

## **Review Article:**

# **A COMPREHENSIVE STUDY OF MEDICINAL PLANTS WITH ANTIDIABETIC PROPERTIES**

### **Abstracts:**

The purpose of this research is to assess the anti-diabetic effects of several medicinal herbs. Herbal medicine has grown in popularity in both developing and developed countries over the last several years, owing to its natural origins and lack of negative effects. Even though medicinal plants have been utilized to treat diabetes mellitus from ancient times, they have been offered as abundant but untapped prospective sources for anti-diabetic medicines. It's a reality that diabetes can't be cured, and no one has ever claimed to be completely free of the disease. Diabetes mellitus is becoming a severe hazard to human health in all regions of the world due to its fast growing occurrence. Furthermore, several novel bioactive compounds derived from plants have demonstrated antidiabetic action with greater efficacy than oral hypoglycemic medicines already utilized in clinical therapy in recent years. Despite the fact that many plants are recommended, further pharmacological and chemical study is needed to fully understand the mechanism of hypoglycemic action.

**Keywords:** Comprehensive review, Diabetes mellitus, Medicinal plants.

### **1. Introduction**

Medicinal plants are still used to treat human illnesses. Over the previous 2500 years, highly powerful traditional medical systems such as Chinese, Ayurvedic, and Unani have emerged and flourished, mostly on the eastern continent [1]. Herbal treatments are gaining popularity on a global scale due to their perceived safety. Traditional traditions are still alive and well, since almost 80% of people in underdeveloped nations depend on these medical systems for their main health care [1-2]. These plants contain compounds that may be employed as therapeutics and as drug precursors. Medicinal herbs have been studied extensively, and it has been revealed that they have different effects on the nervous, circulatory, respiratory, digestive, and urinary systems, as well as the sexual organs, skin, vision, hearing, and taste. Natural products, particularly those of plant origin, are the major focus for discovering promising lead candidates, and they will play an important role in future drug development efforts [2-4]. Plant-based preparations are the major essential player of all current medicines, particularly in rural regions, because of their ease of availability, cheap cost, and minimal adverse effects. Furthermore, many plants have a wealth of bioactive compounds with little adverse effects and potent pharmacological benefits [6-8]. Many of the presently known medications are derived directly or indirectly from plants [9-12]. Many Indian medicinal plants have been demonstrated to help in diabetes therapy. The fact that therapeutic plants are readily available and have few side effects is one of their most enticing features. Plants have long been a good source of pharmaceuticals, and many of the ones on the market today are derived from them, either directly or indirectly.

Diabetes is treated in Unani medicine using a variety of plant-based preparations. Diabetes is a kind of diabetes that affects people of all ages. Diabetes mellitus is described as a metabolic illness with numerous etiologies characterized by persistent hyperglycemia and changes in carbohydrate, lipid, and protein metabolism caused by abnormalities in insulin production, insulin action, or both, according to the World Health Organization. Long-term damage, malfunction, and failure of multiple organs are all side consequences of diabetes mellitus. Thirst, polyuria, impaired eyesight, and weight loss are all common signs of diabetes mellitus [13].

## **2. Types of Diabetes Mellitus(DM)**

2.1. Insulin Dependent Diabetes Mellitus (IDDM, Type-I)

2.2. Non-Insulin Dependent Diabetes Mellitus (NIDDM Type-II)

2.3. Gestational diabetes (Type-III)

Type I diabetes, often known as juvenile diabetes, is an insulin-dependent condition that affects only around 5% of diabetics. Adults over the age of 40 are more likely to acquire Type II diabetes, which is non-insulin dependent. Chronic hyperglycemia caused by diabetes has been linked to long-term damage, malfunction, and finally organ failure, particularly in the eyes, kidneys, nerves, heart, and blood vessels [14].

## **3. Treatment of Diabetes Mellitus**

### **3.1 Insulin and oral hypoglycemic drugs**

Insulin treatment should strive to imitate nature's achievement in minimizing postprandial hyperglycemia and avoiding hypoglycemia between meals. Human insulin, cow insulin, and pig insulin are among the insulin formulations available. Insulin treatment is not without its drawbacks and side effects. When an incorrect dosage of insulin is used and there is a mismatch between meals and insulin injection, the most serious side effects include weight gain and hypoglycemia. They bind to sulfonylurea receptors on the plasma membrane of the  $\beta$ -cell, causing ATP-sensitive potassium channels to close and the cell membrane to depolarize. Sulfonylureas enhance insulin secretion from the pancreas and may also raise insulin levels by reducing hepatic clearance of hormones in type II diabetes patients. When taken orally rather than intravenously, it has been demonstrated to boost peripheral glucose absorption and lower hepatic glucose production by 20-30%. Impaired glucose absorption from the intestine has also been proposed as a mechanism of action [14,15].

### **3.2 Herbal treatment of diabetes**

This condition requires medical diagnosis, treatment, and lifestyle adjustments. It is anticipated to become one of the world's most powerful disablers and killers within the next 25 years. Diabetes management has been a worldwide issue until now, and a suitable cure has yet to be developed. Many synthetic treatments have been produced for patients, but no one has ever been known to have completely recovered from diabetes [15]. Modern oral hypoglycemic medications have a number of unfavorable side effects. As a result, alternative treatment is necessary; a pressing necessity of the hour is to turn to various indigenous plant and herbal compositions [16]. Traditional remedies have a promising future in the treatment of diabetes, and the goal of this study is to compile all relevant data on plants with anti-diabetic activity that have been published in pharmaceutical publications. WHO has a list of 21,000 plants that are utilized for medical reasons all around the world. India has 2500 species, with 150 of them being utilized economically on a considerable basis. India is the world's greatest producer of medicinal plants and is known as the world's botanical garden [14].

#### **4. Screening models for antidiabetic Activity**

##### **4.1 Diabetes induced animal model**

###### **4.1.1. Alloxan**

Alloxan's diabetogenic effect is mediated by reactive oxygen species. With the generation of superoxide radicals, alloxan and its reduction product, dialuric acid, create a redox cycle. Dismutation of these radicals to hydrogen peroxide occurs. The fenton reaction produces extremely reactive hydroxyl radicals after that. The fast death of (beta) cells is caused by reactive oxygen species combined with huge elevations in cytosolic calcium concentration. The fast absorption of alloxan by (beta) cells precedes its activity in the pancreas [17].

###### **4.1.2. Streptozotocin**

*Streptomyces achromogenes* produce streptozotocin, 2-deoxy-2-[methyl-3-nitrosoureidp]-d-glucopyranose, which is used to cause type I and type II diabetes. In practically all species, streptozotocin causes diabetes. The best dosage to induce diabetes in rats was determined to be 50-60 mg/kg i.p. or i.v., in mice 175-200 mg/kg i.p. or i.v., and in dogs 15 mg/kg for 3 days. Rapid intravenous injection seems to be the optimum mode of delivery due to its poor solubility [18].

###### **4.1.3. Ferric nitrilotriacetate induction of diabetes mellitus**

This is a method that is seldom utilized. Diabetic symptoms such as hyperglycemia were seen in rats and rabbits given a significant daily dosage of ferric nitriloacetate. After around 60 days of

therapy, patients with glycosuria, ketonemia, and ketourea had a poor blood insulin response to oral glucose loading [18].

#### **4.1.4. Non insulin dependent diabetes mellitus [NIDD] resembling animal models**

The neonatal STZ-induced rat model of type II diabetes mellitus is established by injecting Wistar rats intravenously [18] or intraperitoneal with 100mg/kg of STZ on the day of their birth.

#### **4.1.5. Hormone induced diabetes**

Growth hormone induced diabetes; in intact adult dogs and cats, repeated administration of growth hormone causes an intensively diabetic condition with all symptoms of diabetes, including severe ketonemia and ketonuria; corticosteroid induced diabetes: hyperglycemia and glycosuria are seen in forced fed rats treated with cortisone; experimental corticoid diabetes in guinea pigs and rabbits;

#### **4.1.6. Insulin deficiency due to insulin antibodies**

Bovine insulin [1mg] is administered subcutaneously into guinea pigs on a monthly basis, and the animals are bled by heart puncture two weeks after the second and subsequent antigen doses. Intravenously injecting guinea pig anti insulin serum (0.25-1.0ml) into rats causes an aldose of dependant rise in blood glucose. This result is caused to insulin antibodies generated by the injected animal neutralizing the impact.

#### **4.1.7. Virus induced diabetes**

Virus infection and -cell specific autoimmunity may cause type 1 diabetes. In male ICR Swiss mice, the d-variant of the Encephala Myocarditis Virus [EMC-D] preferentially infects and kills the -cells (beta), comparable to human insulin-dependent diabetics.

#### **4.1.8. Genetically diabetic animals:**

Several animal species, particularly rodents, have been documented as having hereditary diabetes mellitus, such as spontaneously diabetic rats like the BB rat, WBN/KOB rat, and others [18].

#### **4.1.9. Models of diabetes accelerated atherosclerosis**

In diabetes individuals, accelerated cardiovascular disease is the major cause of morbidity and death. Because the risk of myocardial infarction (MI) is the same in diabetes and non-diabetic individuals with prior MI, aggressive dyslipidemia treatment is required (MI). The most extensively utilized models for studying diabetes and atherosclerosis are now rats and mice.

#### **4.1.10. Genetic models of diabetes**

### **A. Spontaneously develop diabetic rats**

These models allow for the study of a natural product's impact on an animal without the interference of the adverse effects caused by chemical medications like as alloxan and STZ, as described above. The spontaneously diabetic Gotokakizakhi rat, which is a genetic model of type-II diabetes derived via selective breeding of glucose-intolerant non diabetic wister rats over many generations, has been described in many recent articles [19].

### **B. Genetically engineered diabetic mice**

In this case, rodents may be bred to over- or under-express proteins thought to be important in glucose metabolism. Despite significant advances in this field in recent years, particularly with the introduction of transgenic mice, no studies involving natural products have been conducted on these models [18].

## **5. Antidiabetic Drugs and Their Side Effects**

Sulfonylureas, biguanides,  $\alpha$ -glucosidase inhibitors, thiazolidinedione's, and non-sulfonylureas secretagogues are some of the oral hypoglycemic medications that have anti-diabetic actions via distinct mechanisms. Glimepiride and glyburide, for example, are oral sulfonylureas that lower blood sugar by increasing insulin release from the islets of Langerhans. This is accomplished by binding to the sulfonylurea receptor on  $\beta$ -cells (beta), which causes the closure of adenosine triphosphate-dependent potassium channels. As a consequence, the cell membrane depolarizes, allowing calcium to influx and stored insulin to be secreted from secretory granules inside the cells. This process only functions when insulin is present [19, 20]. The biguanides are another kind of oral hypoglycemic medication that works by increasing insulin-stimulated absorption and utilization of sugar to diminish hepatic gluconeogenesis and restore insulin sensitivity in peripheral tissues. Despite this, biguanides are effective in the absence of insulin. Metformin is the greatest example of this class. Acarbose and miglitol are  $\alpha$ -glucosidase (alpha) inhibitors that prevent particular enzymes in the small intestine from breaking down carbs. Hypoglycemic drugs in this class work by slowing the absorption of carbs in the body. Acarbose also inhibits both pancreatic  $\alpha$ -amylase and  $\alpha$ -glucosidase (alpha) enzymes reversibly by binding to the carbohydrate-binding area and interfering with their breakdown into monosaccharides, resulting in delayed absorption and lower postprandial blood sugar levels.

The thiazolidinedione's (TZDs), such as pioglitazone and rosiglitazone, are another major family of oral hypoglycemic medicines, with a mechanism of action that predominantly involves enhancing muscle and adipose tissue sensitivity to insulin and, to a lesser degree, lowering

hepatic glucose production. The nuclear peroxisome proliferator-activated receptor gamma (PPAR) is found in the liver, skeletal muscle, and adipose tissue, and TZDs are powerful and selective agonists. The transcription of insulin-responsive genes involved in the regulation of transportation, manufacturing, and glucose consumption is controlled by the activation of PPAR receptors. TZDs have also been shown to improve  $\beta$ -cell function by reducing free fatty acid levels, which eventually leads to  $\beta$ -cell death [20].

The non-sulfonylurea secretagogues, such as meglitinide and repaglinide, promote insulin secretion from active cells ( $\beta$ ) in a similar fashion as sulfonylureas. This family of oral antidiabetic drugs, on the other hand, binds to a variety of  $\beta$ -cell receptors [21]. Although synthetic oral hypoglycemic medications and insulin are the most common methods for treating diabetes, they do not totally cure the disease's problems and, in addition, they have significant adverse effects. This is the driving factor behind the search for new anti-diabetic medicines [22]. Sulfonylureas, for example, are known to lose their effectiveness in roughly 44 percent of patients after 6 years of therapy, whilst glucose-lowering medications are believed to be unable to manage hyperlipidemia [23]. The hunt for innovative antidiabetic medications from natural sources continues [24] because to many constraints connected with the usage of current synthetic antidiabetic medicines.

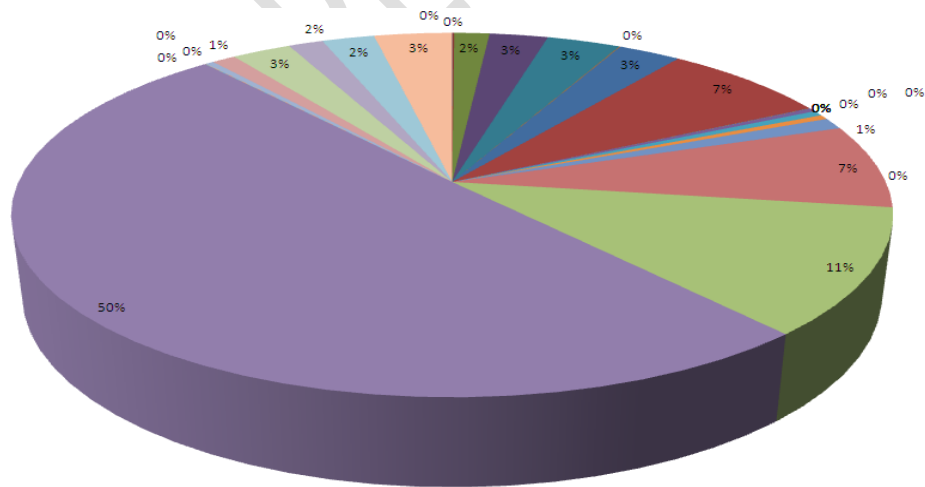
## **6. Medicinal Plants as an Alternative Source of Anti-diabetic Agents**

Insulin and several oral hypoglycemic medications such as sulfonylureas, metformin, glucosidase inhibitors, troglitazone, and others are now available for diabetic treatment. However, significant side effects such as liver issues, lactic acidosis, and diarrhea have been recorded [25]. It presently affects roughly 143 million people [26], and the number of individuals impacted is growing every day; by 2030, it is expected to impact 366 million people globally [27]. There are around 800 plant species that have been documented to have anti-diabetic effects. Native Americans, Chinese, South Americans, and Asian Indians have all employed various plant species to prevent or control diabetes [26]. According to the research, the Asian and African continents account for 56 percent and 17 percent of global distribution of medicinal herbal plants, respectively [28].

Plants that are potent in phenolic, alkaloids, flavonoids, terpenoids, coumarins, and glycosides have beneficial biological benefits. Many classic diabetes treatments, like as metformin, are secretagogues derived from plants, on the other hand. Traditional diabetes drugs work by improving insulin sensitivity, increasing insulin production, and lowering blood glucose levels.

Many medicinal plants have been discovered as potential sources of antidiabetic principles, which are widely used for the treatment of diabetes mellitus in many traditional medical systems across the world, and many of them have been shown to be effective against diabetes. The hypoglycemic action of the plant's pharmacologically active component reduces the impact of -amylase and numerous direct and indirect impacts of various blood parameters that contribute to diabetes development. Figure :1 shows the IC50 values for -amylase (alpha) inhibitors in different plants, with the matching IC50 values in g/ml in parenthesis. There are several anti-diabetic medications available on the market for diabetes and associated complications; however, there is presently no effective treatment available to cure the illness. However, the efficacies of these compounds are questionable owing to undesired side effects, and there is a desire for novel compounds for the treatment of diabetes. Due to its natural origin and fewer side effects, there has been an increasing interest in herbal therapy in the treatment and control of diabetes in both developing and developed nations in recent years [29].

This review article attempts to compile the reported hypoglycemic plants published in various scientific journals, which may be useful to health professionals, scientists, and scholars working in the field of pharmacology and therapeutics in developing evidence-based alternative medicine to treat various types of diabetes in humans and animals. Table 1: shows an analysis of diabetic mellitus therapies derived from various plant sections.



- |  |  |   |
|--|--|---|
| ■ Catharanthus roseus(Apocynaceae) [30]      | ■ Rhizoma fagopyri(Polygonaceae) [31]      | ■ Terminalia arjuna(Combretaceae)[32]       |
| ■ Aegle marmelos(Rutaceae) [32]              | ■ Eugenia cumini(Myrtaceae) [32]           | ■ Ocimum tenuiflorum (Lamiaceae) [33]       |
| ■ Linum usitatissimum(Linaceae) [33]         | ■ Morus alba(Moraceae) [33]                | ■ Pterocarpus marsupium(Legumes) [34]       |
| ■ Santalum spicatum (Santalaceae) [34]       | ■ Beyeria leshnaultii (Euphorbiaceae) [34] | ■ Mucuna pruriens(Fabaceae) [34]            |
| ■ Acacia ligulata (Fabaceae) [34]            | ■ Pterocarpus marsupium (Fabaceae) [34]    | ■ Boerhaavia diffusa (Nyctaginaceae) [34]   |
| ■ Marrubium radiatum (Lamiaceae) [35]        | ■ Salvia acetabulosa (Lamiaceae) [35]      | ■ Aloe vera (Asphodelaceae) [36]            |
| ■ Paronychia argentea (Caryophyllaceae) [36] | ■ Moringa stenopetala (Moringaceae) [37]   | ■ Nelumbo nucifera (Nelumbonaceae) [38]     |
| ■ Costus pictus (Costaceae) [39]             | ■ Juniperus oxycedrus (Cupressaceae) [40]  | ■ Fagonia cretica (Zygophyllaceae) [41]     |
| ■ Eugenia polyantha (Myrtaceae) [42]         | ■ Ludwigia octovalvis (Onagraceae) [43]    | ■ Iostephane heterophylla (Asteraceae) [43] |
| ■ Camellia sinensis (Theaceae) [43]          | ■ Aralia elata (Araliaceae) [44]           | ■ Cinnamomum zeylanicum (Laurels) [45]      |

Figure 1:  $\alpha$ -Amylase inhibitors are reported in several plants, as follows with corresponding IC50 values in  $\mu\text{g/ml}$

## **DISCUSSION**

Diabetes mellitus is expanding at an alarming rate around the globe, affecting three-quarters of the global population, and is regarded as a significant source of substantial economic loss, which might stymie nation-building. Furthermore, untreated diabetes causes a slew of long-term problems, including blindness, heart disease, and renal failure, to name a few. As a result, treatments based on the principles of western medicine (allopathic) are often ineffective, carry the danger of side effects, and are prohibitively expensive, particularly in poor countries. As a result, treating diabetes mellitus using plant-derived chemicals that are readily available and do not need time-consuming pharmaceutical production seems to be very appealing. According to the findings, 85 plant species from 43 families are often used to treat diabetes. The bulk of the studies found that medicinal herbs with hypoglycemic properties are beneficial in the treatment of diabetes mellitus [30]. The comprehensive natural plants are not only used to cure diabetes, but also to cure a variety of other conditions. Other plant components (leaf, root, stem, bark, flower, and whole plant) were also effective for curing. The most often utilized diabetes model was the streptozotocin and alloxan-induced diabetic mouse or rat. In this study, the STZ rat was the most often used animal model. In diverse situations, alloxan mice, glucose tolerance mice, KK-Ay diabetic mice, and diabetic individuals were used as models [31]. Hereditary diabetic mice, such as the KK-Ay mice, have been utilized as a model of type II diabetes with hyperinsulinemia by certain researchers [32]. Flavonoid, Tannin, Phenolic, and Alkaloid are the most typically engaged active ingredients. For these plant extracts, a variety of mechanisms of action have been postulated. Some possibilities center on their impact on pancreatic cell activity (synthesis, release), as well as the increase in insulin sensitivity or insulin-like activity of plant extracts. All of these strategies may have a role in reducing or eliminating diabetes complications.

## **CONCLUSION**

Diabetes mellitus is a sickness defined by a loss of glucose homeostasis due to insulin production and insulin action abnormalities, both of which result in impaired glucose and other energy-yielding fuels such as lipids and proteins metabolism. Many nations are now seeing significant rises in the number of diabetics. In 1985, the World Health Organization estimated that roughly



30 million individuals had diabetes; by 2000, that figure had risen to more than 171 million. By 2030, it is expected that the population would have risen to over 366 million, with considerable increases in emerging nations, particularly among those aged 45 to 64. Plant-based medications and herbal formulations are less toxic and have fewer negative effects than manufactured medications. Hypoglycemic drugs of plant origin used in medicine are significant, according to WHO guidelines. These plants' anti-hyperglycemic properties are linked to their capacity to restore pancreatic tissue function by increasing insulin secretion or decreasing glucose absorption in the intestine. As a result, herbal medication therapy protects cells while also smoothing out fluctuations in glucose levels. In general, there is limited scientific understanding about the precise mechanisms of action in the treatment of diabetes, although most plants have been shown to contain chemicals such as glycosides, alkaloids, terpenoids, flavonoids, and other anti-diabetic compounds. The hunt for alternative therapies (from the plant kingdom) for diabetes mellitus will continue all around the globe, since the condition presents several hurdles to both doctors and researchers.

**Table 1: Analysis of remedies obtained from different plant parts for diabetes mellitus**

Botanical name	Family	Parts used	Solvent (s)	Active chemical constituents	Animal model	Result
<i>Tamarindusindica</i>	Fabaceae	Seed, Fruit	CH <sub>3</sub> OH	Flavonoid, Polysaccharide	STZ-rat	↓Cholesterol, Triglycerides [46]
<i>Aegle marmelos</i>	Rutaceae	Leaf, Seed, Fruit	C <sub>2</sub> H <sub>5</sub> OH, H <sub>2</sub> O	Aegeline-2, Coumarin, Flavonoid, Alkaloid	STZ-rat	↓Glucose, ↓Glycosylated Hemoglobin, ↑Cpeptide, ↑Glucose Tolerance, ↑Glycogen [47,48]
<i>Murrayakoenigii</i>	Rutaceae	Leaf, Fruit	Fruit juice	Carbazole, Alkaloid	ALX-mice	↑Glycogen synthetase, ↓Glycogenolysis, ↓Glycogen phosphorylase, ↓Gluconeogenic enzymes [49]
<i>Allium sativum</i>	Alliaceae	Root	C <sub>2</sub> H <sub>5</sub> OH	Diallyldisulphide oxide, Ajoene, Allyl propyl disulfide, S-allyl cysteine, S-allyl mercaptocysteine	STZ-rat	↓Glucose, ↓Lipid, ↑Insulin, ↓Oxidative stress[50]
<i>Lyciumbarbarum</i>	Solanaceae	Fruit	POLY	Polysaccharide	STZ-rat, ALX-rabbit	↓Glucose, ↓Oxidative stress, ↑GLUT4, ↑Insulin [51]
<i>Psidiumguajava</i>	Myrtaceae	Leaf, Fruit	H <sub>2</sub> O, CH <sub>3</sub> OH	Terpen, Flavonoid, Strictinin, Isostrictinin, Pedunculagin, Polysaccharide	STZ-rat	↓Glucose[52]
<i>Momordicacharantia</i>	Cucurbitaceae	Whole plant	CH <sub>3</sub> OH, H <sub>2</sub> O, CHCl <sub>3</sub>	Charantin, Momordicin, Galactosebinding lectin Non-bitter, Diosgenin, Cholesterol, lan	SZT-mice	↓Glucose, ↓Glycosylated hemoglobin, ↓Oxidative stress,

				osterol, Cucurbitacin glycoside, $\beta$ -sitosterol,		$\downarrow$ Lipid peroxidation, $\uparrow$ Glycogen [53,54]
<i>Momordica cymbalaria</i>	Cucurbitaceae	Fruit	H <sub>2</sub> O	Steroidal glycoside or phenolics	ALX-rat	$\downarrow$ Glucose, $\downarrow$ Cholesterol, $\downarrow$ Triglycerides [55]
<i>Momordica balsamina</i>	Cucurbitaceae	Fruit	CH <sub>3</sub> OH	Momordicin, Vitamin C, Resin acid, Fixed oil, Carotene, Aromatic volatile oil, Alkaloid, Saponin Cucurbitacin,	STZ-rat	Antidiabetic [56]
<i>Phyllanthus emblica</i>	Euphorbiaceae	Fruit	H <sub>2</sub> O	Tannin	ALX-rat	Antidiabetic [57]
<i>Rhus coriaria</i>	Anacardiaceae	Fruit	C <sub>2</sub> H <sub>5</sub> OH	Limonene, Nonanal, Dec-2 (Z)-enal	ALX-rat	Antidiabetic [58]
<i>Musa paradisiaca</i>	Musaceae	Fruit	CH <sub>3</sub> OH	Dietary fibre, Pectin	STZ-rat	Antidiabetic [59]
<i>Aloe vera</i>	Liliaceae	Leaf	C <sub>2</sub> H <sub>5</sub> OH	Pseudoprotinosaponin, Prototinosaponin	STZ-mice	$\downarrow$ Glucose, $\downarrow$ TG, $\downarrow$ LDL, and $\downarrow$ TC and upregulated GLUT-4 mRNA synthesis in NIH/3T3 cells [60,61]
<i>Eugenia jambolana</i>	Asteraceae	Fruit pulp, Seed	H <sub>2</sub> O, C <sub>2</sub> H <sub>5</sub> OH	Pandanus odorosus	STZ-rabbit, STZ-mice	$\downarrow$ Hepatic glucose-6-phosphatase activity, Glucokinase activity [62,63]
<i>Terminalia chebula</i>	Combretaceae	Seed, Fruit	CHCl <sub>3</sub> , H <sub>2</sub> O	Shikimic, Gallic, Triacotanoic, Palmitic acid, $\beta$ -sitosterol, Daucosterol	STZ-rat	$\downarrow$ Glucose [64]
<i>Ziziphusspinachristi</i>	Rhamnaceae	Leaf	N-but	Christinin-A, Fatty acid	STZ-rat, ALX-dog	$\downarrow$ Glucose [65]
<i>Thespesia populnea</i>	Malvaceae	Fruit,	C <sub>2</sub> H <sub>5</sub> OH	Populnetin, Herbacetin, Populneol, Quercetin	ALX-rat	Antihyperglycemic, Hypoglycemic [66]
<i>Diospyros lotus</i>	Ebenaceae	Fruit	H <sub>2</sub> O	Phenolics	STZ-rat	Antidiabetic [67]
<i>Helicteres isora</i>	Sterculiaceae	Fruit	H <sub>2</sub> O	Steroid, Terpenoid,	Glucose	Insulin-

				Alkaloid,Carbohydrate, Phenolics	tolerance- rat	sensitizing,Hypolipide mic activity [68, 69]
<i>Punicagranatum</i>	Punicaceae	Fruit	C <sub>2</sub> H <sub>5</sub> O H	Tannin	ALX-mice	Antidiabetic [71,72]
<i>Panax ginseng</i>	Araliaceae	Fruit	Berry extract	Saponin	Glucose tolerance - mice	Antidiabetic [73]
<i>Anacardiumoccident ale</i>	Anacardiaceae	Leaf	H <sub>2</sub> O, C <sub>2</sub> H <sub>5</sub> O H	Anacardicacid,Cardanol,C ardol, 2-methyl cardol	STZ-rat	Anti- hyperglycemic,Renal protective activities [74]
<i>Annona squamosa</i>	Annonaceae	Seeds, Leaf, Aerial parts	H <sub>2</sub> O, C <sub>2</sub> H <sub>5</sub> O H	Anonaine,Liriodenine, Benzylisoquinoline,Bullat acin	STZ-rat	↑Insulin, ↑utilization of glucose and ↓glucose output from liver [75]
<i>Annona muricata</i>	Annonaceae	Leaf	H <sub>2</sub> O	Linalool,α -terpineol, Linalyl propionate, Calarene	STZ-rat	↑ Insulin immunoreactive β- cells and prevents degeneration of β- cells[76]
<i>Boerhaaviadiffusa</i>	Nyctaginaceae	Leaf	H <sub>2</sub> O	Liriodendrin, Eupalitin	ALX-rat	↓Blood glucose level, ↑Insulin sensitivity [77]
<i>Bougainvillea spectabilis</i>	Nyctaginaceae	Leaf, stem bark	C <sub>2</sub> H <sub>5</sub> O H	Terpinolene,α-(E)- ionone,Methyl salicylate	ALX-rat	↑ Uptake of glucose by enhanced glycogenesis in the liver,↑Insulin sensitivity [78].
<i>Butea monosperma</i>	Papilionaceae	Fruit	H <sub>2</sub> O	Butein, Palasonin, Stigmasterol-3 β-D- glucopyranosid	Type II diabetic patient	Antidiabetic [79]
<i>Brideliandellensis</i>	Euphorbiaceae	Stem Bark	C <sub>2</sub> H <sub>5</sub> O H	2-O-β-D glucosylglycerol	STZ-rat	↓Blood glucose level, Stimulation of islets

						cells [80]
<i>Canavaliaensiformis</i>	Leguminosae	Seeds	H <sub>2</sub> O	Proteins	ALX-rat	↓Blood glucose levels, ↑Triacylglycerol, ↑Cholesterol [81,82]
<i>Cocciniaindica</i>	Cucurbitaceae	Whole plant	C <sub>2</sub> H <sub>5</sub> O H	Pectin, Toluene	ALX-rat	↓Blood glucose [83]
<i>Cocculushirsutus</i>	Menispermaceae	Leaf	H <sub>2</sub> O	β-sitosterol, Ginnol, 28-acetyl betulin	Alloxan-mice	↓Serum glucose level, ↑Glucose tolerance [84]
<i>Ficushispida</i>	Moraceae	Leaf, Bark	CHCl <sub>3</sub> , C <sub>2</sub> H <sub>5</sub> O H	Ficustriol, O-methyl tylophorinidine	ALX-rat	↓ Fasting blood glucose [85]
<i>Mangiferaindica</i>	Anacardiaceae	Leaf, Stem, Bark, Fruit	H <sub>2</sub> O, C <sub>2</sub> H <sub>5</sub> O H	Mangiferin, Phenolics, Flavonoid	STZ-rat, Alloxan-rat	↓α-amylase [86]
<i>Citrus reticulate</i>	Rutaceae	Fruit	Essential oil	Essential oil	ALX-rat	↓Blood cholesterol levels[87]
<i>Feronia elephantum</i>	Rutaceae	Fruit	H <sub>2</sub> O	Bioflavonoid, Bergapten, Terpenoid, Stigma sterol,	ALX-rat	↓Blood glucose level[88]
<i>Limoniaacidissima</i>	Rutaceae	Fruit	CH <sub>3</sub> OH	Polysaccharide	ALX-rat	↓Glucose level, ↓Blood urea, ↑Total protein level [89]
<i>Withaniacoagulans</i>	Solanaceae	Fruit	C <sub>2</sub> H <sub>5</sub> O H	Milk-coagulating enzyme, Esterase, Fatty oil, Essential oil, Alkaloid	T2DM rats	↓Elevated levels of blood glucose, ↓HbA1c, ↓ Insulin [90,91]
<i>Cocciniaindica</i>	Cucurbitaceae	Fruit	C <sub>2</sub> H <sub>5</sub> O H	B-amyrin, Lupeol, Cucurbitacin-B	ALX-rat	↓Blood glucose[92]
<i>Cucumismetuliferus</i>	Cucurbitaceae	Fruit	Fruit extract	B-carotene, Fatty acid	ALX-rat	↓Blood glucose[93]

\*ALX-Alloxan; STZ-Streptozotocin; CH<sub>3</sub>OH-Methanol; C<sub>2</sub>H<sub>5</sub>OH-Ethanol; CHCl<sub>3</sub>-Chloroform; POLY-Polysaccharide; N-but-N-butanol

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