Plants for the Treatment of Diabetes. J Biol Act Prod from Nat. 2023;13(4):316–60.

100) Lee A, Chui PT, Aun CST, Gin T, Lau ASC. Possible interaction between sevoflurane and Aloe vera. Ann Pharmacother. 2004;38(10):1651–4.

101) Basch E, Gabardi S, Ulbricht C. Bitter melon (Momordica charantia): a review of efficacy and safety. Am J Heal Pharm. 2003;60(4):356–9.

102) Patil SM, Shirahatti PS, VB CK, Ramu R, Prasad N. Azadirachta indica A. Juss (neem) as a contraceptive: An evidence-based review on its pharmacological efficiency. Phytomedicine. 2021;88:153596.

103) Saper RB, Phillips RS, Sehgal A, Khouri N, Davis RB, Paquin J, et al. Lead, mercury, and arsenic in US-and Indian-manufactured Ayurvedic medicines sold via the Internet. Jama. 2008;300(8):915–23.

104) Nigam V, Nambiar VS. Therapeutic potential of Aegle marmelos (L.) Correa leaves as an antioxidant and anti-diabetic agent: A review. Int J Pharma Sci Res. 2015;6(3):611–21.

105) Elavarasi S, Saravanan K, Renuka C. A Systematic Review On Medicinal Plants Used To Treat Diabetes Mellitus. Int J Pharm Chem Biol Sci. 2013;3(3).

106) Rosalie IO, Ekype E. Antidiabetic potentials of common herbal plants and plant products: A glance. Int J Herb Med. 2016;4(4):90–7.