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Review

Diabetes Mellitus Management: An Extensive Review of 37 Medicinal Plants

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Abstract: Plants have been used as sources of medicine since ancient times. Natural products have been used extensively in Chinese, ayurvedic and folk medicine. In addition, a significant portion of the world's population still utilizes herbal medicine. Diabetes is a common ailment affecting almost 463 million people in the world. However, current medications exert harmful after-effects on patients, while herbal medicines have fewer adverse effects. Plants possess secondary metabolites, such as alkaloids, flavonoids, tannins, steroids, etc., which exert numerous beneficial effects on health. Extensive research has been conducted over the years investigating and proving the hypoglycemic potential of various plants. The present paper reviews 37 such plants that are rich in phytoconstituents that possess a variety of pharmacological activities and have been experimentally proven to possess potentially hypoglycemic properties in animal models: *Ficus racemosa*, *Agremone mexicana*, *Bombax ceiba*, *Cajanus cajan*, *Coccinia cordifolia*, *Momordica charantia*, *Syzygium cumini*, *Neolamarckia cadamba*, *Mangifera indica*, *Cocos nucifera*, *Tamarindus indica*, *Punica granatum*, *Azadirachta indica*, *Costus speciosus*, *Moringa oleifera*, *Andrographis paniculata*, *Ficus benghalensis*, *Anacardium occidentale*, *Annona squamosa*, *Boerhaavia diffusa*, *Catharanthus roseus*, *Cocculus hirsutus*, *Ficus hispida*, *Terminalia chebula*, *Terminalia catappa*, *Amaranthus tricolor*, *Blumea lacera*, Piper betle leaves, *Achyranthes aspera*, *Kalanchoe pinnata*, *Nelumbo nucifera*, *Mikania cordata*, *Wedelia chinensis*, *Murraya koenigii*, *Aloe barbadensis*, *Bryophyllum pinnatum* and *Asparagus racemosus*. These 37 plant extracts exhibit antidiabetic activities through different mechanisms, including α-amylase and α-glucosidase inhibition, increases in glucose uptake and the stimulation of insulin secretion.

Keywords: diabetes mellitus; management; treatment; ethnomedicine; medicinal plants; Bangladesh

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1. Introduction

Diabetes mellitus, commonly known as diabetes, is a group of metabolic disorders characterized by hyperglycemia due to the faulty production, action or secretion of insulin [1]. Although no successful cure has been found for DM, it can be managed using insulin, diet modification and conventional or synthetic medicines. Despite their efficacy, synthetic drugs often present adverse side effects to patients and are relatively expensive and difficult to obtain. Therefore, there has been increasing research regarding traditional medicinal plants to search for alternative hypoglycemic drugs. Many synthetic medicines are derived from compounds originally found in plants, such as miglitol, an iminosugar derivative. Iminosugars and sugar derivatives are promising antidiabetic agents that regulate blood sugar levels by inhibiting specific enzymes involved in glucose metabolism [2]. For instance, N-hydroxyethyl-1-deoxynojirimycin (Miglitol), a derivative of 1-deoxynojirimycin iminosugar, is already used against type 2 diabetes as an α-glucosidase inhibitor [3].

Chronic hyperglycemia resulting from diabetes is associated with long-term damage to and the dysfunction of multiple organs, as well as complications such as retinopathy,

nephropathy, neuropathy, peripheral vascular diseases, coronary heart disease, etc. [4]. The most common types of diabetes are type 1, type 2 and gestational diabetes. Type 1 diabetes is an autoimmune disease, wherein beta cells in the pancreas are destroyed by the immune system, resulting in absolute insulin deficiency, while Type 2 diabetes results from insulin resistance and the progressive loss of insulin secretion. In contrast, gestational diabetes occurs during pregnancy [5]. Type 2 DM is the most common health burden, particularly in the elderly population, affecting approximately 25% of people over the age of 65 years as of 2021, with the number of affected people expected to increase drastically over the next decades owing to increased life expectancy [6].

Plants produce secondary metabolites, such as alkaloids, flavonoids, tannins, terpenoids, ferulic acid, etc., which have proven to possess hypoglycemic activity. Alkaloids inhibit alpha-glucosidase and decrease glucose transport through the intestinal epithelium, lowering blood glucose. Flavonoids suppress glucose levels and increase hepatic glucose activity, most likely by enhancing insulin release from pancreatic islets. Saponins, triterpenoids and steroidal glycosides stimulate insulin release and block the formation of glucose in the bloodstream. Polysaccharides increase serum insulin levels, improve glucose tolerance and reduce blood glucose levels. Compounds such as ferulic acid stimulate insulin secretion [7].

Additionally, herbal medicine is cheaper and safer, with fewer adverse effects, than synthetic medicine. Furthermore, in herbal medicine, the whole plant or parts of the plant are treated instead of a single isolated active ingredient, as in conventional medicine. The use of the whole plant is believed to produce a better synergistic effect due to all the chemicals in the plant working together to produce a combined and more beneficial effect. Herbalists also claim that the synergistic effect reduces the toxicity of plants due to buffering [7,8]. Plants have significant potential as alternative hypoglycemic medicines due to their safety, efficacy, affordability and availability, as well as the rich array of potential hypoglycemic phytocompounds. This article attempts to give a brief overview of some plants that contain hypoglycemic phytoconstituents and have exhibited anti-diabetic activity in animal models.

2. Retrieval of Published Research

An exhaustive scientific-publication search was conducted for this review article covering the years up to 2022 on different databases, including PubMed, Scopus, Google Scholar, Science Direct, Web of Science and ResearchGate. During the search, no time limits or filters were applied to the publications, but recent publications relevant to this review's scope were given priority during screening. The purpose of the initial search was to determine the medicinal plants with antidiabetic properties using different combinations of the following keywords: "medicinal plant", "plant", "herbal medicine", "diabetes", "hyperglycemia", "antidiabetic", "antihyperglycemic", "hypoglycemic", and "insulin". In total, 37 plants with antidiabetic properties were finalized as subjects of this review. Further, 37 plants were searched individually for their antidiabetic activity, mechanism, relevant bioactive compounds and toxicity, using keywords such as "diabetes", "hyperglycemia", "antidiabetic", "antihyperglycemic", "hypoglycemic", "insulin sensitivity", "insulin secretion", "mechanism", "pathway", "pancreatic beta cells", "insulin mimetics", "glucosidase", "amylase", "phytochemistry", "bioactive compound", "toxic", "toxicity" and "cytotoxic" in different combination with the individual scientific names of 37 plants. Boolean operators such as AND, OR and NOT were used for different combinational searches. The full scientific names of 37 plants were used as keywords. A manual search was also conducted for additional studies in the reference lists of relevant articles and reviews. In total, 239 articles were identified, which were further screened based on their relevance to the topic of interest; 198 articles were considered relevant to the scope of this review. Only publications about antidiabetic activity, bioactive compounds and toxicity of the selected 37 plants with full texts available in English are considered in this review.

3. Plants in the Management of Diabetes Mellitus

3.1. Achyranthes aspera

Achyranthes aspera (Figure 1; all figures are taken from authors from different areas of Bangladesh) is an Amaranthaceae-family plant commonly known as Devil's horsewhip. The plant's root is known to be used as a cure for jaundice [9]. The plant contains phytochemicals such as alkaloids, oleanolic acid, β-sitosterol, saponins, D-glucuronic acid, quercetin-3-O-β-D-galactoside dihydroxy ketones, aliphatic alcohol, benzoquinone, hydroquinone, asarone, eugenol, etc. It is reported to have hepatoprotective, laxative, antiasthmatic and anti-allergic properties [10]. In a study conducted by Vijayaraj et al. (2016), the administration of 300 mg/kg and 600 mg/kg body weight of the ethanolic seed extract of *A. aspera* in STZ-induced diabetic rats for 28 days significantly reduced blood glucose levels ($p < 0.001$) compared to the standard drug, glibenclamide (5 mg/kg body weight) [11]. Furthermore, *A. aspera* may have antidiabetic effects by either reducing glucose absorption from the gut or increasing glucose transport from the blood [12]. Sadashiv and Krishna (2011) investigated the acute toxicity of leaf powder and a methanolic extract from the leaves of *A. aspera* in Swiss albino mice according to OECD guidelines. The powder was administered to the rats in doses of 2, 4, 6 and 8 gm/kg body weight and the extract was administered in doses of 2, 4, 6 and 8 mg/kg body weight. The rats were observed for signs of toxicity or mortality for the first 24 h and the next 14 days. No signs of toxicity or mortality were observed, which confirmed that the leaf powder and methanolic extract were safe [13].

Figure 1. *Achyranthes aspera*.

3.2. Aloe barbadensis

Aloe barbadensis (Figure 2), commonly known as Aloe, lily of the desert or burn plant, is a perennial succulent plant of the Asphodelaceae family and is used for a variety of medicinal purposes, including in the treatment of allergic reactions, wounds, burns, rheumatoid arthritis, rheumatic fever, diabetes, inflammation, etc. The plant has phytoactive compounds, such as flavonoids, terpenoids and polysaccharides, including pectins, hemicelluloses, glucomannan, sterols β-sitosterol, lupeol, tannins, etc., with analgesic, antioxidant, anti-cancer and anti-inflammatory properties [14]. Lanjhiyana et al. (2011) demonstrated

that the administration of the methanolic extract of 300 mg/kg body weight of Aloe vera gel in alloxan-induced diabetic rats for 21 days significantly reduced blood glucose levels ($p < 0.05$) compared to the reference drug, glibenclamide (0.25 mg/kg body weight). The acute oral toxicity of the extract was examined according to the OECD guidelines. The extract was administered to overnight-fasted rats in single oral doses of 5, 50, 300 and 2000 mg/kg body weight and observed for signs of mortality or toxicity for the next 30 min and the subsequent 14 days. The extract conferred no mortality or toxicity upon the rats [15]. Chysalodin, an anthraquinone dimer isolated from *A. barbadensis*, is a potent α-glucosidase inhibitor and can thus be used as an antidiabetic agent [16]. Again, the mechanism of the antidiabetic effect of *A. barbadensis* involves dipeptidyl peptidase (DPP)-IV-enzyme inhibition in type 2 diabetes. This DPP-IV inhibition may be caused by a dipyrrole derivative, 3,6-dioxo-3,3a,6,6a-tetrahydropyrrolo[3,4-c]pyrrole1,4-dicarboxamid, isolated from *A. barbadensis* leaves [17].

Figure 2. *Aloe barbadensis.*

3.3. Amaranthus tricolor

Amaranthus tricolor (Figure 3) belongs to the family Amaranthaceae and is commonly known as edible amaranth. The plant is used to cure leprosy, bronchitis, piles, leucorrhea and constipation [18]. The plant is known to have anti-hyperglycemic, antihyperlipidemic, anti-diabetic and antioxidant properties. It contains flavonoids, amino acids, alkaloids, carbohydrates, saponins, phenolic compounds and tannins [19]. The plant also contains phytic acid, with diabetes-related enzyme-inhibition properties [20]. According to a study by Clemente et al. (2011), 200 mg/kg and 400 mg/kg body weight of the aqueous leaf extract of the plant showed reduced serum glucose levels in a dose-dependent manner in diabetic rats [21]. Further studies are needed to determine the exact molecular mechanism of the antidiabetic effect. Aneja et al. (2013) conducted research in which they administered a single dose of 2000 mg/kg body weight of aqueous extract of *A. tricolor* roots to Wistar albino rats after fasting overnight. The animals were closely observed for signs of toxicity or mortality during the first 30 min post-treatment, periodically for the next 24 h and once daily for the next 14 days. No lethality was conferred by the extract at 2000 mg/kg body weight [19].

Figure 3. *Amaranthus tricolor*.

3.4. Anacardium occidentale

Locally known as *kaju badam* and commonly known as cashew nut, *Anacardium occidentale* (Figure 4) is a plant in the sumac family. The bark of this plant has been reported to have hypoglycemic and antihypertensive properties and was thus used in African communities to treat diabetes mellitus. The herb leaves' consumption has also been associated with improvements in diabetes-associated kidney problems by reducing the amount of mucopolysaccharide [22]. The plant's stem, leaves and bark are rich in phenolics, saponin, flavonoids, vitamins and selenium. The *A. occidentale* plant contains alkaloids, anthocyanidins, tannins, essential oils, glycosides, myricetin, pentoside, lactone, quercetin hexoside, xanthones, chalcones, 4-hydroxy dodecanoic acid, palmitate, sitosterol, stigmasterol, 3-O-βD-galactopyranoside, etc., which are responsible for its antibacterial, antimutagenic and antifungal activities [23]. According to a study conducted by Ukwenya et al. (2012), the administration of 300 mg/kg body weight of methanolic extract of *A. occidentale* leaves to STZ-induced Wistar rats significantly reduced blood glucose ($p < 0.05$), with 1 I U/kg body weight of insulin also significantly reducing the blood glucose ($p < 0.05$) [24]. *Anacardium occidentale* seeds showed potent antidiabetic efficacy. Seed extracts enhance glucose uptake in skeletal muscle cells via AMPK activation, increases in Glut4 synthesis and translocation to the plasma membrane. Additionally, they may increase glycolysis by impairing mitochondrial oxidative phosphorylation [25]. Konan et al. (2007) administered a hydroethanolic extract of *A. occidentale* leaves to rats with a dose limit of 2000 mg/kg. They monitored the rats closely for the next 3 h and, subsequently, for 14 days, to observe any signs of mortality or toxicity. The animals were sacrificed after 14 days. There was no mortality or apparent changes in the animals' vital organs or behavioral patterns, even at the highest dose of 2000 mg/kg body weight [26].

Figure 4. *Anacardium occidentale*.

3.5. Andrographis paniculata

Commonly known as green chiretta, *Andrographis paniculata* (Figure 5) is a plant in the Acanthaceae family, native to Southern Asia. The plant has been reported to have anti-inflammatory, antioxidant, anti-diabetic and anti-infective properties. It is deemed a natural antibiotic, containing compounds such as terpenoids, flavonoids, iridoids, ferulic acid and, in particular, diterpenoid lactones, such as andrographolide, 14-deoxyandrographolide and 14-Deoxy-11,12-dehydroandrographolide, which are ferulic acids [27]. Andrographolide has been reported to have anti-diabetic properties. In a study conducted by Akter et al. (2013), the administration of 1000 mg/kg of ethanolic extract of *A. paniculata* leaves in Alloxan-induced diabetic Wistar rats significantly reduced their elevated blood glucose ($p < 0.01$). To test the acute toxicity of the extract, it was administered to rats orally and intraperitoneally at 4000 mg/kg body weight; the animals were observed for the next 24 h and then for 10 days for signs of mortality. The extract conferred no toxicity [28]. A study by Augustine et al. (2014) suggested that *A. paniculata* lowers blood glucose levels by regulating glucose uptake and oxidation, restoring insulin-signaling molecules in the liver and reducing serum lipid levels [29].

Figure 5. *Andrographis paniculata*.

3.6. Annona squamosa

Annona squamosa (Figure 6), also known as custard apple, is a tropical plant in the Annonaceae family, cultivated in India, Brazil, Egypt, the West Indies, Ecuador, South and Central America and Brazil. The leaves of the plant possess a wide variety of phytochemicals, such as flavonoids, alkaloids, phenols, saponins, tannins, glycosides, diterpenes, etc., which confer anti-diabetic, antioxidant, antimicrobial, antiviral and anti-tumor properties [30]. According to a study conducted by Rout et al. (2013), the administration of 200 mg/kg and 400 mg/kg body weight of hydroethanolic extract from *A. squamosa* leaves to STZ-induced hyperglycemic rats brought about a significant decrease ($p < 0.05$) in blood sugar compared to the standard drug, metformin (300 mg/kg body weight) (Table 1) [31]. Extracts from *A. squamosa* leaves show antidiabetic properties by enhancing insulin secretion or action, inhibiting starch digestion and protein glycation, delaying glucose absorption and suppressing DPP-IV enzyme activity [32]. In an acute-toxicity study by Onwusonye et al. (2014), a methanolic extract of *A. squamosa* was administered orally to mice up to a dose limit of 5000 mg/kg as a single dose for 24 h, after which the animals were monitored for 30 days. A sub-acute study was also carried out by orally administering the extracts at doses of 200, 400, 600, 800 and 1000 mg/kg body weight to each of the five groups of mice for 30 days. No mortality or pathological alterations were found, with the LD50 of the *A. squamosa* leaves greater than 5000 mg/kg body weight, indicating that the extract was well tolerated [33].

Figure 6. *Annona squamosa*.

Table 1. Summary of the Bangladeshi diabetes plants with utilized parts, model organisms, solvents, dosages, reference drugs and others.

Scientific Name	Common Name	Family	Parts Used	Model Organism	Solvent	Dosage	Reference Drug	Result	References
Ficus racemosa	Cluster fig, *Dumur*	Moraceae	Leaves	STZ-induced diabetic rats	Petroleum ether	200 mg/kg body weight and 400 mg/kg body weight	Glibenclamide	Reduction in blood glucose levels ($p < 0.001$)	[34]
Asparagus racemosus	*Satamuli*	Liliaceae	Whole plant	STZ-induced diabetic Wistar rats	Ethanol	200 and 400 mg/kg body weight	Glibenclamide 10 mg/kg body weight	Decreased blood glucose level ($p < 0.05$)	[35]
Bombax ceiba	*Shimul*, red silk-cotton tree	Bombacaceae	Bark	STZ-induced diabetic rats	Ethyl-acetate extract	600 mg/kg body weight	Glibenclamide (10 mg/kg body weight)	Displayed significant hypoglycemic activity ($p < 0.001$)	[36]
Cajanus cajan	*Arhar*, pigeon pea	Fabaceae	Root	Alloxan-induced diabetic mice	Methanol	200 mg/kg body weight or 400 mg/kg body weight	Metformin (50 mg/kg body weight)	Significantly lowered fasting serum glucose ($p < 0.001$) and blood glucose level ($p < 0.001$)	[37]
Coccinia cordifolia	*Telakucha*, Ivy gourd	Cucurbitaceae	Leaves	STZ-induced diabetic rats	Petroleum ether, ethyl acetate	150 mg/kg body weight	Metformin HCl (150 mg/kg body weight)	Reduced blood glucose levels by 50.39% and 50% at the 10th and 24th hours, respectively ($p < 0.001$)	[38]
Momordica charantia	*Korola*, bitter gourd	Cucurbitaceae	Seed	STZ-induced diabetic rats	Water	150 mg/kg body weight	Glibenclamide (600 µg/kg)	Significantly reduced plasma glucose ($p < 0.05$)	[39]
Syzygium cumini	*Kalojam*, Java plum	Myrtaceae	Whole fruit, Leaves	STZ-induced diabetic albino Wistar rats STZ-induced diabetic rats	Ethanol Ethanol	200 mg/kg body weight 250 mg/kg body weight	Glibenclamide (200 mg/kg body weight)	Decreased blood glucose levels ($p < 0.01$) Significantly decreased blood glucose concentration, increased muscle glycogen store ($p < 0.001$)	[40,41]
Neolamarckia cadamba	Burflower tree, *Kodom*	Rubiaceae	Leaves	Glucose-loaded hyperglycemic mice	Methanol	200 mg/kg body weight and 400 mg/kg body weight	10 mg/kg body weight of glibenclamide	Reduced elevated blood glucose ($p < 0.05$)	[42]

Table 1. *Cont.*

Scientific Name	Common Name	Family	Parts Used	Model Organism	Solvent	Dosage	Reference Drug	Result	References
Mangifera indica	Mango, *Aam*	Anacardiaceae	Leaves	Alloxan-induced diabetic rats	Water	200 mg/kg body weight and 400 mg/kg body weight	Gliclazide 2 mg/kg body weight and 4 mg/kg body weight	Significantly lowered the fasting blood glucose ($p < 0.0001$)	[43]
Cocos nucifera	Coconut	Arecaceae	Spadix	STZ (STZ)-induced diabetic rats	Hydromethanol	250 mg/kg body weight and 500 mg/kg body weight	0.5 mg/kg body weight glibenclamide	Significantly lowered fasting blood glucose ($p < 0.001$)	[44]
Tamarindus indica	Tamarind	Fabaceae	Seed	STZ-induced diabetic Long–Evans rats	-	1.25 g/kg	Glibenclamide (5 mg/kg body weight)	Demonstrated anti-hyperglycemic properties ($p < 0.03$)	[45]
Punica granatum	Pomegranate	Lythraceae	Leaves Fruit	STZ-induced type 2 diabetic rats Alloxan-induced diabetic Wistar rats	Methanol Water	100, 200, 400 and 600 mg/kg body weight 100 mg/kg, 200 mg/kg and 350 mg/kg body weight	Glibenclamide (1 mg/kg body weight) -	Demonstrated anti-diabetic activity ($p < 0.05$) Reduced fasting blood glucose ($p < 0.001$)	[46,47]
Azadirachta indica	*Neem*	Meliaceae	Leaves	STZ (STZ)-induced diabetic rats	Ethanol	200 mg/kg body weight	Glibenclamide (0.25 mg/kg body weight)	Normalized glucose levels after STZ-induced hyperglycemia ($p < 0.05$)	[48]
Costus speciosus	Crepe Ginge	Costaceae	Rhizome Root	Alloxan-induced diabetic rats	Ethanol	200 mg/kg body weight 300 and 450 mg/kg body weight	Glibenclamide (2.5 mg/kg body weight) Glibenclamide (600 µg/kg)	Enhanced insulin secretion lowered blood glucose concentration, decreased glyconeogenesis, increased glycogenesis	[49,50]
Moringa oleifera	Drumstick tree	Moringaceae	Leaves	STZ-induced Sprague-Dawley rats	Ethyl acetate	200 mg/kg body weight	Glibenclamide (5 mg/kg body weight)	Significantly reverses the effects of STZ on serum glucose and insulin, demonstrating anti-diabetic activity ($p < 0.05$)	[51]
Andrographis paniculata	Green chiretta	Acanthaceae	leaves	Alloxan-induced diabetic Wistar rats	Ethanol	1000 mg/kg body weight	Glimepiride (4 mg/kg) body weight	Significantly reduced blood glucose ($p < 0.01$)	[28]

Table 1. *Cont.*

Scientific Name	Common Name	Family	Parts Used	Model Organism	Solvent	Dosage	Reference Drug	Result	References
Ficus benghalensis	Banyan	Moraceae	Leaves Bark	Alloxan-induced diabetic albino rats STZ-induced diabetic rats	Ethanol Ethanol	200 mg/kg body weight and 400 mg/kg body weight 150 mg/kg body weight, 300 mg/kg body weight, 500 mg/kg body weight	Glibenclamide (5 mg/kg body weight) Glibenclamide 0.5 mg/kg body weight	Reduced triglyceride, cholesterol and glucose levels Reduction in blood glucose levels by stimulating insulin secretion ($p < 0.01$)	[52,53]
Anacardium occidentale	Cashew nut, *kaju badam*	Sumac	Leaves	STZ-induced diabetic Wistar rats	Methanol	300 mg/kg body weight	1 IU/kg body weight insulin	Significantly reduced blood glucose ($p < 0.05$)	[24]
Annona squamosa	Custard apple	Annonaceae	Leaves	STZ-induced rats	Water and ethanol	200 mg/kg body weight, 400 mg/kg body weight	Metformin (300 mg/kg body weight)	Reduced blood glucose ($p < 0.05$)	[31]
Boerhaavia diffusa	Hogweed	Nyctaginaceae	Leaves	STZ-induced diabetic rats	Chloroform	50, 100, 200 mg/kg body weight	Glibenclamide9 (25 µg/kg body weight)	Reduced blood glucose, possibly through rejuvenation of pancreatic β-cells	[54]
Catharanthus roseus	*Nayantara*	Apocynaceae	Leaf	Alloxan-induced diabetic rat	Juice	0.5, 0.75, 1.0 mL/kg body weight	Glibenclamide (40 µg/kg body weight)	Lowered blood glucose ($p < 0.01$)	[55]
Cocculus hirsutus	Broom creeper, *Daikhali, Jalajmani*	Menispermaceae	Leaf	Alloxan-induced diabetic rat	Water	250, 500, 1000 mg/kg body weight	Glyburide (10 mg/kg body weight)	Reduced serum glucose level ($p < 0.01$)	[56]
Ficus hispida	Hairy fig	Moraceae	Bark	Alloxan-induced diabetic albino rat	Ethanol	1.25 g/kg body weight	Glibenclamide (0.5 mg/kg body weight)	Reduced blood glucose ($p < 0.001$)	[57]
Terminalia chebula	Myrobalan	Combretaceae	Fruit	STZ-induced diabetic rats	Ethanol	200 mg/kg body weight	Glibenclamide (600 µg/kg body weight)	Stimulated insulin and lowered blood glucose ($p < 0.05$)	[58]
Terminilia catappa	*Bangla badam*	Combretaceae	Leaf	Alloxan-induced diabetic Wistar albino rats	Water, cold extract	Aqueous extract (43 mg/kg body weight) Cold extract (46 mg/kg body weight)	Glibenclamide (10 mg/kg body weight)	Regenerated pancreas	[59]
Amaranthus tricolor	Edible amaranth	Amaranthaceae	Leaf	Alloxan-induced diabetic male albino rats	Water	400 mg/kg body weight	-	Reduced serum glucose levels ($p < 0.001$)	[21]

Table 1. *Cont.*

Scientific Name	Common Name	Family	Parts Used	Model Organism	Solvent	Dosage	Reference Drug	Result	References
Blumea lacera	Lettuce leaf blumea	Asteraceae	Leaf	Swiss albino mice	Methanol	50–400 mg/kg body weight	Glibenclamide (10 mg/kg body weight)	Reduced blood glucose ($p < 0.0001$)	[60]
Piper betle leaves	Betel leaf	Piperaceae	Leaf	STZ-induced diabetic rats	Ethanol	100, 200, 300, 1500 mg/kg body weight	Tolbutamide (22.5 mg/kg body weight)	Reduced blood glucose significantly ($p < 0.050$)	[61]
Achyranthes aspera	Devil's horsewhip	Amaranthaceae	Seed	STZ-induced diabetic rat	Ethanol	300, 600 mg/kg body weight for 24 days	Glibenclamide (5 mg/kg body weight)	Reduced blood glucose level ($p < 0.001$)	[11]
Kalanchoe pinnata	Cathedral bells, life plant	Crassulaceae	Leaf	Alloxan-induced diabetic rats	Ethanol	5.8, 11.6 and 33.2 mg/kg body weight	Glibenclamide (1.35 mg/kg body weight), acarbose (13.5 mg/kg body weight)	Significantly powered fasting blood glucose ($p < 0.05$), increased number of pancreatic β-cells	[62]
Nelumbo nucifera	Indian lotus	Nymphaeaceae	Flower	STZ-induced diabetic male Wistar rat	Ethanol	250 mg/kg body weight	Glibenclamide (0.25 mg/kg body weight)	Lowered fasting blood glucose	[63]
Mikania cordata	Bitter vine	Asteraceae	Leaf	Alloxan-induced diabetic rat	Ethanol	200 mg/kg, 400 mg/kg body weight	Metformin hydrochloride (100 mg/kg body weight)	Reduced blood glucose ($p < 0.05$, $p < 0.01$)	[64]
Wedelia chinensis	Wedelia	Asteraceae	Leaf	Alloxan-induced diabetic Swiss albino mice	Methanole	100 mg/kg, 200 mg/kg body weight	Glibenclamide (5 mg/kg body weight)	Reduced blood glucose levels ($p < 0.01$)	[65]
Murraya koenigii	Curry tree	Rutaceae	Leaf	STZ-induced and nicotinamide-induced hyperglycemic rats	Ethaol	200 mg/kg, 400 mg/kg body weight	Glibenclamide (1 mg/kg body weight)	Decreased blood glucose ($p < 0.01$)	[66]
Aloe barbadensis	Aloe	Asphodelaceae	Gel	Alloxan-induced diabetic rat	Methanol	300 mg/kg body weight	Glibenclamide (0.25 mg/kg body weight)	Reduced blood glucose level ($p < 0.05$)	[15]
Bryophyllum pinnatum	Goethe	Crassulaceae	Leaf	Alloxan-induced diabetic rat	Ethanol	200 mg/kg, 400 mg/kg body weight	Glibenclamide (2.5 mg/kg body weight)	Reduced blood glucose level ($p < 0.05$)	[67]
Agremone mexican	Mexican prickly poppy, *Sialkanta*	Papaveraceae	Aerial parts	Alloxan-induced diabetic rat	Ethanol, water	200 mg/kg, 400 mg/kg body weight	Glibenclamide (5 mg/kg body weight)	Demonstrated significant anti-diabetic effect ($p < 0.05$)	[68]

3.7. Argemone mexicana

Argemone mexicana (Figure 7), commonly known as Mexican prickly poppy and locally known as *Sialkanta*, is a herb in the Papaveraceae family. The plant's roots, stem and latex are used as diuretics and in treating skin diseases, jaundice and diabetes [69]. The roots' stems, curry, latex and juice are consumed for medicinal purposes [70]. The plant contains several isoquinoline alkaloids and phenolic compounds, such as berberine, cheilanthifoline, coptisine, cryptopine, sanguinarine, stylopine, coptisine, tetrahydroberberine, protopine, benzophenathridines, sanguinarine and dihydrosanguinarine, as well as palmitic acid, oleic acid, myristic acid, linoleic acids and β-sitosterol [71,72]. It also contains amino acids, fatty acids, tannins, saponins, flavonoids and phytosterols [73]. It has been reported to have analgesic, anti-diabetic, anthelmintic, antioxidant, anti-inflammatory, antimicrobial, antimutagenic and anti-cancer properties [74]. Although the roots and other parts of the plant are generally non-toxic, *A. mexicana* has been proven to be toxic and lethal [75] and the consumption of its seeds causes epidemic dropsy, as characterized by a case in Delhi, India [76]. The administration of *argemone* seeds in the diet of the roof rat (*Rattus rattus* L.) for 10 days leads to sedation, abdominal jerking, sluggishness, corneal opacity, hind leg edema, etc., with 14 of the 16 rats dying at the end of the experiment [75]. However, the root extract of the plant was found to be non-toxic, as the administration of root powder in the aqueous slurry in Swiss albino mice demonstrated no signs of toxicity on cage observation, even at the highest dose level (7.0 gm/kg body weight), thereby proving that it had no significant toxic effects on mice [77]. According to a study conducted by Nayak et al. (2011), the administration of 200 mg/kg and 400 mg/kg body weight of ethanolic and aqueous extracts of the aerial parts of *Argemone mexicana* had a significant anti-diabetic effect ($p < 0.05$) on alloxan-induced hyperglycemic rats [68]. Therefore, *A. mexicana* has significant therapeutic potential, but caution must be undertaken regarding the usage of its seeds.

Figure 7. *Argemone mexicana*.

3.8. Asparagus racemosus

Asparagus racemosus (Figure 8), commonly known as *Satamuli*, is a plant in the Liliaceae family. The roots and whole parts of the plants are used to treat diabetes, urinary diseases, jaundice and urinary disease. The juice of the plant's roots is used to treat diabetes, jaundice and diarrhea [69,70]. The plant contains several bioactive phytoconstituents, which are responsible alone or in conjunction for its various pharmacological properties, such as its anti-diabetic, antioxidant, neuroprotective and anti-ulcer activities. The main phytoconstituents of the plant are saponins and flavonoids. Furthermore, *A. racemosa* has triterpenoids, steroidal saponins such as shatavarin IV (asparanin B), shatavarin V, shatavarin VI, shatavarin VII, shatavarin VIII, immunoside, schidigeras-

aponin D5 (asparanin A), racemoside A, racemoside B and racemoside C, etc., alkaloids such as asparagamine A, quercetin, quercetin glycosides such as quercetin-3-O-rutinoside and quercetin 3-O-galactoside, isoflavones and sapogenins [78]. The flavonoids and triterpenoids in the plant may be responsible for inhibiting α-amylase and α-glucosidase [79]. According to a study by Vadivelan (2012), the ethanolic extract of *Asparagus racemosus* significantly alleviated the blood glucose in Wistar rats with STZ-induced diabetes when administered at dosages of 200 mg/kg and 400 mg/kg body weight for 21 days [35]. The ethanolic extracts of *A. racemosus* demonstrate more potent hypoglycemic activity than other plant extracts. The plant has also decreased serum glucose levels in in vitro antidiabetic studies [80]. *Asparagus racemosus* exhibits antihyperglycemic activity by inhibiting carbohydrate digestion and absorption, boosting insulin secretion and enhancing its action in peripheral tissues [81]. The intracellular Ca^{2+} levels are increased by *A. racemosus* root extracts, which stimulates the physiological pathways that induce insulin release. Furthermore, *A. racemosus* extracts stimulate insulin release in β-cells through a secretory mechanism involving an inhibitory effect on KATP channels [82]. In another study by Kumar et al. (2010), aqueous extracts of *A. racemosus* did not produce any fatalities in rats, even when used at high doses of 3200 mg/kg body weight [83]. In addition, *A. racemosus* was found to be non-toxic, even after long-term administration [84].

Figure 8. *Asparagus racemosus*.

3.9. Azadirachta indica

Azadirachta indica (Figure 9), locally known as *Neem*, is a plant in the Meliaceae family [85]. The tree is primarily found in Southern Asia and Africa. The leaves, bark, oil, flowers, fruit and gum have been used to treat heart disease, cancer, diabetes and hypertension [86]. The *A. indica* plant consists of phenols, flavonoids, saponins, tannins, alkaloids, glycosides, carbohydrates, triterpenoids, β-sitosterol, ferulic acid, etc.; it has been reported to have antimicrobial, antioxidant, hepatoprotective and other properties [87,88]. The medicinal characteristics of the plant can be attributed to its DNA-repair, detoxification, cell-cycle-alteration, anti-inflammatory and anti-metastatic activities [89]. In an acute toxicity study conducted by Kanagasanthosh, Shanmugapriyan and Kavirajan (2015), ethanolic extracts of *A. indica* leaves were administered to Swiss albino mice at 20 mg/kg, 200 mg/kg and 2000 mg/kg body weight. The mice were observed for signs of mortality within the

first 24 h and for other signs of toxicity for 14 subsequent days. No adverse effects were observed, even at 2000 mg/kg body weight of the ethanolic extract, indicating the safety of the usage of the extract for medicinal purposes [90]. A study by Bisht and Sisodia (2010) involved the administration of 200 mg/kg body weight of ethanolic extract of *A. Indica* to STZ (STZ)-induced diabetic rats. It was demonstrated that the extract normalized glucose levels after STZ-induced hyperglycemia ($p < 0.05$) [48]. *Azadirachta indica* leaf extracts exhibit antihyperglycemic activity by increasing insulin-receptor protein expression, insulin-receptor substrate-1 and its tyrosine phosphorylation (Tyr632), as well as the activity of AKT and GLUT4 proteins [91]. Meliacinolin, a tetranortriterpenoid extracted from *A. indica*, can inhibit α-glucosidase and α-amylase activities, improving insulin resistance [92].

Figure 9. *Azadirachta indica*.

3.10. Blumea lacera

Blumea lacera (Figure 10), commonly known as lettuce-leaf blumea, is a plant in the family Asteraceae [93]. The plant has significant medicinal value and has been used as a stimulant, astringent, anthelmintic drug and diuretic, as well as in the treatment of hemorrhoids [94]. The *B. lacera* plant consists of several phytochemicals, such as β-sitosterol, cineol, artemisinin, lupeol, β-caryophyllene and protocatechuic acid, as well as other alkaloids, flavonoids, tannins, terpenoids, flavones, triterpenes, etc. [94]. According to a study by Hassan et al. (2015), the oral administration of 50–400 mg/kg body weight of leaf methanolic extract to Swiss albino mice significantly reduced blood glucose compared to the reference drug, glibenclamide (10 mg/kg body weight) ($p < 0.0001$). The possible mechanisms include an increase in pancreatic insulin secretion [60]. The exact mechanism should be explored to consider this plant as a potent antidiabetic drug. Hossen et al. (2021) conducted a study on the acute oral toxicity of a methanolic extract of *B. lacera* leaves. The extract was administered to overnight-fasted rats in a single oral dose (500–5000 mg/kg body weight). The rats were kept under close observation for the first 30 min after the treatment and then for the next 72 h to check for any signs of toxicity, such as behavioral changes, allergenic symptoms or mortality. The extract did not demonstrate toxicity, even at the highest dose of 5000 mg/kg body weight [95].

Figure 10. *Blumera lacera*.

3.11. Boerhaavia diffusa

Boerhaavia diffusa (Figure 11), also known as hogweed, is a species of flowering plant in the Nyctaginaceae family. Various parts of the plant, particularly the roots, have been associated with anti-diabetic, anti-cancer, gastroprotective and hepatoprotective properties. The plant contains steroids such as ecdysteroids, alkaloids, lignan glycosides, phenolic glycosides, flavonoids, isoflavonoids such as rotenoids, etc. [96]. According to a study conducted by Nalamolu (2003) et al., the chloroform extract of *B. diffusa* leaves reduced the blood glucose in STZ-induced diabetic rats in a dose-dependent manner when used in daily doses of 50 mg/kg, 100 mg/kg and 200 mg/kg body weight compared to the standard drug, glibenclamide. The blood glucose was probably reduced by the rejuvenation of pancreatic β-cells [54]. The ethanol extract of *Boerhaavia diffusa* exhibits therapeutic potential against type 2 diabetes by inhibiting small intestinal glucose absorption and stimulating muscle glucose uptake [97]. In an acute-toxicity study by Hiruma-Lima (2000), extracts obtained from lyophilized decoction and the juice of fresh leaves of *B. diffusa* were administered in doses of up to 5000 mg/kg body weight in mice after 12 h fasting. The animals were subsequently observed for 14 days. No signs of toxicity or mortality were observed until the dose of 5000 mg/kg body weight [98].

Figure 11. *Boerhaavia diffusa*.

3.12. Bombax ceiba

Bombax ceiba (Figure 12), locally known as *Shimul* and commonly known as the red silk-cotton tree, is a plant in the Bombacaceae family. The bark and roots of the plants are used to treat excessive menstrual discharge, dysentery and diabetes [69]. The *B. ceiba* plant contains alkaloids, flavonoids, glycosides, β-sitosterol, kaempferol, hentriacon-

tane, hentriacontanol, quercetin, shamimin (2-(2,4,5-trihydroxyphenyl)-3,5,7-trihydroxy-6-C-glucopyranosyloxy-4H-1-benzopyran-4-one), ceiba naphthoquinone, etc. [99]. In a study by Wanjari et al. (2016), the acute toxicity of the aqueous extract of *B. ceiba* flowers was investigated by administering the extract to healthy Wistar rats up to a dose of 2000 mg/kg body weight, according to the OECD 423 guidelines. The rats were observed for signs of toxicity for the first 2 h, 24 h, 72 h and 14 days. The extract did not confer toxicity or mortality up to a dose of 2000 mg/kg body weight [100]. According to a study conducted by Bhavsar and Talele (2013), the administration of 600 mg/kg of *B. ceiba* bark extract to STZ-induced diabetic rats demonstrated significant hypoglycemic activity ($p < 0.001$). This hypoglycemic activity may be attributed to the presence of triterpenoid compounds in the extract (Table 2) [36]. One possible mechanism of hypoglycemic activity is α-amylase inhibition, as ethyl-acetate extracts of *Bombax ceiba* leaves showed a 66.69 ± 0.95% α-amylase inhibition [101]. Another possible mechanism, suggested by Guang-Kai et al. (2017), is that the hypoglycemic effect may be due to an increase in insulin levels by protecting pancreatic β-cells and stimulating insulin secretion from the remaining β-cell [102]. A network-pharmacology analysis found several pathways, such as PPAR signaling, the activation of the oncogenic chemical receptor and fatty-acid metabolism, through which *Bombax ceiba* flowers help to treat type 2 diabetes mellitus [103]. The proposed possible mechanisms should be further explored to determine the exact mechanism of action of this plant's antihyperglycemic effect.

Figure 12. *Bombax ceiba*.

Table 2. List of plants with potential hypoglycemic compounds.

Name of Plant	Potential Hypoglycemic Compounds	References
Ficus racemosa	β-Sitosterol, stigmasterol, lanosterol, flavonoids (gluanol acetate and racemosic acid)	[104]
Asparagus racemosa	Flavonoids, Saponins-shatavarin IV (asparanin B), shatavarin V, shatavarin VI, shatavarin VII, shatavarin VIII, immunoside, schidigerasaponin D5 (asparanin A), racemoside A, racemoside B and racemoside C, triterpenoids, alkaloids-asparagamine A, quercetin, quercetin glycosides-quercetin-3-O-rutinoside, quercetin 3-O-galactoside, isoflavones, sapogenins	[78]
Bombax ceiba	alkaloids, flavonoids, glycosides, β-sitosterol, kaempferol, hentriacontane, hentriacontanol, quercetin, shamimin (2-(2,4,5-trihydroxyphenyl)-3,5,7-trihydroxy-6-C-glucopyranosyloxy-4H-1-benzopyran-4-one)	[99]

Table 2. *Cont.*

Name of Plant	Potential Hypoglycemic Compounds	References
Cajanus cajan	B-sitosterol, flavonoids- luteonin, vitexin, apigenin, genistic, ononin, sissiotrin, 2′-hydroxygenistein, stilbenes-cajanusin A, cajanusin B, cajanusin C, cajanusin D, cajanstilbene H, cajanolactone A, cajanonic acid A, canjanotone	[105]
Coccinia cordifolia	saponin, glycoside, alkaloid compounds (catharanthin, leurosine, lochnerine, vindoline and vindolinine), flavonoids, tannins, phenols, terpenoids	[38,106]
Momordica charantia	Diosgenin, saponins, alkaloids, trtiterpenes, proteins, steroids	[107]
Syzygium cumini	alkaloids, tanins, flavonoids, carotenoids, glycosides, saponins, steroids, triterpenoids, anthocyanins, phenols, oxalic acid, phytosterols, myrcetin, gallic acid	[108,109]
Neolamarckia cadama	Phenolics, alkaloids, Cadambine, Chlorogenic acid, Dihydrocinchonine, flavonoids, saponins, triterpenes, indole alkaloids, triterpenoid glycosides, 3α-dihydrocadambine, isodihydrocadambine, isocadamine	[110–112]
Mangifera indica	Mangiferin, flavonoids, phenolic acids, xanthones, gallic acid, catechins, kaempferol, carotenoids-luteoxanthine, zeaxantine, β-carotene, terpenoids- careen, myrcene, terpinoline, terpenoid saponins- indicoside A and B	[113,114]
Cocos nucifera	phenols, tannins, β-sitosterol, flavonoids, noctinic acid, folic acid, riboflavin, biotin, triterpenes, alkaloids, steroids, saponins, tannins, catechins, epicatechins	[115]
Tamarindus indica	phenolic compounds, β-sitosterol, proanthocyanins, apigenins tartaric acid, cardiac glycosides, mucilage, pectin, eicosanoic acid, β-sitosterol, palmitic acid, oleic acid, succininc acid, formic acid, β-amyrin, apigenin, epicatechins, catechins, taxifolin, eriodictoyl, naringenin	[116]
Punica granatum	flavonols, triterpenoids, fatty acids, organic acids- citric acid, malic acid, ascorbic acid, tannins- gallagic acid, punicalin, punicalagin, flavonoids-luteolin, quercetin, kaempferol, magnesium, alkaloids, catechin, gallic acid	[117]
Azadirachta indica	phenols, flavonoids, saponins, tannins, alkaloids, glycosides, carbohydrates, triterpenoids, β-sitosterol, ferulic acid	[87,88]
Costus speciosus	alkaloids, glycosides, flavonoids, steroids, polyphenols, tannins, β-sitosterol, gracillin, dioscin, diosgenin	[118]
Moringa oleifera	β-sitosterol, saponins, steroids, alkaloids- moringine and moringinine, flavonoids- rhamnetin, isoquercitrin, kaempferitrin, saccharides, phenolic acids, tannins, terpenoid, alpha-carotene	[119–121]
Andrographis paniculata	terpenoids, flavonoids, iridoids, ferulic acid, diterpenoid lactones, andrographolide, 14-deoxyandrographolide, 14-Deoxy-11,12-dehydroandrographolide, fersulic acids	[27]
Ficus benghalensis	anthocyanidin derivatives, aliphatic long-chain ketones, glycosides, flavonoids, amino acids, steroids, saponins, carbohydrates, tannins	[122,123]
Anacardium occidentale	phenolics, saponin, flavonoids, alkaloids, anthocyanidins, tannins, essential oils, glycosides, myricetin, pentoside, lactone, quercetin hexoside, canthones, chalcones, 4-hydroxydodecanoic acid, palmitate, sitosterol, stigmasterol, 3-O-βD-galactopyranoside	[23]
Annona squamosa	flavonoids, alkaloids, phenols, saponins, tannins, glycosides, diterpenes	[30]
Boerhaavia diffusa	steroids, ecdysteroid, alkaloids, lignan glycosides, phenolic glycosides, flavonoids, isoflavonoids, rotenoids	[96]
Catharanthus roseus	alkaloids, catharanthine, tetrahydroalstonine, vindoline, kaempferol, lochnerine, flavonoids	[124]
Cocculus hirsutus	β-sitosterol, ginnol, flavonoids such as luteolin, kaempferol and quercetin, glycosides, carbohydrates, tannins, saponins, steroids	[125]
Ficus hispida	flavonoids, saponins, steroids, glycosides, alkaloids, alkanes	[126,127]
Terminalia chebula	B-sitosterol, flavonoids, tannins, sterols, gallic acid, chebulanin, corilagin, ellagic acid, chebulinic acid, amino acids, fructose, resin, triterpenoids, glycosides	[128]
Terminilia catappa	tannins, saponins, phenolics, flavonoids, triterpenoids, kaempferol, geraniin, punicalin, quercetin, gentisic acid, tercatain, tergallagin, β-carotene, cyanidin-3-glucoside, ellagic acid, gallic acid	[59,129]
Amaranthus tricolor	flavonoids, amino acids, alkaloids, carbohydrates, saponins, phenolic compounds, tannins, phytic acid	[19,20]
Blumea lacera	β-sitosterol, artemesinin, lupeol, β-caryophyllene, protocatechuic acid, alkaloids, flavonoids, tannins, terpenoids, flavones, triterpenes	[94]
Piper betle leaves	glycosides, quercitin, alkaloids, saponins, steroids, tannins, diterpenes, eugenol, chavibetol, flavonoids, hydroxychavicol	[130]
Achyranthes aspera	Alkaloids, oleanolic acid, saponins, D-Glucuronic Acid, dihydroxy ketones, quercitin, β-sitosterol, aliphatic alcohol, benzoquinone, hydroquinone, asarone and eugenol	[10]

Table 2. *Cont.*

Name of Plant	Potential Hypoglycemic Compounds	References
Kalanchoe pinnata	β-sitosterol, flavonoids, kaempferol, quercetin, alkaloids, tannins, phenolic compounds, caffeic acid, syringic acid, luteolin, rutin, para-coumaric acid, ferulic acid, stigmaterol, astragalin, campesterol	[131]
Nelumbo nucifera	asteroidal triterpenoid, alkaloids, phenolic bases, flavonoids, quercetin, glycoside, kaempferol, nuciferin, roemerin, armepavine, β-sitosterol glucopyranoside	[132,133]
Mikania cordata	saponins, alkaloids, flavonoids, tannins, steroids	[134]
Wedelia chinensis	flavonoids, alkaloids, saponins, phytosterols, mucilage, tannins	
Murraya koenigii	carbazole alkaloids, mahanimbine, flavonoids, sterols, koenimbine, koenine, girinimbine	[135]
Aloe barbadensis	flavonoids, terpenoids, polysaccharides, pectins, hemicelluloses, glucomannan, sterols β-sitosterol, lupeol, tannins	[14]
Bryophyllum pinnatum	flavonoids, alkaloids, reducing sugars, tannins, bufadienolides, glycosaponins, polyphenols, steroidal glycosides	[136]
Agremone mexicana	Berberine, cheilanthifoline, coptisine, cryptopine, sanguinarine, stylopine, tetrahydroberberine, protopine, sanguinarine, dihydrosanguinarine, palmitic acid, oleic acid, myristic acid, linoleic acids, β-sitosterol, amino acids, fatty acids, tannin, saponins, flavonoids, phytosterols	[71–73]

3.13. Bryophyllum pinnatum

Commonly known as Goethe, *Bryophyllum pinnatum* (Figure 13) is a plant in the Crassulaceae family and grows in the temperate regions of Asia, the West Indies, Pacific, Hawaii, Australia, etc. The plant is rich in phytochemicals, such as flavonoids, alkaloids, reducing sugars, tannins, bufadienolides, glycosaponins, polyphenols and steroidal glycosides, which are responsible for its antioxidant, anti-tumor, anti-inflammatory, analgesic, anti-diabetic and hepatoprotective properties [136]. According to a study by Ezeagu et al. (2017), 200 mg/kg and 400 mg/kg body weight of ethanolic leaf extract from *B. pinnatum* significantly reduced the blood glucose levels in alloxan-induced diabetic rats compared to the standard drug (2.5 mg/kg body weight of glibenclamide) [67]. The serum-glucose-lowering mechanism involves α-amylase and α-glucosidase inhibition by kaempferol and quercetin isolated from *B. pinnatum* leaves [137]. In a study conducted by Afzal, Kazmi and Anwar (2013), the acute toxicity of ethanolic and aqueous extracts of *B. pinnatum* was conducted according to OECD guideline 420 and administered to Swiss albino mice orally in doses of 5 mg/kg, 50 mg/kg and 500 mg/kg body weight. The animals were observed for the first 2 h and the next 24 h for signs of toxicity or mortality. The extract was non-toxic, weighing up to 2000 mg/kg [138].

Figure 13. *Bryophyllum pinnatum*.

3.14. Cajanus cajan

Cajanus cajan (Figure 14), locally known as *Arhar* and commonly known as pigeon pea, is a shrub in the Fabaceae family. The juice from the plant's roots is used to treat diabetes [69]. The plant contains over 40 bioactive compounds, with flavonoids and stilbenoids the chief bioactive constituents [139]. The plant contains β-sitosterol, flavonoids such as luteolin, vitexin, apigenin, genistic, ononin, sissotrin, 2′-hydroxygenistein, etc., as well as stilbenes such as cajanusin A, cajanusin B, cajanusin C, cajanusin D, cajanstilbene H, cajanolactone A, cajanonic acid A, canjanotone, etc. [105]. Tang et al. (2017) administered aqueous and ethanolic extracts of *C. cajan* in Sprague–Dawley rats in doses of 1.5, 3.0 and 6.0 g/kg body weight for four weeks and observed them for the two weeks after the treatment to check for symptoms of toxicity. No mortality, behavioral changes or weight alterations were observed. The study demonstrated the lack of acute toxicity from *C. cajan* in rats [139]. Extracts from *C. cajan* are used for the treatment of diabetes, dysentery, hepatitis, measles, wounds, bedsores, malaria, etc. According to a study conducted by Nahar et al. (2014), the administration of 200 mg/kg or 400 mg/kg of methanolic extract from the plant's roots in alloxan-induced diabetic rats for two weeks significantly lowered the fasting serum glucose ($p < 0.001$) and blood glucose levels ($p < 0.001$) [37]. Increased insulin secretion may mediate the extract's hypoglycemic effect [140]. However, there is still insufficient evidence of the glucose-lowering mechanism, so more studies are required to consider the significance of *Cajanus cajan* as a potent antidiabetic agent.

Figure 14. *Cajanus cajan*.

3.15. Catharanthus roseus Linn.

Locally known as Nayantara, *Catharanthus roseus* Linn. (Figure 15) belongs to the Apocynaceae family. The whole plant, is reported to have shown anti-cancer and anti-diabetic properties, especially the leaves [126]. The plant contains alkaloids, catharanthine, tetrahydroalstonine, vindoline, kaempferol, lochnerine and flavonoids, as well as pharmacological properties such as anti-microbial, antioxidant, anti-ulcer and wound-healing effects [124]. Research conducted by Nammi et al. (2003) demonstrated that 0.5 mL/kg, 0.75 mL/kg and 1.0 mL/kg body weight of leaf juice from *C. roseus* Linn. lowered the blood glucose in alloxan-induced diabetic rats, with 1.0 mL/kg body weight of glibenclamide used as a control. The maximum reduction in blood glucose was produced by

1.0 mL/kg body weight of *C. roseus* at 31.9% ($p < 0.01$) [55]. Several mechanisms of the antihyperglycemic effect have been reported [141]. The most significant mechanism is the enhancement of the glucose-transport gene (GLUT-2 and GLUT-4) expression, through which *Catharanthus roseus* seeds showed a potent antihyperglycemic effect [142]. In a study conducted by Vutukuri et al. (2017), the acute toxicity of an ethanolic extract from *C. roseus* leaves was assessed, according to the OECD 420 guidelines, in female albino Wistar rats. The extract was administered to groups of five rats in single oral doses of 5, 50, 300 and 2000 mg/kg body weight. The rats were kept under observation for the subsequent 14 days for signs of toxicity. No mortality was observed at the highest dose of 2000 mg/kg body weight, although slight tremors and restlessness were observed at the highest dose [143].

Figure 15. *Catharanthus roseus* Linn.

3.16. Coccinia cordifolia

Coccinia cordifolia (Figure 16), locally known as *Telakucha* and commonly known as Ivy gourd, is a plant in the Cucurbitaceae family [69]. The Cucurbitaceae family is a plant family consisting of 960 species and is considered to be one of the essential plant families, possessing potent hypoglycemic properties. Plants in this family were applied in the treatment of diabetes mellitus in both modern and ancient Ayurvedic medicine [144]. In a study conducted by Islam et al. (2011), 150 mg/kg body weight of ethanolic extract from *Coccinia cordifolia* leaves administered to STZ-induced diabetic rats for 24 h reduced blood glucose levels by 50.39% and 50% at the 10th and 24th hours, respectively ($p < 0.001$). Many of the hypoglycemic activities of the plant may be related to the phytochemicals saponin and glycoside, alkaloid compounds (catharanthin, leurosine, lochnerine, vindoline and vindolinine) and flavonoids [38]. The hypoglycemic activities of different parts of this plant are mediated through various mechanisms, including β-cell regeneration, insulin secretion stimulation, glucose-uptake enhancement, antioxidant-enzyme restoration, metabolic-enzyme regulation, digestive-enzyme inhibition and lipid-profile improvement [145]. A chemical analysis showed that the plant is rich in nutrients, mainly antioxidant compounds, such as total phenol, vitamin C and β-carotene. Phytochemical screening showed that the methanolic extract contains bioactive constituents, such as tannins, saponins, phenols, flavonoids and terpenoids [106]. In a study by Jha (2010), the acute oral toxicity of aqueous extracts from *C. cordifolia* was carried out according to the OPPTS (Office of Prevention, Pesticides and Toxic Substances) guidelines. The extracts were administered orally to albino

Wistar rats at a dose of 2000 mg/kg. When no toxicity or mortality were observed, the dose was increased to 5000 mg/kg body weight, which also did not confer toxicity [146].

Figure 16. *Coccinia cordifolia*.

3.17. Cocculus hirsutus Linn.

Locally known as Daikhai or Jalajmani and commonly known as Broom creeper, *Cocculus hirsutus* (Figure 17) belongs to the family Menispermaceae. Its root and leaf extracts have been reported to show laxative and antiperiodic properties and alleviate symptoms of eczema and gonorrhea. The plant contains alkaloids, β-sitosterol, ginnol, flavonoids such as luteolin, kaempferol, quercetin, glycosides, carbohydrates, tannins, saponins and steroids, among others and possesses anti-diabetic, antibacterial, anti-cancer and antifungal activities [125]. A study conducted by Badole et al. (2006) demonstrated that the administration of 250 mg/kg, 500 mg/kg and 1000 mg/kg body weight of aqueous extract from *C. hirsutus* leaves in alloxan-induced diabetic mice for 28 days significantly reduced serum glucose levels ($p < 0.01$), with 10 mg/kg body weight p.o. of glyburide used as the standard drug [56]. The exact mechanism of the glucose-lowering effect of this plant extract is yet to be established. Bothara, Marya and Saluja (2011) performed an acute toxicity test for *C. hirsutus* methanolic and aqueous extracts in male Wistar albino rats, in which the LD50 of the extract was found to be 3000 mg/kg body weight [147].

Figure 17. *Cocculus hirsutus*.

3.18. Cocos nucifera

Cocos nucifera (Figure 18), commonly known as coconut, belongs to the Arecaceae family. The plant's fruit has been used in the treatment of syphilis, jaundice, diabetes and cholera [69]. The plant has multiple phytoconstituents, such as phenols, tannins, β-sitosterol, flavonoids, nicotinic acid, folic acid, riboflavin, biotin, triterpenes, alkaloids, steroids, saponins, tannins, catechins, epicatechins, etc. [115]. *Cocus nucifera* can improve insulin secretion and blood glucose utilization, which is used in managing diabetes [148]. In a study conducted by Naskar et al. (2011), 250 mg/kg and 500 mg/kg of hydromethanol extract from *Cocus nucifera* was administered to STZ (STZ)-induced diabetic rats for 14 days (Table 1). The hydromethanolic extract from *C. nucifera* significantly lowered fasting blood glucose in the diabetic rats and had an effect comparable to 0.5 mg/kg glibenclamide ($p < 0.0001$) [44]. Salil et al. (2011) found that coconut-kernel protein (CKP) contains arginine in significant amounts and that it demonstrated potent anti-diabetic activity. As proposed by Salil et al. (2011), the mechanisms of anti-diabetic activity of CKP may include increasing glycogen and insulin levels while reducing serum glucose levels, the efficient degradation of carbohydrates by β-D-galactosidase and the inhibition of the regeneration of β-pancreatic cells by arginine, resulting in increased insulin secretion and subsequent increases in glycogen levels in blood serum [149]. Paul et al. (2012) administered petroleum ether, chloroform and methanol extracts from *C. nucifera* leaf extracts to Swiss albino mice to investigate the extracts' acute toxicity. No mortality or toxic effects were observed at doses of up to 2000 mg/kg body weight in the acute toxicity studies, demonstrating that *C. nucifera* is non-toxic in adult albino mice [150].

Figure 18. *Cocos nucifera*.

3.19. Costus speciosus

Commonly known as Crepe Ginger, *Costus speciosus* (Figure 19) is a Costaceae-family plant with anti-diabetic, anti-microbial, antioxidant and anti-inflammatory activities [151]. The *C. speciosus* plant contains phytochemicals such as alkaloids, glycosides, flavonoids, steroids, polyphenols, tannins, etc. It also contains compounds such as β-sitosterol, gracillin, dioscin, diosgenin, etc. Diosgenin possesses anti-diabetic properties [118]. The rhizomes of *C. speciosus* are the primary sources of diosgenin, along with leaves. The plant's leaves possess significant hypoglycemic properties and can lower blood glucose [152]. In a study conducted by Revathy, Abdullah and Kumar (2014), the administration of 200 mg/kg

per body weight of ethanolic extract of *C. speciosus* enhanced insulin secretion in alloxan-induced diabetic rats [49]. Another study, conducted by Bavarva and Narasimhacharya (2008), demonstrated that doses of 300 mg/kg and 450 mg/kg body weight of ethanolic root extracts from *C. speciosus* lowered the concentration of blood glucose, decreased glyconeogenesis and increased glycogenesis, reinstating normal levels of glucose in the blood when administered to alloxan-induced diabetic rats [50]. An oligosaccharide called raffinose, which was isolated from the *C. speciosus* rhizome, increases glucose uptake in a dose-dependent manner. Through an increase in Glut4 translocation via IRβ/PI3K/Akt phosphorylation, its ability to increase insulin sensitivity was observed. Raffinose's capacity to inhibit the activation of GSK3 for glycogen synthesis provides additional proof that it has therapeutic potential for treating diabetes [153]. In a study conducted by Mar (2019), 70% ethanolic extracts of *C. speciosus* rhizome were administered to albino mice, according to the OECD 423 guidelines. No mortality or toxicity were observed in the animal models, even with a maximum dose of 5000 mg/kg body weight over an observation period of 14 days, indicating the safe usage of the *C. specious* [57].

Figure 19. *Costus speciosus*.

3.20. Ficus benghalensis L.

Ficus benghalensis (Figure 20), commonly known as Banyan, is a large evergreen semi-deciduous tree in the Moraceae family. All the parts of the plant contain latex, which is used in the treatment of toothache, dysentery and diarrhea. The tree's bark is also used to treat diabetes [22]. The tree has been reported to possess anti-helminthic, anti-inflammatory, anti-diabetic, antimicrobial and analgesic properties. The phytochemicals derived from the plant include anthocyanidin derivatives, aliphatic long-chain ketones and glycosides [122]. It also contains phytoconstituents, such as flavonoids, amino acids, steroids, saponins, carbohydrates and tannins [123].

A study conducted by Saraswathi et al. (2013) demonstrated that the administration of 200 mg/kg and 400 mg/kg body weight of ethanolic extract from *F. benghalensis* leaves in alloxan-induced diabetic albino rats reduced blood glucose, cholesterol and triglyceride levels [52]. In another study, by Kasireddy et al. (2021), it was reported that an ethanolic extract of *F. benghalensis* lowered blood glucose in STZ-induced diabetic rats by stimulating insulin secretion from the Islets of Langerhans $p < 0.01$ [53]. The bark of *F. benghalensis* shows an anti-diabetic effect through a mechanism that includes the inhibition of the carbohydrate-hydrolyzing enzymes, α-amylase and α-glucosidase [154]. A network-pharmacology study suggested that *F. benghalensis* bark extract increases glucose uptake and insulin secretion through the PI3K/Akt signaling pathway, supporting other wet-laboratory research [155]. Gabhe, Tatke and Khan (2006) investigated the acute toxicity of the methanolic extract of *F. benghalensis* by orally administering a single dose of 2000 mg/kg body weight of the extract to rats and observing them for signs of toxicity for the next 14 days. The study's results demonstrated that the LD50 of the methanolic extract of *F. benghalensis* was more than 2000 mg/kg body weight [123].

Figure 20. *Ficus benghalensis*.

3.21. Ficus hispida Linn.

Commonly known as hairy fig, *Ficus hispida* (Figure 21) is a plant in the Moraceae family. The plant is rich in phytochemicals, such as flavonoids, saponins, steroids, glycosides, alkaloids, alkanes, etc. It has been reported for wound healing, anti-inflammatory, sedative, anti-ulcer and anti-diabetic activity, as well as being used to alleviate symptoms of dysentery, ulcers, dysentery, ulcers, psoriasis, anemia, piles, jaundice, etc. [126,127]. In a study by Ghosh et al. (2004), the ethanolic extract of *F. hispida* was administered in doses of 1.25 g/kg body weight to normal and alloxan-induced diabetic albino rats with 0.5 mg/kg body weight of glibenclamide as a standard drug (Table 1). The blood glucose was estimated by the glucose-oxidase method 2 h prior to and 2 h post-treatment. The *F. hispida* extract demonstrated significant hypoglycemic activity, as it significantly reduced blood glucose in both the normal ($p < 0.01$) and diabetic ($p < 0.001$) rats, but the effect was weaker than that of glibenclamide. The extract also increased the blood glucose uptake by the hemidiaphragm, increased the glycogen content in the liver and demonstrated other hypoglycemic activities [57]. In a study by Swathi, Sreedevi and Bharathi (2011), an acute-toxicity study of a methanolic extract from the fresh fruits of *F. hispida* was carried out following CPCSEA guideline 420. The extracts were administered to Wistar albino rats in doses of up to 1000 mg/kg body weight and conferred no mortality or toxicity [156].

Figure 21. *Ficus hispida.*

3.22. Ficus racemosa

Ficus racemosa (Figure 22), commonly known as cluster fig, or locally as *Dumur*, is a plant in the Moraceae family. The plant is used to treat diabetes, dry cough, kidney and spleen diseases, bronchitis, menorrhagia and hemoptysis. The plant's unripe fruit is often cooked in curries and consumed by diabetic patients, in addition to the use of its sap as a tonic [22]. According to a study by Mandal et al. (1997), 200 mg/kg and 400 mg/kg petroleum-ether extract from *Ficus racemosa* leaves exhibited hypoglycemic activity in Streptozotocin-induced diabetic rats when dispensed orally (Table 2) [34]. Isolated from *F. racemosa*, β-sitosterol is a compound with potential anti-diabetic activity. Other potential pharmacological products isolated from the plant include flavonoids, triterpenes such as gluanol acetate and racemosic acid, alkaloids and tannins. In a study conducted by Kushwaha et al. (2015), β-sitosterol, stigmasterol and lanosterol isolated from the petroleum-ether extract of *F. racemosa* leaves significantly reduced the blood glucose in STZ-induced diabetic rats with an action comparable to that of glibenclamide [104]. *Ficus racemosa* bark extracts exhibited potent antidiabetic effects through multiple mechanisms, such as inhibiting α-amylase, adsorbing and trapping glucose in its fiber matrix to prevent glucose diffusion and enhancing glucose transport across cell membranes [157]. In a study by Bhaskara Rao et al. (2002), the acute toxicity of the methanolic extract of *F. racemosa* bark was determined according to the methodology of Lorke (1983). The extracts did not confer any mortality or toxicity up to 3.2 g/kg body weight, indicating that the extract was non-toxic [158].

Figure 22. *Ficus racemosa*.

3.23. Kalanchoe pinnata

Kalanchoe pinnata (Figure 23), commonly known as cathedral bells, life plant, etc., belongs to the family Crassulaceae [159]. The plant contains phytochemicals such as flavonoids, kaempferol, quercetin, alkaloids, tannins, phenolic compounds, caffeic acid, syringic acid, luteolin, rutin, para-coumaric acid, ferulic acid, β-sitosterol, stigmasterol, astragalin, campesterol, etc. The plant's extracts have been used in ethnomedicine to cure respiratory-tract infections, insect bites, fever, constipation, piles, etc. Furthermore, it is also known to have anti-cancer, antifungal and anti-diabetic activities [131]. In a study conducted by Indah (2016), an ethanolic extract of *K. pinnata* leaves was administered to alloxan-induced diabetic rats in doses of 5.8 mg/kg, 11.6 mg/kg and 33.2 mg/kg body weight, with glibenclamide (1.35 mg/kg body weight) and acarbose (13.5 mg/kg body weight) as standard drugs. After the treatment, the fasting blood glucose of the rats was recorded every day for 5 days; the animals were sacrificed at the end of the study for histopathological examination. The extract significantly lowered the fasting blood glucose ($p < 0.05$) and increased the number of pancreatic beta Langerhans cells, albeit not in a dose-dependent manner [62]. *Kalanchoe pinnata* has anti-oxidative, as well as α-amylase- and α-glucosidase-inhibitory activities, which enhance glucose uptake, thereby indicating its antidiabetic potential [160]. Quazi et al. (2011) investigated the acute toxicity of *K. pinnata* leaves by orally administering a single dose of 2000 mg/kg body weight of the ethanolic leaf extract of the plant to Wistar rats, which were kept under subsequent observation for signs of toxicity/mortality for the next 14 days. No signs of mortality, morbidity or histopathological changes were noted with the administration of the extract. The acute-toxicity study revealed that the extract was safe for use in doses greater than 2000 mg/kg of the rats' body weight [131].

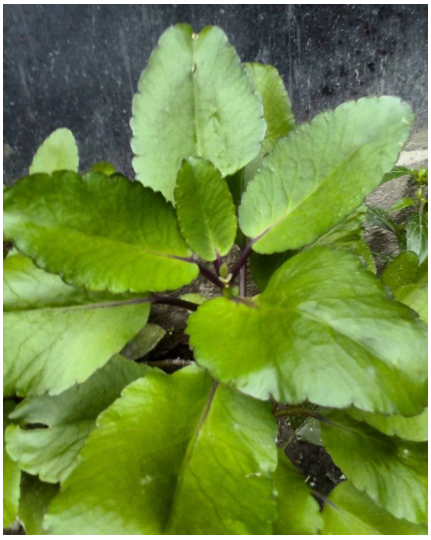

Figure 23. *Kalanchoe pinnata*.

3.24. Mangifera indica

Mangifera indica (Figure 24), commonly known as mango and locally known as *Aam*, is a plant from the Anacardiaceae family. The plant has been used as an antidote to poison, as well as in the treatment of edema, dysentery and diabetes [85]. It is native to tropical Asia and commonly used in Ayurvedic medicine. The plant consists of Mangiferin, a polyphenolic antioxidant, as well as glucosyl xanthone, with hypotensive, antidegenerative and anti-diabetic properties [113]. The most abundant phytoconstituents of the plant are flavonoids, phenolic acids and xanthones. The major polyphenolic compounds found in the plant include gallic acid, catechins, kaempferol, ellagic acids, anthocyanins and ascorbic acid, carotenoids such as luteoxanthine, zeaxantine, β-carotene, terpenoids such as careen, myrcene, terpinoline, terpenoid and saponins such as indicoside A and B, etc. [114]. John et al. (2012) administered aqueous ethanolic extracts from *M. indica* stem bark orally to rats with doses of 1000, 1500, 3000, 4000 and 5000 mg/kg, respectively. They observed signs of toxicity over the next 48 h. The LD50 of the extract was determined at >5000 mg/kg body weight. The extract showed low toxicity at 5000 mg/kg body weight, as there were no clinical indications of toxicity or mortality after 48 h of administration (Table 3) [161]. In a study conducted by Madhuri and Mohanvelu (2017), 200 mg/kg and 400 mg/kg of aqueous extracts of *Mangifera indica* leaves were administered to alloxan-induced diabetic rats for 15 days. The experiment was conducted using the aqueous extract of *M. indica* alone, gliclazide (a hypoglycemic drug) and a combination of both. When used alone, both the *M. indica* extract and the gliclazide significantly lowered the fasting blood glucose of the rats ($p < 0.0001$). However, the most significant lowering of fasting blood glucose was observed when the extract and drug were used in conjunction [43]. This commercially available plant has been studied widely and several mechanisms have been proposed for its anti-diabetic effect. Insulin-stimulated processes, such as glucose transport and glycogen synthesis, which stimulate glucose uptake, are regulated by the activation of the PI3K pathway [162]. Ethyl-acetate extracts and 3β-taraxerol from *Mangifera indica* stimulate insulin-stimulated glucose uptake through PI3K activation in 3T3-L1 adipocyte cells. This PI3K-pathway activation leads to the activation of the glucose transporter GLUT4 and of PKB, along with the suppression of GSK3β, which is responsible for increased glycogen synthesis [163].

Figure 24. *Mangifera indica*.

Table 3. Summary of the key studies conducted with Bangladeshi diabetes plants.

Name of Plant	Solvent	Part of Plant	Model	Highest Safe Dose with No Toxicity (mg/kg Body Weight)	LD50 (Median Lethal Dose) (mg/kg Body Weight)	References
Ficus racemosa	Methanol	Bark	Normal and alloxan-induced diabetic rat	3200 mg/kg	3200 mg/kg	[158]
Asparagus racemosus	Water	Roots	Rats	3200 mg/kg		[83]
Bombax ceiba	Water	Flower	Wistar rats	2000 mg/kg		[100]
Cajanus cajan	Water, ethanol	Leaf	Sprague–Dawley rats	6000 mg/kg		[139]
Coccinia cordifolia	Water	Aerial parts	Wistar rats	5000 mg/kg		[146]
Momordica charantia	Ethanol	Fruit	Sprague–Dawley rats	2000 mg/kg		[39]
Syzygium cumini	Methanol, water	Bark, root, seed, leaf	Albino mice		2000 mg/kg (seed extract-200 mg/kg)	[164]
Neolamarckia cadama	Methanol	Bark	Mouse	3000 mg/kg		[112]
Mangifera indica	Water	Bark	Rat		>5000 mg/kg	[161]
Cocos nucifera	Petroleum ether, chloroform, methanol	Leaf	Swiss albino rat	2000 mg/kg		[150]
Tamarindus indica	Water	Pulp	Albino rats	4500 mg/kg		[165]
Punica granatum	Ethanol	Whole fruit, seeds	Swiss albino mice	2000 mg/kg		[166]

Table 3. *Cont.*

Name of Plant	Solvent	Part of Plant	Model	Highest Safe Dose with No Toxicity (mg/kg Body Weight)	LD50 (Median Lethal Dose) (mg/kg Body Weight)	References
Azadirachta indica	Ethanol	Leaf	Swiss albino mice	2000 mg/kg		[90]
Costus speciosus	Ethanol	Rhizome	Albino mice	5000 mg/kg		[57]
Moringa oleifera	Ethanol, water	Roots	Swiss albino mice		Ethanolic extract—1780 mg/kg; aqueous extract—1590 mg/kg	[167]
Andrographis paniculata	Ethanol	Leaf	Wistar rats	4000 mg/kg		[28]
Ficus benghalensis	Methanol	Roots	Rats		>2000 mg/kg	[123]
Anacardium occidentale	Water, ethanol	Leaf	Rats	2000 mg/kg		[26]
Annona squamosa	Methanol	Leaf	Rat		>5000 mg/kg	[33]
Boerhaavia diffusa	Juice	Leaf	Mice	5000 mg/kg		[98]
Catharanthus roseus	Ethanol	Leaf	Wistar rat	2000 mg/kg		[143]
Cocculus hirsutus	Water, methanol	Root	Wistar albino rat		>3000 mg/kg	[147]
Ficus hispida	Methanol	Fruit	Wistar albino rat	1000 mg/kg		[156]
Terminalia chebula	Water	Fruit	Rat	5000 mg/kg		[168]
Terminilia catappa	Water	Leaf	Sprague-Dawley rats	3000 mg/kg		[169]
Amaranthus tricolor	Water	Root	Wistar albino rat	2000 mg/kg		[19]
Blumea lacera	Methanol	Leaf	Rat	5000 mg/kg		[95]
Piper betle leaves	Methanol	Leaf	Mice	5000 mg/kg		[170]
Achyranthes aspera	Methanol	Leaf	Swiss albino mice	8000 mg/kg		[13]
Kalanchoe pinnata	Ethanol	Leaf	Wistar rat	>2000 mg/kg		[131]
Nelumbo nucifera	Ethanol	Flower	Wistar rat	2000 mg/kg		[63]
Mikania cordata	Ethanol	Leaf	Rat	2000 mg/kg		[64]
Wedelia chinensis	Ethanol	Whole plant	Mice		>1600 mg/kg	[171]
Murraya koenigii	Petroleum ether, chloroform, ethanol	Leaf	Rat		2500 mg/kg	[172]
Aloe barbadensis	Methanol	Gel	Rat	2000 mg/kg		[15]
Bryophyllum pinnatum	Ethanol, water	Aerial parts	Swiss albino mice	2000 mg/kg		[138]
Agremone mexicana	Aqueous slurry of root-bark powder	Root bark	Swiss albino mice	7000 mg/kg		[77]

3.25. Mikania cordata

Mikania cordata (Figure 25), commonly known as bitter vine, heartleaf hempvine, etc., is a wild plant in the Asteraceae family. The plant has been reported to have antibacterial, anti-cancer and anti-inflammatory properties and contains saponins, alkaloids, flavonoids, tannins and steroids [134]. In a study conducted by Nasrin et al. (2015), 200 mg/kg and 400 mg/kg body weight of ethanolic leaf extracts from *M. cordata* were administered to alloxan-induced diabetic rats for 14 days and demonstrated significant hypoglycemic activity compared to the control drug, metformin hydrochloride (100 mg/kg body weight) ($p < 0.05$ and $p < 0.01$). The extracts (200 mg/kg and 400 mg/kg body weight) reduced the blood glucose levels of the mice by 38.04% and 47.72%, respectively, demonstrating that *M. cordata* has anti-diabetic properties. The acute-toxicity study of the extract was carried out by following OECD-423 guidelines and administering the extract at doses of 5, 50, 300 and 2000 mg/kg body weight. The female mice were observed for the next 24 h and then for 14 days for signs of toxicity or mortality. The extract did not confer toxicity or mortality, even at doses up to 2000 mg/kg body weight [64].

Figure 25. *Mikania cordata*.

3.26. Momordica charantia

Momordica charantia (Figure 26), locally known as *Korola* or bitter gourd, is a member of the Cucurbitaceae family. It is a climber, with its flowering time spanning from January to December. The juice made from the plant's leaves is used to treat chickenpox and rheumatism, while the unripe fruit is used to treat diabetes [69]. The plant contains biologically active phytoconstituents, such as saponins, alkaloids, triterpenes, proteins and steroids. In addition, it contains several phytochemicals, such as diosgenin (a compound that alleviates hypoglycemia), momorcharins, momordenol, momordicin, charantin, charine, cucurbitin, gentisic acid, etc. Since the hypoglycemic chemicals in the plant are concentrated in its fruits, these fruits have significant hypoglycemic properties [107]. According to a study conducted by Sathishsekar et al. (2005), 150 mg/kg body weight of aqueous extract of *M. charantia* seeds significantly ($p < 0.05$) reduced plasma glucose levels when administered to STZ (STZ)-induced diabetic rats for 30 days [173]. The anti-diabetic effects of *M. charantia* involve several mechanisms, such as the stimulation of insulin resistance, the suppression of MAPKs and NF-κβ in pancreatic cells, the activation of the AMPK pathway, the promotion of glucose and fatty-acid catabolism, the enhancement of fatty acid absorption, the inducement of insulin production and the inhibition of glucose-metabolism enzymes such as fructose-1,6-bisphosphate and glucose-6-phosphatase [174]. Husna et al. (2013) administered single doses of 300 mg/kg and 2000 mg/kg body weight of ethanolic extract from *M. charantia* in Sprague–Dawley rats to determine the acute toxicity. The treated rats demonstrated dizziness and depression for the first 30 min after the dose's administration. However, no marked differences were observed between the behavioral patterns or body

weights thereafter. However, in the treatment group, which received 2000 mg/kg body weight of the extract, the hemoglobin counts and relative liver weights were significantly decreased compared to the control. The study demonstrated that the extract was safe to use at 2000 mg/kg body weight [136] and below.

Figure 26. *Momordica korola.*

3.27. Moringa oleifera

Moringa oleifera (Figure 27), commonly known as the Drumstick tree, is a tree in the Moringaceae family. It is a valued medicinal plant indigenous to Southeast Asia that has been reported to have analgesic, anti-diabetic, gastroprotective, antimicrobial and wound-healing properties. It contains β-sitosterol, saponins, steroids, alkaloids such as moringine and moringinine, flavonoids such as rhamnetin, isoquercitrin, kaempferitrin, saccharides, phenolic acids, tannins, terpenoid and alpha-carotene [119–121]. In a study by Kasolo et al. (2019), ethanolic and aqueous extracts from *M. oleifera* roots were administered to Swiss albino mice. The aqueous extracts were administered at 10, 15, 20, 25 and 35 g/kg body weight and the ethanolic extracts were administered ats 10, 15, 20, 25 and 30 g/kg body weight to different groups. The animals were observed for behavioral changes for the subsequent 12 h and for mortality in the 24 h following treatment. The LD50 levels of the ethanolic extract and aqueous extract were 17.8 g/kg body weight and 15.9 g/kg body weight, respectively. This demonstrated that the plant is relatively non-toxic (Table 3) [167]. According to a study conducted by Bamagous et al. (2018), 200 mg/kg body weight of ethyl-acetate-extract fraction from *M. oleifera* leaves administered to STZ-induced Sprague–Dawley rats for 30 days significantly reversed the effects of STZ on serum glucose and insulin, demonstrating anti-diabetic activity ($p < 0.05$) [51]. Extracts from *M. oleifera* leaves reduce hyperglycemia in type 2 diabetes by modulating hyperinsulinemia, PPAR-γ and inflammatory cytokines [175]. The inhibition of α-amylase and α-glucosidase activity, increases in glucose uptake in the muscles and liver, the inhibition of glucose uptake from the intestine, decreases in gluconeogenesis in the liver and increases in insulin secretion and sensitivity are some of the other proposed mechanisms for the antidiabetic effect of *M. oleifera* [176].

Figure 27. *Moringa oleifera*.

3.28. Murraya koenigii

Commonly known as the curry tree, *Murraya koenigii* (Figure 28) is a tropical tree native to Asia and belongs to the family Rutaceae. The leaves and roots of the plant are rich in bioactive phytocompounds, including carbazole alkaloids such as mahanimbine, flavonoids, sterols, koenimbine, koenine, girinimbine and mukoeic acid, which have antioxidant, antimicrobial, anti-helminthic, anti-diabetic and hepatoprotective properties. They have been used to treat night blindness, diarrhea, dysentery, etc. [135]. According to a study conducted by Husna et al. (2018), the administration of 200 mg/kg body weight and 400 mg/kg body weight of *M. koenigii* extract leaves in STZ- and nicotinamide-induced hyperglycemic rats led to a significant decrease ($p < 0.05$) in blood glucose levels compared to the standard drug glibenclamide (1 mg/kg body weight). This antidiabetic effect may have been due to its antioxidant properties and reduced insulin resistance [66]. Darvekar et al. (2011) conducted a study on the acute toxicity of petroleum ether, chloroform and ethanol extracts of *Murraya koenigii* according to OECD guidelines. The extracts were suspended in saline and administered orally in single doses of 500 mg/kg, 1000 mg/kg and 2500 mg/kg body weight to different groups of rats each; the rats were monitored for the next 24 h. The LD50 of the extracts was found to be 2500 mg/kg body weight [172].

Figure 28. *Murraya koenigii*.

3.29. Nelumbo nucifera

Nelumbo nucifera (Figure 29), commonly known as Indian Lotus, is a plant in the family Nymphaeaceae. It is an aquatic crop grown throughout Asia. The plant has been used in Ayurvedic and Chinese traditional medicine. Its rhizome extract possesses asteroidal triterpenoid, which gives it anti-diabetic and anti-inflammatory properties. It has also been used to treat hematuria, hemoptysis, diarrhea, cholera, fever, etc. [132]. The plant consists of phytoconstituents, such as alkaloids, phenolic bases, flavonoids, quercetin, glycoside and kaempferol. Its other compounds include nuciferine, roemerine, armepavine, β-sitosterol glucopyranoside, etc. [133]. A study conducted by Sakuljaitrong et al. (2013) investigated the hypoglycemic, hypolipidemic and possible acute toxicity of ethanolic extracts from *N. nucifera* flowers. On the acute-toxicity test, the extract was administered orally in doses of 0, 500, 1000, 1500 and 2000 mg/kg body weight to healthy adult male Wistar rats, which were observed for a subsequent 24 h and then 14 days for signs of toxicity or morbidity. The extract was also administered in 250-mg/kg-body-weight doses to STZ-induced male Wistar rats with 0.25 mg/kg body weight glibenclamide as a reference drug to investigate its possible hypolipidemic and hypoglycemic activities. The extract significantly ($p < 0.05$) lowered fasting blood glucose, total cholesterol, triglycerides and low-density lipoprotein. The acute-toxicity test revealed that the extract did not confer any toxicity or mortality, even at 2000 mg/kg body weight [63]. *Nelumbo nucifera* leaf extract was evaluated for its antidiabetic efficacy by Sharma BR et al. (2016). The results suggested that leaf extracts reduce the toxicity of pancreatic β-cells in type 1 diabetes, followed by the increased secretion of insulin from pancreatic β-cells [177]. This mechanism of action clearly indicates its antidiabetic potential.

Figure 29. *Nelumbo nucifera.*

3.30. Neolamarckia cadamba

Neolamarckia cadamba (Figure 30), also known as the Burflower tree and locally known as *Kodom*, is an evergreen tropical tree from the Rubiaceae family. It is found in Bangladesh, India, Sri Lanka, Nepal and Myanmar. The phenolics and alkaloids, cadambine, chlorogenic acid and dihydrocinchonine, present in the plant give it anti-diabetic properties [110,111]. Its other phytoconstituents include flavonoids, saponins, triterpenes, indole alkaloids, triterpenoid glycosides, 3α-dihydrocadambine, isodihydrocadambine, isocadamine, etc. Dubey et al. (2011) investigated the acute toxicity of *N. cadamba* barks by administering methanolic extracts from the plant in mouse models. The mice had no mortality for doses up to 3000 mg/kg, with acute toxicity demonstrated only at doses above 3000 mg/kg body weight [112]. According to a study by Ahmed et al. (2011), a methanolic extract from *Neolamarckia cadamba* reduced glucose-induced hyperglycemic mice's elevated blood glucose. In the study, the methanolic extract of *Neolamarckia cadamba* was administered to glucose-loaded mice at 200 mg/kg

and 400 mg/kg body weight. The dosage of 400 mg/kg body weight demonstrated the greatest anti-hyperglycemic activity, which was comparable to 10 mg/kg of glibenclamide ($p < 0.05$) [42].

Figure 30. *Neolamarckia cadamba*.

3.31. Piper betle Leaves

Piper betle (Figure 31) is a Piperaceae-family plant commonly known as the betel leaf. Betel leaves are respiratory depressants and have anti-diabetic, antitumor, antimutagenic, carminative and stomachic properties. They are also commonly used as mouth fresheners [178]. The plant consists of several phytochemicals, such as glycosides, alkaloids, saponins, steroids, tannins, diterpenes, eugenol, quercetin, chavibetol, flavonoids, hydroxychavicol, etc. Many toxicity tests have been carried out on *Piper betel* extracts, confirming their safety for human use [130]. In a study by Avijit et al. (2005), 100, 200, 300 and 1500 mg/kg body weight of hot and cold ethanolic extracts from *P. betle* leaves were administered to STZ-induced diabetic rats, with the drug tolbutamide (22.5 mg/kg body weight) used as the standard drug. Both extracts significantly ($p < 0.05$) reduced the fasting blood glucose in the rats, suggesting that the extract had hypoglycemic activity [61]. The inhibition of α-glucosidase and α-amylase inhibition and the insulin-mimetic properties of *Piper betle* extract constitute the proposed mechanism behind the hypoglycemic effect [61,179]. In a study conducted by Al-Adhroey et al. (2010), following the OECD 423 guideline, "Acute oral toxicity–acute toxic class method", the acute toxicity of methanolic extracts from *P. betel* leaves was studied. The extracts were administered to mice at doses of up to 5000 mg/kg body weight. The mice were observed for mortality or signs of toxicity twice, 1, 3 and 4 h after administration. They were then observed twice daily for 14 days, after which they were sacrificed for necropsy and histopathological study. The extract demonstrated no toxicity at 5000 mg/kg body weight, demonstrating that it is safe for use [170].

Figure 31. *Piper betle*.

3.32. Punica granatum

Punica granatum (Figure 32), commonly known as pomegranate, is a plant in the Lythraceae family. The leaves, fruits and seeds of the plant have been used in the treatment of dysentery, diabetes, heart diseases, etc. [180]. The *P. granatum* plant consists of flavonols, triterpenoids, fatty acids, organic acids such as citric acid, malic acid, ascorbic acid, tannins such as gallagic acid, punicalin, punicalagin, flavonoids such as luteolin, quercetin, kaempferol, magnesium and alkaloids such as pelletierine, etc. [117]. In an acute toxicity study by Bhandary et al. (2013), 2000-mg/kg-body-weight ethanolic extracts from the whole fruit and seeds of *P. granatum* were orally administered to mice. There were no behavioral changes and no significant changes in biochemical or hematological parameters, with no mortality in the treated groups. The LD50 was greater than 2000 mg/kg body weight, so the extracts' oral consumption was deemed non-toxic [166]. According to a study conducted by Pottahil et al. (2020), a methanolic extract from *Punica granatum* leaves was administered to STZ-induced type 2 diabetic rats at doses of 100, 200, 400 and 600 mg/kg body weight daily for 45 days. The *P. granatum* extract demonstrated significant anti-diabetic activity ($p < 0.05$) due to the presence of the antioxidants gallic acid, ellagic acid and apigenin [46]. In another study, conducted by Gharib and Kouhsari (2019), an aqueous extract of *P. granatum* fruit noticeably reduced fasting blood glucose compared to a diabetic control in alloxan-induced diabetic Wistar rats ($p < 0.001$) [47]. The understanding of the mechanism of action of *Punica granatum* flower extracts has improved. *Punica granatum* flowers contain gallic acid, which activates the PPAR-γ pathway to improve insulin-receptor sensitivity [181]. *Punica granatum* flowers' phenolic extracts can lower glucose levels in type 2 diabetes by activating the Akt/GSK3β signaling pathway and inhibiting endoplasmic reticulum (ER) stress. The mechanism of ER-stress inhibition involves a decrease in IRE1 (inositol-requiring kinase1) phosphorylation and XBP-1 (X-box-binding protein-1) splicing. This mechanism leads to improved insulin sensitivity [182].

Figure 32. *Punica granatum*.

3.33. Syzygium cumini (L.)

Syzygium cumini (Figure 33), locally known as *Kalojam* and commonly known as Java plum, is a plant in the Myrtaceae family. The bark and seeds of the plant are used to treat wounds, dysentery and diabetes [69]. The plant consists of bioactive phytoconstituents, such as alkaloids, tannins, flavonoids, carotenoids, glycosides, saponins, steroids, triterpenoids, anthocyanins, phenols, oxalic acid, phytosterols, myricetin, gallic acid etc., which endow it with anti-inflammatory, antibacterial, antioxidant, hypoglycemic and hypolipidemic properties [108,109]. Deb et al. (2013) administered methanolic and aqueous extracts from the bark, roots, seeds and leaves of *S. cumini* in albino mice of both sexes, according to the OECD 423 guidelines. The median lethal dose (LD50) cut-off for all the extracts was 2000 mg/kg body weight, except for the methanolic seed extract, for which the LD50 cut-off was 200 mg/kg body weight (Table 3). No common side effects, such as mild diarrhea, weight loss or depression, were reported within 7 days of the administration of the extracts [164]. A study conducted by Gupta and Saxena (2011) demonstrated that a single oral dose of 200 mg/kg body weight of 95% ethanolic extract from the whole fruit of *Syzygium cumini* in STZ-induced diabetic rats led to a significant decrease in blood glucose concentration ($p < 0.01$), increases in muscle glycogen stores and degranulation in pancreatic β-cells, demonstrating hypoglycemic activity [40]. In another study, by Schoenfelder et al. (2008), a crude ethanolic extract from *Syzygium cumini* leaves was administered in normal, hyperglycemic and alloxan-induced diabetic rats. The extract significantly ($p < 0.001$) decreased blood glucose levels in the alloxan-induced diabetic rats at dosages of 125 mg/kg and 250 mg/kg [41]. There are several mechanisms of action in the antidiabetic activity of *Syzygium cumini* in type 2 diabetes, such as the improvement of insulin resistance and β-cell dysfunction through the modulation of PPARγ and the reduction in dyslipidemia, oxidative stress and TNF-α [183].

Figure 33. *Syzygium cumini.*

3.34. Tamarindus indica

Tamarindus indica (Figure 34), commonly known as Tamarind, is a leguminous tree in the Fabaceae family. The leaves and fruits of the plant have been used to treat diabetes [85]. The plant is native to the Indian subcontinent and most tropical countries. It has been used to treat diarrhea, dysentery, wound healing, bacterial and parasitic infections. It contains essential amino acids and phytochemicals and possesses antimicrobial, antivenom and anti-diabetic properties [184]. Furthermore, *T. indica* consists of phenolic compounds, β-sitosterol, proanthocyanidins, apigenin, tartaric acid, cardiac glycosides, mucilage, pectin, eicosanoic acid and β-sitosterol, as well as essential elements such as calcium, copper, iron, manganese, magnesium, palmitic acid, oleic acid, succinic acid, formic acid, β-amyrin, apigenin, epicatechins, catechins, taxifolin, eriodictyol, naringenin, etc. [116]. Abukakar et al. (2008) administered aqueous pulp extract to adult albino rats for acute-toxicity testing. No toxicity was observed in the tests up to 900–4500 mg/kg body weight. However, at higher doses of 2700–4500 mg/kg, mild behavioral changes, such as anorexia, restlessness, sensitivity to sound, etc., were observed. Nevertheless, no mortality was observed at these concentrations, with no apparent histopathological alterations. Therefore, the plant had no apparent toxic effects in animal models, which supported its safe usage as a medicine [165]. In a study conducted by Parvin et al. (2013), 1.25 g/kg of *T. indica* seed powder was administered to non-diabetic and STZ-induced diabetic Long–Evans rats and demonstrated anti-hyperglycemic properties ($p < 0.03$) (Table 1) [45]. The antidiabetic property of *Tamarindus indica* seeds may be due to the presence of phenols and flavonoids, as they have insulin-mimetic properties and stimulate glucose uptake [185]. A recent study by Costa et al. (2022) also suggested this insulin-mimetic effect [186]. The specific molecular mechanism involves increases in the expression of glucose transporter (GLUT-2 and GLUT-4) genes, which increase glucose uptake and help to maintain glucose homeostasis. Furthermore, the compounds in *T. indica* increase the concentration of Ca^{2+} in islets of Langerhans cells, stimulating β-pancreatic cell proliferation and enhancing insulin secretion [185].

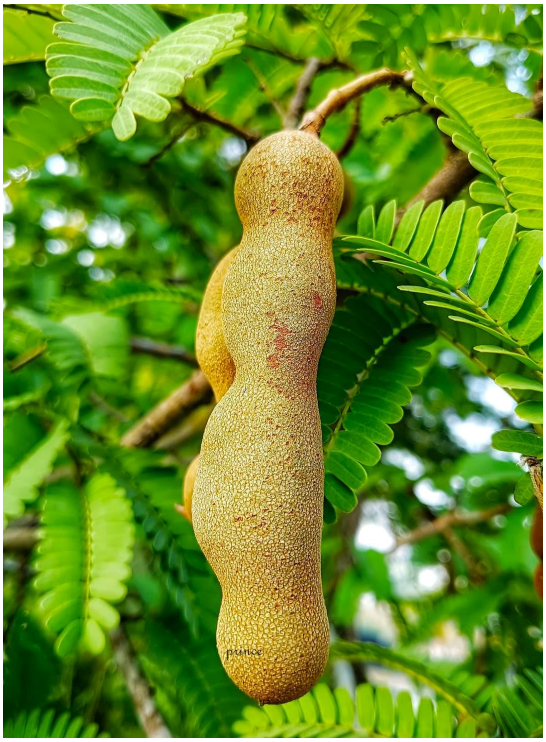

Figure 34. *Tamarindus indica*.

3.35. Terminalia catappa

Terminalia catappa (Figure 35) belongs to the family Combretaceae and is locally known as Bangla badam [187]. The juice of its leaves is used to treat skin conditions, such as leprosy and scabies. It is also ingested to alleviate symptoms of stomach ache and headache. Furthermore, it has antimicrobial, anti-inflammatory, antioxidant and anti-cancer activities, alongside its anti-diabetic properties [129]. The plant contains tannins, saponins, phenolics, flavonoids, triterpenoids, punicalin, punicalagin, kaempferol, geraniin, punicalin, quercetin, gentisic acid, tercatain, tergallagin, β-carotene, cyanidin-3-glucoside, ellagic acid, gallic acid, etc. [59,129].

Figure 35. *Terminalia catappa*.

According to a study by Ahmed et al. (2005), aqueous and cold plant-leaf extracts reduced fasting blood sugar levels in alloxan-induced diabetes rats, with glibenclamide (10 mg/kg body weight) used as a control. The regeneration of the pancreas was confirmed by the results of histological tests [59]. The anti-diabetic properties of *Terminalia catappa* leaf extract involve the activation of the PI3K/AKT pathway, the reversal of insulin resistance and the enhancement of glucose transport in type 2 diabetes [188]. Azrul et al. (2013) conducted a toxicity study in which they investigated the primary and secondary toxicity of a crude aqueous extract from *T. catappa* in Sprague–Dawley rats by administering 0.5, 1.0 and 3.0 g/kg body weight of the extract to the rats for 14 days. No mortality or signs of toxicity were noted in the rats [169].

3.36. Terminalia chebula

Terminalia chebula (Figure 36), commonly known as Myrobalan, is a plant in the Combretaceae family [189]. The plant's leaves are known to have antihyperglycemic properties and are thus reportedly used to treat diabetes by traditional health practitioners [180]. The plant contains flavonoids, β-sitosterol, tannins, sterols, gallic acid, chebulanin, corilagin, ellagic acid, chebulinic acid, amino acids, fructose, resin, triterpenoids, glycosides, etc. The plant has laxative, carminative, anti-diabetic, anti-cancer, antimutagenic and antiviral properties [58,128]. According to a study by Kumar et al. (2006), STZ-induced rats were orally administered with 200 mg/kg body weight of the fruit extract of the plant. Within 30 days of the administration, the rats showed lowered blood glucose levels. The fruit extract was linked with insulin stimulation and its effectiveness was comparable with the hypoglycemic drug, glibenclamide (600 µg/kg body weight) ($p < 0.05$) [58]. The bioactive compounds present in *Terminalia chebula* fruit exhibit insulin-like actions and inhibit the α2 receptors of pancreatic β-cells, increasing insulin secretion [190]. In an acute-toxicity study of *T. chebula* conducted by Panunto et al. (2010), aqueous extracts from dried fruits from the plant were orally administered to five male and five female rats at a single dose of 5000 mg/kg body weight. The extract did not confer any mortality, behavioral changes or changes in the internal organs, demonstrating that the extract was non-toxic [168].

Figure 36. *Terminalia chebula*.

3.37. Wedelia chinensis

Wedelia chinensis (Figure 37), also known as Wedelia, is a climbing wetland herb from the Asteraceae family native to India, China and Japan. Furthermore, is reported to have anti-cancer, antimicrobial, antioxidant and anti-inflammatory properties and contains flavonoids, alkaloids, saponins, phytosterols, mucilage, carbohydrates and tannins [171,191]. Bari et al. (2020) demonstrated that the administration of 100 mg/kg and 200 mg/kg body weight of methanolic extract of *W. chinensis* to alloxan-induced hyperglycemic Swiss albino mice significantly reduced blood glucose levels ($p < 0.01$), in addition to improving the lipid profiles (TG, LDL, TC, VLDL and HDL) compared to standard the drug (glibenclamide 5 mg/kg body weight) [65]. Compounds isolated from *W. chinensis* leaves, especially flavonoids, have significant α-amylase- and α-glucosidase-inhibitory activity, which is an effective mechanism for managing type 2 diabetes [192]. In a study conducted by Umasankar et al. (2010), the toxicity of the ethanolic extract from *W. chinensis* was investigated following the methods of Litchfield and Wilcoxon (1949). The extracts were each administered in doses of 100, 200, 400, 800 and 1600 mg/kg body weight to five different groups of mice. The mice were observed for mortality for the subsequent 72 h. The extract did not confer mortality or toxicity, indicating that the LD50 value of the extract was >1600 g/kg body weight [171].

Figure 37. *Wedelia chinensis*.

4. Plant-Based Treatments: Current Progress and Future Prospects

Plants are natural sources of bioactive compounds, with various health-beneficial pharmacological activities [193]. The comparatively low or almost no toxicity of the 37 plants discussed above is the main advantage of plant-based treatments. With the progress in the understanding of the mechanisms through which plant extracts can be used to treat different conditions, researchers are conducting clinical trials. A randomized, double-blind, placebo-controlled clinical trial on sixty type 2 diabetes mellitus (T2DM) patients was conducted by Ghafouri et al. (2020) to evaluate the hypoglycemic effect of *Rheum ribes* extracts. The consumption of *Rheum ribes* extracts improved the diabetic patients' insulin sensitivity, malondialdehyde levels and high-sensitivity C-reactive protein levels significantly [194]. In a clinical trial, the widely used synthetic antidiabetic drug metformin's efficacy was improved by a Ginkgo biloba extract as an adjuvant [195]. Another recent development in the management of T2DM is the use of herbal nanoformulations of plant-based natural products, which have been proven to be better than crude extracts [196]. Plant-based vaccines have shown significant therapeutic potential to treat respiratory diseases in recent years [197]. This is evidence that in the future, plant-based treatments will greatly influence the discovery of novel drugs and treatments. However, the mechanism of action behind different pharmacological activities is yet to be established for many plants; this is one of the main limitations of plant-based

treatments. A caveat to the use of medicinal plants is that approximately 15,000 species are in danger of becoming extinct due to habitat loss and overharvesting, highlighting the urgent need for conservation efforts [198]. The implementation of biotechnological techniques, such as tissue culture, micropropagation, synthetic seed technology and molecular-marker-based approaches can enhance the yield and modify the potency of medicinal plants. These advances can be complemented with conservation strategies to ensure the sustainable use of these resources [198]. The phytoconstituents responsible for the pharmacological activities and their mechanism of action with safety measures should be studied more extensively, followed by clinical trials. This will lead to the development of plant-based treatments that are accepted by medical science.

5. Conclusions

There is potential for plant medicine to become an established form of alternative medicine in Bangladesh due to its effectiveness, affordability and accessibility. It is encouraged to undertake further research and studies to maximize the potential of these plants for use in the management of diabetes mellitus, a widespread affliction in Bangladesh and the wider world. As the world is searching for new natural sources of drugs to treat diabetes mellitus, plants for which the mechanism behind their antidiabetic effect has already been established and clearly understood may be chosen for developing antidiabetic drugs. Further clinical trials can be conducted to prove their efficacy.

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