Pharmacologically Active Phytomolecules Isolated from Traditional Antidiabetic Plants and Their Therapeutic Role for the Management of Diabetes Mellitus

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Abstract: Diabetes mellitus is a chronic complication that affects people of all ages. The increased prevalence of diabetes worldwide has led to the development of several synthetic drugs to tackle this health problem. Such drugs, although effective as antihyperglycemic agents, are accompanied by various side effects, costly, and inaccessible to the majority of people living in underdeveloped countries. Medicinal plants have been used traditionally throughout the ages to treat various ailments due to their availability and safe nature. Medicinal plants are a rich source of phytochemicals that possess several health benefits. As diabetes continues to become prevalent, health care practitioners are considering plant-based medicines as a potential source of antidiabetic drugs due to their high potency and fewer side effects. To better understand the mechanism of action of medicinal plants, their active phytoconstituents are being isolated and investigated thoroughly. In this review article, we have focused on pharmacologically active phytomolecules isolated from medicinal plants presenting antidiabetic activity and the role they play in the treatment and management of diabetes. These natural compounds may represent as good candidates for a novel therapeutic approach and/or effective and alternative therapies for diabetes.

Keywords: medicinal plants; traditional medicine; phytoconstituents; diabetes; pharmacology

1. Introduction

Diabetes mellitus is one of the most common endocrine metabolic disorders characterized by chronic hyperglycemia caused by varying degrees of insulin resistance, deficiency in insulin secretion, or both [1]. Nearly 10.5% of the worldwide population is affected by diabetes, with its prevalence increasing at an alarming rate. According to data collected from the International Diabetes Federation (IDF), about 783.2 million people are estimated to be diagnosed with diabetes by 2045 [2]. Diabetes mellitus can be classified into two major categories: Type 1 and Type 2 diabetes, where Type 2 diabetes accounts for about 90% of all cases. Type 1 diabetes, previously known as insulin-dependent diabetes, is an autoimmune disorder that occurs due to the destruction of the pancreatic beta cells leading to significantly reduced secretion of insulin [3]. It is a non-hereditary genetic condition that mainly affects the juvenile under thirty years of age. Type 2 diabetes, also known as non-insulin-dependent diabetes, is the most common form of diabetes, with its prevalence rapidly rising worldwide [4]. It is a hereditary condition caused as a result of insulin resistance, insufficient insulin secretion, or a combination of both, largely affecting an older population than Type 1 diabetes [5]. Both forms of diabetes alter carbohydrate, protein, and fat metabolism. The effect of insulin resistance leads to high blood sugar levels...
by hindering the uptake and efficient use of glucose by most cells of the body [6]. The progression of the disease is accompanied by tissue or vascular damage resulting in severe complications, including retinopathy, diabetic neuropathy, nephropathy, cardiovascular, pulmonary, cerebral, and peripheral vascular diseases, ulcers, and thyroid gland disorders, leading to serious morbidity and mortality [1,7–9]. Available therapies currently in use for the treatment and management of diabetes include insulin and several oral hypoglycemic agents such as metformin, sulfonylureas, α-glucosidase inhibitors, meglitinide analogues, thiazolidinediones, DPP-IV inhibitors, SGLT-2 inhibitors, and GLP-1 mimetics. However, these drugs, intended to boost insulin sensitivity and increase insulin secretion together with the reduction in circulatory plasma glucose levels by increasing glucose excretion or uptake in adipose tissue, are usually associated with many side effects. These include, among others, weight gain, hypoglycemia, gastrointestinal tract disturbances, liver injury, renal failure, hypersensitivity reactions, flatulence, diarrhea, and abdominal bloating [1,10,11]. In addition, these drugs have been known to have other major disadvantages, including drug resistance, and there is also a lack of therapies to prevent the long-term complications of the disease.

The complications associated with insulin and oral antidiabetic agents, together with limited drug tolerability, adverse effects, and cost, have accelerated the search for alternative medicines with better efficacy, potency, and fewer side effects [12]. Interestingly, there has been an increase in popularity surrounding drug discovery research into natural antidiabetic agents, especially those derived from medicinal plants, which could enhance β-cell function and treat diabetes-associated complications with fewer adverse side effects [13].

Herbal medicines contain a diversity of phytochemicals and have been traditionally used for treating a wide variety of diseases. They are considered to be naturally safe and efficacious with fewer side effects [12]. The control and management of diabetes using herbal drugs have proven to be more advantageous over synthetic medicines due to their accessibility, reduced cost, lesser complications, and lower side effects. Herbal medicines act via different mechanisms aiming at reducing insulin resistance, increasing insulin secretion, protecting pancreatic beta cells, and thereby lowering circulating blood glucose levels [14].

Throughout the years, thousands of plant species have been used for their medicinal uses as integrative medicines for various diseases, of which more than 800 plants have been reported to exhibit antidiabetic effects [15]. Such plants have been examined for their use in the treatment of the different types of diabetes and could be potential sources for new natural antidiabetic drug discovery research [16]. A number of medicinal plants used traditionally for their antidiabetic activity are currently under investigation to be formulated commercially as modern drugs. This is particularly the case in developing countries where the cost of allopathic medicine is high, and the traditional use of plants to treat diabetes is common practice [15]. Traditional natural medicines are extensively prescribed in Asian countries (e.g., China, India, Bangladesh, Pakistan, Sri Lanka, Thailand, Nepal, Bhutan, Japan, and others) [17]. Among the medicinal plants possessing hypoglycemic effects, the most common ones used as remedies for diabetes include Acacia arabica, Aegle marmelos, Allium cepa, Allium sativum, Aloe vera, Ammona squamosa, Azadirachta indica, Berberis vulgaris, Camellia sinensis, Capsicum frutescens, Cassia alata, Cinnamomum zeylanicum, Eucalyptus globulus, Eugenia jambolana, Helicteres isora, Momordica charantia, Panax ginseng, Punica granatum, Swertia chirayita, Trigonella foenum-graecum, and others [15,16,18,19]. The antidiabetic activity of these plants is thought to be mediated via various mechanisms, including the stimulation of insulin secretion from pancreatic β-cells, increasing insulin binding to receptors, reduction in insulin resistance, and improving glucose tolerance. Other modes of action include enhancing glucose metabolism, improving β-cell mass and function, and increasing plasma insulin, thus decreasing circulating blood glucose levels [20–23]. In addition to being used to treat diabetes, these plants have also been traditionally employed to treat other conditions such as ulcers, wounds, inflammation, infections, diarrhea, dysentery, malaria, rheumatism, hypertension, obesity, pneumonia,
and kidney diseases [12,19,24–26]. The main objective of this review is to explore the
traditional plant-based therapies and/or their phytoconstituents available for the treatment
of diabetes. These could provide the basis for the discovery of new antidiabetic drugs with
fewer side effects and stronger efficacy than currently available medicines.

2. Methods

A literature search was carried out via Google Scholar, ScienceDirect, Scopus, and
PubMed databases to accumulate data for this review article using the keywords “Diabetes
mellitus,” “Medicinal Plants,” “Traditional medicine,” “Antidiabetic phytochemicals,” and
“Plant-based antidiabetic therapy.” The data search was not restricted to a specific time
period; however, around 98% of the gathered data were published between 2000 and
2022, and only 2% were published before 2000. Our data collection began in early January
until late May 2022. More than 700 papers were found relevant to our study, and after
performing a primary screening, around 400 papers were selected to be critically examined.
An overview of the key findings has been presented in this current review.

3. Ethnomedicines and Their Scope in the Modern World

Ethnomedicine is a traditional health care practice followed by indigenous people con-
cerned with human health. It is the origin of all other traditional medical systems, including
Ayurveda, Siddha, Unani, Nature Cure, as well as modern medicine [27]. Knowledge of
plants presenting therapeutic properties has been passed on by experimenting through
trials and errors from one generation to the next for more than hundreds of years. Eth-
nomedicines are highly prevalent in the rural and native communities of several developing
countries [28]. According to information collected from the World Health Organization,
about 80% of the global population relies upon traditional remedies [29]. Medicinal plants
have always been recognized as a major source of raw materials for both conventional and
traditional medicines [30]. In India, the poor and rural residents are dependent upon na-
atural herbal remedies since they are easily obtainable to them. Indeed, plant-based medicines
are the sole source of medical management for people living in remote areas. In countries
such as Russia, Africa, and a few European countries, ethnomedicines are being studied
by various botanists, anthropologists, folklorists, and medical scientists [27]. The inability
for people to access adequate healthcare, alongside financial restrictions, has resulted in
the under-provision of modern health care for a majority of the people in underdeveloped
countries. [31]. Numerous folk remedies are recorded as being effective in treating various
diseases (such as digestive tract disorders, skin diseases, renal and liver diseases, malaria,
ulcers, heart diseases, pneumonia, diabetes, and many others), and thus, even developed
countries have also considered utilizing these medicines [32].

4. Plant-Based Medicine versus Synthetic Medicine

Many drugs that are currently available have been derived directly or indirectly from
natural sources such as medicinal plants and animals [33,34]. Plant-derived natural prod-
ucts have played and continue to play a prominent role in drug discovery and development
programs. The increase in the number of herbal drug manufacturing companies, linked to
the current increase in interest and demand for herbal medicines, can be largely expanded
because of the toxicity and numerous adverse effects of allopathic medicines [35]. The
convenience of accessibility, availability, inexpensiveness, and relatively low risks of side
effects, have caused plant-based medicines to be an important alternative source of exist-
ing therapies, especially in rural and/or developing regions [33]. Plant-based medicines
also provide a rich source of biologically active compounds that possess pharmacological
activity with minimal undesirable effects [33].

Over the centuries, plant-based medicines have been widely used to treat the ailments
of local communities of many developing countries that have easy access to these sources.
Densely populated countries, such as China and India, have especially contributed to the
advancement of sophisticated traditional medical systems such as acupuncture, ayurvedic
medicine, and herbal medicine [36]. Many factors should be considered when selecting the appropriate medications for the management and treatment of diabetes. This includes efficacy, adverse effects, cost, and potential to contribute to weight gain, risks associated with hypoglycemia, comorbidities, and patient compliance. Even though oral antihyperglycemic agents can lower plasma glucose levels by improving insulin secretion or reducing insulin resistance, they are associated with many other adverse effects. Metformin, the mainstay of treatment in type 2 diabetes, has a high safety profile, yet it is still associated with mild side effects such as low risks of hypoglycemia and gastrointestinal tract disturbances (nausea, diarrhea, dyspepsia). Previous studies have shown that continuous use of metformin may result in vitamin B12 and folic acid deficiency in humans [37]. DPP-IV inhibitors such as sitagliptin, saxagliptin, and linagliptin, have been found to cause headaches, nasopharyngitis, and upper respiratory tract infections [38]. The most common adverse effect of sulfonylureas such as glimepiride and gliclazide is hypoglycemia. These drugs are also associated with minor side effects such as weight gain, nausea, headaches, drowsiness, and hypersensitivity reactions. The most serious complication of insulin injections is hypoglycemia. Insulin may also cause weight gain or loss, dizziness, confusion, and sweating [38]. In contrast to synthetic drugs, plant-based medicines do not interrupt the body’s natural healing process; instead, they accelerate the recovery process by strengthening the healing process, ultimately leading to a steady recovery. Alongside their ability to help the body recover to a healthy status, herbal medicines are also known for boosting the immune system. The use of highly effective herbal medicines showing fewer side effects and a strong immune system together with a healthy lifestyle promotes better body metabolism with increased nutritional absorption from the diet [35]. Whether they have insulinotropic, insulin-mimetic, or any other antihyperglycemic effects, medicinal plants are considered safer and more effective alternatives to synthetic antidiabetic drugs [39].

5. Pharmacological Activity of Plant-Based Medicines

Although knowledge of many plant-based therapies has been transmitted through generations, only a few of these have started to come to the fore recently. However, there is still some uncertainty regarding their pharmacological activity as well as their acute/chronic side effects due to such medicines being broadly underreported [40]. Few plants have proven to be efficacious for which they were intended, whilst some were not strongly therapeutically effective and/or sufficient scientific data were lacking to support their expected effects [41]. The increase in the widespread use of plant-based therapies has led to an urgent need for a detailed scientific examination of the chemicals responsible for pharmacological activity. Indeed, such a study of the pharmacological properties and phytoconstituents of plant-based medicines may lead to the discovery of new pharmacological characteristics previously unknown or used in traditional medicine [42]. Herbal medicines have been suggested to exert their mechanism of action by concurrently targeting multiple physiological processes via interactions between different biochemicals and cellular proteins [43].

Herbal medications may be able to alter the biological systems from disease to a healthy state by causing the interactions between multi-component and multi-target. Because of the therapeutic properties of the phytomolecules, a lower dosage may be used, resulting in less toxicity and adverse effects. [43]. The antidiabetic activity of medicinal plants is dependent upon the phytochemicals that act through multiple pathways, such as cAMP: which stimulates insulin secretion without affecting the K\textsubscript{ATP} channel [44]; PI3K: which facilitates glucose uptake by the translocation of the glucose transporter in skeletal muscles, adipose tissue, or liver [45]; AMPK: The activation of 5′-adenosine monophosphate-activated protein kinase pathway improves insulin sensitivity by limiting lipolysis and lipogenesis, and AMPK also enhances glucose uptake in skeletal muscles by translocating GLUT4-containing intracellular vesicles across the plasma membrane [46,47]. For example, phlorizin obtained from the bark of apple and pear trees increases glucose excretion in urine by decreasing glucose reabsorption in the kidneys via the inhibition of SGLT and thus, lowers plasma
glucose concentration \[48\]. Some of the phytomolecules have the potential to regenerate and protect pancreatic beta cells from destruction by reducing the glucose load \[49\], inhibiting \(\alpha\)-amylase and \(\alpha\)-glucosidase activity, inducing glucose uptake in 3T3L1 cells \[50,51\], inhibiting aldose reductase enzyme activity, glycogen metabolizing enzymes, exerting hepato-pancreatic protective activity, inhibiting glucose-6-phosphate and DPP-IV, reducing lactic dehydrogenase, \(\gamma\)-glutamyl transpeptidase, glycosylated hemoglobin levels, and inhibiting glycogenolysis and gluconeogenesis in the liver \[20,52\]. As an example, a summary of the different pathways involved in the antidiabetic activity of flavonoids is illustrated in Figure 1. A summary of antidiabetic medicinal plants and their pharmacological actions has been shown in Table 1.

**Figure 1.** Flavonoids exerting antidiabetic activity via different mechanistic pathways: Flavonoids increase insulin secretion and improve \(\beta\)-cell function via the PI3K/AKT signaling pathway; increase GLUT-4 translocation through AMPK activation to increase glucose uptake in adipose tissues and skeletal muscles; activate PPAR-\(\gamma\) expression to decrease insulin resistance; activate cAMP/PKA pathway to reduce blood glucose levels and improve glucose tolerance; increase glutathione peroxidase activity to reduce HbA1c levels; decrease G-6-Pase, PEPCK, glycogen phosphorylase, fructose 1,6-biphosphatase and DPP-IV activity in liver to decrease gluconeogenesis, glycogenolysis, and glycosylation; inhibit SGLT pathway in kidney to decrease renal glucose reabsorption; inhibit GLUT-2, \(\alpha\)-amylase and \(\alpha\)-glucosidase activity to decrease glucose absorption in the small intestine.
Table 1. Traditional uses and pharmacological effects of antidiabetic medicinal plants.

| Medicinal Plants     | Parts           | Traditional Uses                                      | Pharmacological Effects                                                                 | References |
|----------------------|-----------------|-------------------------------------------------------|------------------------------------------------------------------------------------------|------------|
| 1. Abrus precatorius | Leaves, seeds   | Diabetes, wounds, fever, cough, cold, tetanus         | Improves β-cell function, inhibits α-amylase and α-glucosidase activity                  | [53,54]    |
| 2. Acacia arabica    | Bark, roots     | Diabetes, astringent, diarrhea, parasitic worms, diuretic, liver tonic | Lowers blood glucose levels, increases insulin secretion, improves glucose uptake and glucose tolerance | [24,55]    |
| 3. Acacia catechu    | Bark            | Diabetes, asthma, bronchitis, diarrhea, obesity, dysentery, skin diseases | Lowers blood glucose levels, increases insulin secretion                                  | [56–58]    |
| 4. Aegle marmelos    | Leaves          | Diabetes, dysentery, inflammation, ulcer, diarrhea, asthma | Lowers blood glucose levels, increases insulin secretion, glucose uptake and metabolism, inhibits aldose reductase and DPP-IV enzyme activity | [56,59,60] |
| 5. Aframomum melegueta | Fruit, leaves  | Diabetes, cough, diarrhea, stomach ache, leprosy, hypertension, measles | Lowers plasma glucose levels, inhibits α-amylase and α-glucosidase activity                | [61,62]    |
| 6. Ageratum conyzoides | Leaves         | Diabetes, fever, rheumatism, cardiovascular diseases, malaria, wounds, spasms | Lowers blood glucose levels, improves β-cell function, increases insulin secretion        | [63,64]    |
| 7. Albizia lebbeck  | Bark, pods      | Diabetes, asthma, diarrhea, infections, dysentery, inflammation | Lowers blood glucose levels, increases insulin secretion, enhances glucose uptake         | [56,65,66] |
| 8. Albizia adianthifolia | Bark, leaves | Diabetes, eye problems, hemorrhoids, skin diseases, wounds, malaria diarrhea, indigestion | Lowers blood glucose levels, improves glucose tolerance                                   | [16,67]    |
| 9. Allium cepa       | Bulb            | Diabetes, bronchitis, hypertension, skin infections, swelling, lower cholesterol level | Increases insulin secretion and insulin sensitivity, improves glucose uptake               | [68,69]    |
| 10. Allium sativum   | Bulb            | Diabetes, fever, hypertension, rheumatism, dysentery, bronchitis, intestinal worms | Increases insulin secretion and insulin sensitivity to cells                               | [70,71]    |
| 11. Aloe vera        | Leaves          | Diabetes, constipation, infections, ulcer, dysentery, piles, rheumatoid arthritis | Lowers blood glucose levels, increases insulin secretion, reduces insulin resistance, improves glucose tolerance | [72,73]    |
| 12. Anacradium occidentale | Leaves, stem bark | Diabetes, fever, hypertension, rheumatism, toothache, piles, dysentery | Lowers blood glucose levels, reduces oxidative stress, decreases total cholesterol and triglyceride levels | [74–76]    |
| Medicinal Plants              | Parts       | Traditional Uses                                      | Pharmacological Effects                                                                 | References |
|------------------------------|-------------|-------------------------------------------------------|-----------------------------------------------------------------------------------------|------------|
| 13. *Anemarrhena asphodeloides* | Rhizome     | Diabetes, fever, cough, inflammation, infections, night sweats, dementia | Lowers blood glucose levels, increases insulin sensitivity, improves glucose uptake       | [77,78]    |
| 14. *Annona salzmannii*      | Leaves, bark | Diabetes, inflammation, tumors                         | Lowsers blood glucose levels, improves β-cell function, increases insulin secretion        | [79,80]    |
| 15. *Annona squamosa*        | Leaves      | Diabetes, wounds, inflammation, hypertension, malaria, insect bites | Lowsers blood glucose levels, increases insulin secretion, improves glucose tolerance and β-cell function | [10,81]    |
| 16. *Anogeissus latifolia*   | Bark        | Diabetes, diarrhea, hemorrhoids, dysentery, snake bites, stomach disorders, skin diseases, leprosy | Decreases blood glucose levels, improves β-cell function, increases insulin secretion, inhibits DPP-IV enzyme activity | [56,82,83] |
| 17. *Arachis hypogaea*       | Seeds       | Diabetes, inflammation, heart diseases, coagulation, rheumatism, hypertension, Alzheimer’s disease | Increases insulin secretion and insulin sensitivity, improves glucose tolerance            | [84–86]    |
| 18. *Artemisia absinthium*   | Rhizome     | Diabetes, wounds, indigestion, gastritis, anemia, hepatitis, cardiovascular diseases, gall bladder disorders | Increases insulin sensitivity, improves glucose uptake, enhances GLUT-4 translocation | [87–89]    |
| 19. *Artocarpus heterophyllus* | Leaves, rhizome | Diabetes, diarrhea, malaria, wounds, anemia, inflammation | Lowsers blood glucose levels, decreases glycosylated hemoglobin levels                    | [78,90]    |
| 20. *Asparagus racemosus*    | Roots       | Diabetes, constipation, ulcers, stomach disorders, cough, inflammation | Increases insulin secretion and action, improves β-cell function, inhibits carbohydrate digestion and absorption | [91–94]    |
| 21. *Atractylodes japonica*  | Rhizome     | Diabetes, rheumatism, gastrointestinal diseases, influenza, night blindness, diuretic, stomachic | Lowsers blood glucose levels, reduces insulin resistance, improves glucose uptake         | [95,96]    |
| 22. *Azadirachta indica*     | Leaves      | Diabetes, malaria skin diseases, infections, cardiovascular diseases, intestinal worms | Lowsers blood glucose levels, increases insulin secretion, improves pancreatic β-cell function, inhibits α-amylase and α-glucosidase activity, enhances glucose uptake | [56,97,98] |
| 23. *Balanites aegyptiaca*   | Fruit       | Diabetes, wounds, asthma, malaria, diarrhea, hemorrhoids, fever, infections | Increases insulin secretion, improves glucose uptake, inhibits α-glucosidase activity     | [99,100]   |
| 24. *Berberis vulgaris*      | Root, bark  | Diabetes, eye infections, piles, wounds, snake bites, hemorrhoids, dysentery | Reduces blood glucose levels, increases insulin secretion                                | [101,102]  |
| Medicinal Plants          | Parts                  | Traditional Uses                                                                 | Pharmacological Effects                                                                                                                                                                                                                                                                                                                                 | References            |
|---------------------------|------------------------|-----------------------------------------------------------------------------------|                                                                                                                                                                                                                                                                                                                                                           |                      |
| 25. *Bidens pilosa*       | Root                   | Diabetes, wounds, hepatitis, diarrhea, urinary tract infections, cold, glandular sclerosis | Increases plasma insulin, improves glucose tolerance, protects or prevents islet degeneration                                                                                                                                                                                                                                                                                                                  | [103,104]             |
| 26. *Bougainvillea spectabilis* | Flowers, leaves     | Diabetes, inflammation, ulcers, sore throat, infections, contraceptive            | Regenerates β-cell function, increases plasma insulin levels, reduces intestinal glucosidase activity                                                                                                                                                                                                                                                                                                              | [105,106]             |
| 27. *Brassica juncea*     | Leaves, seeds          | Diabetes, arthritis, rheumatism, back pain, coughs, paralysis                     | Increases insulin secretion and glucose utilization                                                                                                                                                                                                                                                                                                                                                                  | [16,107]              |
| 28. *Bridelia ferruginea* | Leaves, stem bark      | Diabetes, headache, arthritis, fever, inflammation                               | Lowers blood glucose levels, inhibits α-amylase and α-glucosidase activity                                                                                                                                                                                                                                                                                                                                          | [108,109]             |
| 29. *Bunium persicum*     | Seeds                  | Diabetes, diarrhea, gastrointestinal disorders, inflammation, obesity, asthma     | Lowers blood glucose levels, improves glucose uptake and utilization                                                                                                                                                                                                                                                                                                                                               | [56,110,111]          |
| 30. *Caesalpinia decapetala* | Leaves                | Diabetes, indigestion, flatulence, stomach aches, constipation, fever             | Lowers blood glucose levels, protects pancreatic beta cells, decreases oxidative stress                                                                                                                                                                                                                                                                                                                               | [112,113]             |
| 31. *Calendula officinalis* | Leaves, bark           | Diabetes, fever, infections, wounds, menstrual irregularity, poor eyesight, inflammation, ulcers | Lowers blood glucose levels, increases plasma insulin levels                                                                                                                                                                                                                                                                                                                                                      | [114,115]             |
| 32. *Camellia sinensis*   | Leaves                 | Diabetes, heart diseases, diuretic, astringent, stimulant, flatulence             | Increases insulin secretion and action, inhibit insulin glycation, DPP-IV enzyme, and α-amylase activity, improves glucose tolerance                                                                                                                                                                                                                                                                              | [116,117]             |
| 33. *Capsicum frutescens* | Whole plant            | Diabetes, gastrointestinal disorders, toothache, pain, muscle spasms, fever, infections | Increases insulin secretion and insulin sensitivity, improves glucose uptake                                                                                                                                                                                                                                                                                                                                         | [118,119]             |
| 34. *Carica papaya*       | Fruit, leaves          | Diabetes, gastrointestinal disorders, dengue, malaria, nerve pains, insomnia, constipation | Lowers blood glucose levels, increases insulin secretion, suppresses glucagon secretion                                                                                                                                                                                                                                                                                                                             | [120,121]             |
| 35. *Cassia alata*        | Leaves, seeds          | Diabetes, skin diseases, rheumatism, constipation, ringworm, infections, inflammation | Lowers blood glucose levels, inhibits α-glucosidase activity                                                                                                                                                                                                                                                                                                                                                      | [122,123]             |
| 36. *Cassia fistula*      | Stalk                  | Diabetes, wounds, constipation, piles, skin diseases, asthma, liver diseases, rheumatism, leprosy | Lowers blood glucose levels, increases insulin secretion, improves glucose uptake and utilization                                                                                                                                                                                                                                                                                                                      | [56,124–127]          |
Table 1. Cont.

| Medicinal Plants | Parts         | Traditional Uses                                      | Pharmacological Effects                                                                                                      | References   |
|------------------|---------------|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|--------------|
| 37. *Catharanthus roseus* | Leaves, roots | Diabetes, hypertension, menstrual irregularity, cancer, wounds, muscle pain | Lowers blood glucose levels, increases insulin sensitivity, improves glucose uptake and utilization                            | [128–130]    |
| 38. *Cecropia obtusifolia* | Root bark     | Diabetes, asthma, bronchitis, heart diseases, inflammation, wounds, hypertension | Lowers blood glucose levels, decreases glycosylated hemoglobin levels                                                        | [78,131]     |
| 39. *Cichorium intybus* | Bark, leaves  | Diabetes, constipation, wounds, liver diseases        | Increases insulin secretion and insulin sensitivity, improves glucose uptake                                                  | [78,132]     |
| 40. *Cinnamomum zeylanicum* | Bark          | Diabetes, common cold, flu, gastrointestinal disorders, bacterial infections, headache, stomach pain | Increases plasma insulin levels, increases insulin sensitivity, inhibits α-amylase activity                                      | [133,134]    |
| 41. *Citrus limon* | Fruit         | Diabetes, hypertension, infections, scurvy, sore throat, rheumatism | Lowers plasma glucose levels, inhibits α-amylase activity                                                                     | [135,136]    |
| 42. *Citrus x aurantium* | Fruit         | Diabetes, insomnia, indigestion, constipation, heartburn, nausea, cardiovascular diseases | Lowers blood glucose levels, increases insulin secretion                                                                      | [137,138]    |
| 43. *Cola nitida* | Seeds         | Diabetes, dysentery, fatigue, CNS stimulant, morning sickness, migraine, indigestion, wounds | Lowsers blood glucose levels, increases serum insulin levels                                                                | [139,140]    |
| 44. *Coptis chinensis* | Rhizome       | Diabetes, sore throat, whooping cough, dysentery, neurodegenerative diseases | Lowers blood glucose levels, increases insulin sensitivity, improves glucose uptake                                           | [141,142]    |
| 45. *Cornus officinalis* | Fruit, seeds  | Diabetes, pain, inflammation, cardiovascular diseases, liver, and kidney diseases | Lowsers blood glucose levels, increases insulin secretion, inhibits α-glucosidase activity, increases GLUT-4 expression | [143,144]    |
| 46. *Curcuma longa* | Rhizome       | Diabetes, gastric, inflammation, infections, cough, pain, liver diseases | Lowsers blood glucose levels, inhibits α-amylase and α-glucosidase activity, increases insulin secretion, improves peripheral glucose uptake, reduces insulin resistance | [78,145,146] |
| 47. *Cudrania cochinchinensis* | Bark, roots   | Diabetes, hepatitis, scabies, bruises, gonorrhea, jaundice, rheumatism | Lowsers blood glucose levels, increases insulin secretion, improves glucose uptake and utilization, inhibits DPP-IV enzyme and α-glucosidase activity | [56,147,148] |
| Medicinal Plants | Parts           | Traditional Uses                                                                 | Pharmacological Effects                                                                 | References         |
|------------------|-----------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|--------------------|
| 48.              | *Cyamopsis tetragonoloba* | Fruit Diabetes, night blindness, arthritis, sprains, constipation, asthma, liver diseases, obesity | Increases insulin secretion, protects pancreatic beta cells, decreases glycosylated hemoglobin levels | [149,150]          |
| 49.              | *Dalbergia sissoo*   | Bark Diabetes, stomach disorders, dysentery, skin diseases, syphilis, nausea, gonorrhea | Lowers blood glucose levels, reduces serum triglyceride and cholesterol levels            | [56,151,152]       |
| 50.              | *Eriobotrya japonica* | Leaves, seeds Diabetes, bronchitis, inflammation, cough                           | Lowers blood glucose levels, reduces insulin resistance, improves glucose tolerance       | [153,154]          |
| 51.              | *Eucalyptus citriodora* | Leaves Diabetes, fever, pain, sinusitis, bronchitis, asthma, chronic rhinitis,     | Increases insulin secretion, improves glucose uptake, inhibits insulin glycation and DPP-IV enzyme activity, decreases starch digestion | [155,156]          |
| 52.              | *Eucalyptus globulus* | Leaves Diabetes, cough, cold, wounds, fungal infections, fever, sore throat, pain | Increases insulin secretion, improves glucose uptake                                      | [157,158]          |
| 53.              | *Euclea undulata*    | Root, bark Diabetes, cough, chest pain, diarrhea, headache, toothache             | Lowers blood glucose levels, inhibits α-glucosidase activity                              | [78,159]           |
| 54.              | *Eugenia jambolana*  | Seeds Diabetes, skin ulcers, gastritis, constipation, sore throat, liver, and kidney diseases | Lowers blood glucose levels, improves pancreatic β-cell function, increases insulin secretion, inhibits sucrase and maltase activity, improves glucose uptake and metabolism | [56,160,161]       |
| 55.              | *Euphorbia hirta*    | Leaves Diabetes, respiratory diseases, diarrhea, jaundice, tumors, gonorrhea      | Increases insulin release from beta cells, inhibits α-glucosidase activity                | [162,163]          |
| 56.              | *Ficus benghalensis*  | Bark, leaves Diabetes, hypertension, dysentery, diarrhea, pain, ulcers, asthma     | Decrease carbohydrate digestion and absorption, lowers blood glucose levels               | [164,165]          |
| 57.              | *Garcinia kola*      | Seeds Diabetes, diarrhea, food poisoning, bacterial infections, cough, liver diseases | Inhibits α-amylase activity, decreases glycosylated hemoglobin levels                     | [166,167]          |
| 58.              | *Glycine max*       | Seeds Diabetes, cardiovascular diseases, obesity, cancer                           | Reduces insulin resistance, improves glucose tolerance                                  | [168,169]          |
| Medicinal Plants | Parts | Traditional Uses | Pharmacological Effects | References |
|------------------|-------|------------------|-------------------------|------------|
| Glycyrrhiza glabra | Roots | Diabetes, epilepsy, respiratory diseases, paralysis, jaundice, rheumatism | Lowers blood glucose levels, increases insulin secretion | [56,170] |
| Gymnema sylvestre | Leaves | Diabetes, asthma, bronchitis, constipation, jaundice, dyspepsia, hemorrhoids, obesity | Lowers blood glucose levels, regenerates beta cells, increases insulin secretion, improves glucose tolerance | [171,172] |
| Harungana madagascariensis | Leaves | Diabetes, cancer, hernia, hypertension, jaundice, malaria, yellow fever | Lowers blood glucose levels, inhibits α-amylase activity | [16,173] |
| Helicteres isora | Roots | Diabetes, diarrhea, snake bites, gastrointestinal disorders, spasms | Lowers blood glucose levels, improves glucose uptake | [174,175] |
| Heritiera fomes | Bark | Diabetes, diarrhea, constipation, dysentery, dermatitis, scabies, goiter | Decreases carbohydrate digestion and glucose absorption, lowers blood glucose levels, increases insulin secretion, improves glucose tolerance, inhibits DPP-IV enzyme activity | [26,51,176] |
| Hibiscus esculentus | Roots, seeds | Diabetes, gastric irritations, inflammatory diseases, wounds, and boils | Lowers blood glucose levels, improves β-cell function, increases insulin secretion | [177,178] |
| Hibiscus rosa-sinensis | Leaves | Diabetes, cough, diarrhea, dysentery, pain, contraceptive | Reduces glucose absorption, lowers blood glucose levels, increases insulin secretion and hepatic glucose utilization, improves glucose tolerance, inhibits DPP-IV activity | [179,180] |
| Jatropha curcas | Leaves | Diabetes, fever, bacterial and fungal infections, jaundice, muscle pain | Lowers fasting blood glucose levels, improves glucose uptake and utilization | [181,182] |
| Lantana camara | Leaves | Diabetes, asthma, malaria, chicken pox, hypertension, measles | Lowers elevated blood glucose levels, improves glucose tolerance | [183,184] |
| Linum usitatissimum | Seeds | Diabetes, diarrhea, gastrointestinal infections, asthma, bronchitis, atherosclerosis | Lowers blood glucose levels, increases insulin secretion, improves glucose uptake and metabolism | [56,185] |
| Mangifera indica | Leaves, seeds | Diabetes, constipation, piles, dysentery, asthma, anemia, hypertension, hemorrhage, | Lowers blood glucose levels, increases insulin secretion, improves glucose uptake, inhibits α-glucosidase and DPP-IV activity | [56,186,187] |
### Table 1. Cont.

| Medicinal Plants | Parts      | Traditional Uses                                         | Pharmacological Effects                                                                 | References |
|------------------|------------|----------------------------------------------------------|----------------------------------------------------------------------------------------|------------|
| 70. Momordica charantia | Leaves, seeds | Diabetes, malaria, hypertension, scabies, liver diseases, obesity, ulcers, measles | Lowers blood glucose levels, increases insulin secretion and glucose uptake, improves glucose tolerance, decreases gluconeogenesis, inhibits α-glucosidase activity | [56,134,188] |
| 71. Moringa oleifera | Leaves    | Diabetes, asthma, enlarged liver, bacterial infections, eye problems, piles, influenza, diuretic | Reduces glucose absorption, lowers blood glucose levels, improves glucose uptake, inhibits α-amylase activity | [189,190] |
| 72. Murraya koenigii | Leaves    | Diabetes, piles, dysentery, itching, bruises, inflammation | Lowers blood glucose levels, inhibits α-amylase and α-glucosidase activity | [78,191] |
| 73. Musa sapientum | Flowers   | Diabetes, dysentery, ulcers, hypertension, pain, inflammation, snake bites | Lowers blood glucose levels, increases insulin secretion, decreases glucosylated hemoglobin levels | [192,193] |
| 74. Nigella sativa | Seeds     | Diabetes, hypertension, gastrointestinal disorders, back pain, paralysis, heart diseases, bacterial infections, malaria | Decreases carbohydrate digestion and absorption, lowers blood glucose levels, increases insulin secretion and sensitivity, improves glucose uptake and utilization | [194,195] |
| 75. Ocimum basillicum | Leaves    | Diabetes, headaches, constipation, coughs, kidney diseases, warts | Inhibits α-amylase and α-glucosidase activity, reduces oxidative stress, inhibits glycogenolysis | [196–198] |
| 76. Ocimum sanctum | Leaves    | Diabetes, ringworm, skin diseases, dysentery, dyspepsia, bronchitis, asthma | Increases insulin secretion, improves glucose uptake and utilization | [149,199] |
| 77. Olea europaea | Leaves    | Diabetes, constipation, urinary tract infections, asthma, hypertension, intestinal diseases | Lowers blood glucose levels, increases antioxidant activity | [200,201] |
| 78. Panax ginseng | Roots     | Diabetes, insomnia, anorexia, confusion, hemorrhage | Improves peripheral insulin action, increases insulin sensitivity, decreases carbohydrate absorption | [202,203] |
| 79. Panda oleosa | Stem bark  | Diabetes, HIV/AIDS, wounds, rheumatism, intestinal parasites | Lowers blood glucose levels, improves glucose tolerance | [16,204] |
| 80. Phaseolus vulgaris | Seeds     | Diabetes, hypertension, obesity, blood cancer | Reduces insulin resistance, inhibits α-amylase and DPP-IV enzyme activity | [149,205] |
| 81. Phyllanthus amarus | Leaves    | Diabetes, spleen, liver and kidney diseases, gonorrhea, stomach problems | Lowers blood glucose levels, increases insulin secretion, improves insulin sensitivity | [206,207] |
Table 1. Cont.

| Medicinal Plants    | Parts       | Traditional Uses                                                                 | Pharmacological Effects                                                                 | References          |
|---------------------|-------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|---------------------|
| 82. *Plantago ovata*| Husk        | Diabetes, constipation, diarrhea, hypercholesterolemia, hypertension, hemorrhoids| Improves glucose tolerance, decreases carbohydrate digestion and glucose absorption    | [208,209]          |
| 83. *Pterocarpus marsupium*| Bark | Diabetes, dysentery, cough, diarrhea, skin diseases, wounds, ulcer | Improves pancreatic β-cell function, increases insulin secretion, improves glucose uptake | [149,210,211]       |
| 84. *Punica granatum*| Flowers    | Diabetes, urinary tract infections, arthritis, sore throat, skin diseases, anemia | Improves β-cell function, increases insulin secretion                                 | [210,212,213]       |
| 85. *Rehmannia glutinosa*| Roots    | Diabetes, anemia, obesity, kidney diseases, osteoporosis                        | Improves pancreatic β-cell function, increases insulin secretion, improves glucose uptake, decreases oxidative stress | [214,215]          |
| 86. *Santalum album*| Bark       | Diabetes, jaundice, diarrhea, dysentery, liver tonic, inflammation, hypertension | Lowers blood glucose levels, increases insulin secretion, improves glucose uptake and utilization | [56,216]          |
| 87. *Selaginella bryopteris*| Leaves | Diabetes, fever, epilepsy, constipation, colitis, cancer, urinary tract infections | Lowers blood glucose levels, increases insulin secretion, improves glucose uptake and utilization | [56,217]          |
| 88. *Sesamum indicum*| Seeds      | Diabetes, constipation, hypertension, high cholesterol, athlete’s foot           | Inhibits α-amylase and α-glucosidase activity, exerts antioxidant activity             | [56,218,219]       |
| 89. *Solanum nigrum*| Leaves     | Diabetes, pneumonia, toothache, stomach ache, fever, tumor, tonsillitis         | Lowers blood glucose levels, increases insulin secretion, decreases gluconeogenesis, increases glycogenesis | [220,221]         |
| 90. *Spirulina platensis*| Whole plant | Diabetes, hypercholesterolemia, atherosclerosis, obesity | Lowers blood glucose levels, increases insulin secretion, improves glucose tolerance, inhibits DPP-IV activity | [222,223]         |
| 91. *Swertia chirayita*| Bark, leaves | Diabetes, malaria, hypertension, epilepsy, liver diseases, weight loss         | Lowers blood glucose levels, increases insulin secretion, improves glucose uptake and metabolism, inhibits α-amylase and α-glucosidase | [56,224]         |
| 92. *Tamarindus indica*| Seeds      | Diabetes, diarrhea, dysentery, constipation, abdominal pain, wounds, malaria    | Lowers blood glucose levels, increases insulin secretion                               | [56,225]         |
| 93. *Terminalia arjuna*| Bark       | Diabetes, cardiotoxic, anemia, viral infections, venereal diseases, ulcers      | Lowers blood glucose levels, increases insulin secretion, improves glucose uptake and utilization | [56,226]         |
### Table 1. Cont.

| Medicinal Plants       | Parts               | Traditional Uses                                      | Pharmacological Effects                                                                 | References       |
|------------------------|---------------------|-------------------------------------------------------|----------------------------------------------------------------------------------------|------------------|
| 94. *Terminalia chebula* | Fruit              | Diabetes, fever, astringent, constipation, dementia    | Improves β-cell function, increases insulin secretion, reduces glycosylated hemoglobin levels | [227,228]       |
| 95. *Tinospora cordifolia* | Leaves, roots, stem | Diabetes, dysentery, diarrhea, snake bites, asthma, fever, jaundice | Increases insulin secretion, inhibits gluconeogenesis, increases insulin sensitivity     | [149,229]       |
| 96. *Trigonella foenum-graecum* | Seeds             | Diabetes, bronchitis, pneumonia, indigestion, dysentery, high cholesterol | Lowers blood glucose levels, increases insulin secretion, improves glucose uptake and utilization | [56,134,230,231] |
| 97. *Urtica dioica*    | Leaves              | Diabetes, cardiovascular diseases, anemia, rhinitis, arthritis, gout, wounds | Increases insulin sensitivity, improves glucose tolerance                              | [232,233]       |
| 98. *Vernonia amygdalina* | Leaves            | Diabetes, gastrointestinal disorders, amoebic dysentery, malaria, helminth infections | Lowers elevated blood glucose levels, inhibits gluconeogenesis and glycogenolysis   | [234,235]       |
| 99. *Withania coagulans* | Fruit              | Diabetes, insomnia, impotence, nervous exhaustion, asthma, liver diseases | Lowers blood glucose levels, improves glucose tolerance                               | [56,236]        |
| 100. *Zingiber officinale* | Rhizome           | Diabetes, nausea, high cholesterol, heartburn, indigestion, diarrhea, asthma | Lowers fasting blood glucose levels, increases insulin secretion                       | [119,237]       |
6. Phytochemicals and Their Impact on Diabetes

Plants are the primary source of biologically active compounds that may ultimately lead to the discovery and development of potential new drugs [238]. Plants produce both primary and secondary metabolites. Carbohydrates, proteins, and lipids are considered primary metabolites, necessary for the growth and development of plants and involved in essential metabolic pathways, such as photosynthesis and glycolysis. Secondary metabolites are not required for the growth and development of plants; rather, they are responsible for interactions between plant species and the environment and have highly specific functions in plants [239].

Over 13,000 secondary metabolites have been purified and isolated from medicinal plants. These phytochemicals can be categorized into various chemical classes such as alkaloids, flavonoids, terpenoids, phenolics, tannins, saponins, xanthones, and glycosides [78]. Many of these phytochemicals are known to exhibit medicinal properties, including antidiabetic activity [78]. Several phytochemicals isolated from various plant species have been scientifically validated for their contribution to treating and managing diabetes by exerting antihyperglycemic activity and reducing the complications associated with diabetes [171]. For example, the flavonoid rutin, present in the leaves of numerous plants, including Annona squamosa and Azadirachta indica (neem), has been reported to possess many beneficial effects such as anti-inflammatory, anti-cancer, anti-allergic, antiviral, and antioxidative properties [240]. Rutin-containing plants have also been shown to protect against heart disease, hepatotoxicity, and diabetes mellitus [240]. Rutin exerts its antidiabetic effect by lowering plasma glucose, improving the function of pancreatic β-cells, and enhancing glucose tolerance [10]. Two other flavonoids found in the leaves of Annona squamosa, namely quercetin and isoquercetin, have also been reported to possess antihyperglycemic activity by inhibiting α-glucosidase and lowering blood glucose levels [241]. Alongside rutin and quercetin, the tetranortriterpenoid meliacinolin, isolated from the leaves of A. indica, has been found to inhibit α-glucosidase and α-amylase in Type 2 diabetic mice [98]. Nimbidin, extracted from neem seeds, is another phytochemical exhibiting hypoglycemic properties [98]. Quercetin, allicin, allyl-propyl disulfide, cysteine sulfoxide, and S-allyl cysteine sulfoxide from Allium sativum (garlic) have been reported to stimulate insulin secretion from pancreatic β-cells, increase insulin sensitivity to target cells, and prevent insulin activation triggered by the liver [71]. Alliin, from garlic, has been reported to mimic the function of glibenclamide and insulin [71]. Epigallocatechin-3-gallate, epigallocatechin, epicatechin-3-gallate, and epicatechin present in Camellia sinensis (tea) leaves can also lower plasma glucose levels by improving β-cell function, increasing insulin secretion, and enhancing glucose metabolism [117]. These phytomolecules may exert their antidiabetic activity in multiple manners, most commonly by being insulinitropic, insulin-mimetic, and by improving β-cell function, increasing insulin sensitivity, improving glucose tolerance and metabolism, as well as inhibiting various enzyme activities. A summary of antidiabetic medicinal plants and their phytochemicals with potential antidiabetic effects is provided in Table 2. The chemical structures of the antidiabetic phytoconstituents of medicinal plants are given in Table 3.
| Medicinal Plants | Parts          | Phytoconstituents                          | Pharmacological Effects                                                                                     | References          |
|------------------|----------------|--------------------------------------------|-------------------------------------------------------------------------------------------------------------|---------------------|
| 1. *Abrus precatorius* | Leaves, seeds  | Luteolin, lupenone, 24-methylene cycloartenol | Maintains blood glucose levels, promotes insulin secretion, prevents oxidative stress, inhibits inflammation in pancreatic tissues | [16,242,243]       |
| 2. *Acacia arabica*  | Bark, roots    | Quercetin, kaempferol, catechin            | Lowers blood glucose levels, increases insulin secretion, reduces insulin resistance, improves glucose tolerance, reduces oxidative stress | [24,244]            |
| 3. *Acacia catechu*  | Bark           | Catechin, epicatechin, catechu tannic acid, gallocatechin, kaempferol | Lowers blood glucose levels, increases plasma insulin levels, reduces insulin resistance, and improves glucose uptake, inhibits α-amylase and α-glucosidase activity | [24,244–247]       |
| 4. *Aegle marmelos* | Leaves         | Rutin, β-sitosterol, aegelinosides A and B, aegeline, marmelosin | Lowers plasma glucose levels, reduces insulin resistance, decreases glycosylated hemoglobin levels, inhibits α-glucosidase activity, improves β-cell function | [248–252]          |
| 5. *Aframomum melegueta* | Fruit, leaves | 6-paradol, 6-shogaol, 6-gingerol, oleanolic acid | Decreases blood glucose and cholesterol levels, improve glucose tolerance and utilization, inhibits lipid synthesis by adipocytes | [16,253–255]       |
| 6. *Ageratum conyzoides* | Leaves        | Kaempferol, precocene II                   | Lowers blood glucose levels, increases plasma insulin levels, improves glucose uptake                          | [16,256]           |
| 7. *Albizia lebbeck*  | Bark, pods     | Lupeol, oleanolic acid, docosanoic acid, β-sitosterol, catechin, friedelin | Decreases blood glucose and glycosylated hemoglobin levels, reduces nitric oxide, increases insulin levels, activates GLUT2 and GLUT4 | [244,250,255,257–259] |
| 8. *Albizia adianthifolia* | Bark, leaves  | β-caryophyllene, viridiflorol              | Lowers blood glucose levels, increases insulin secretion and sensitivity, reduces glucose absorption, triglyceride, and cholesterol levels | [67,260]           |
| 9. *Allium cepa*     | Bulb           | Alliin, quercetin, S-methyl cysteine sulfoxide | Reduces fasting glucose levels, increases insulin secretion and sensitivity, decreases triglyceride levels | [16,261,262]       |
| 10. *Allium sativum* | Bulb           | Allicin, alliin, diallyl disulfide, quercetin, allyl propyl disulfide | Lowers blood glucose levels, increases insulin secretion and sensitivity, decreases cholesterol and triglyceride levels | [71,261–263]       |
| 11. *Aloe vera*      | Leaves         | Lophenol, aloin, aloeic acid, emodin, glucomannan | Lowers blood glucose levels, increases insulin secretion, improves glucose tolerance, prevents oxidative stress | [16,264–266]       |
### Table 2. Cont.

| Medicinal Plants         | Parts            | Phytoconstituents                  | Pharmacological Effects                                                                 | References       |
|--------------------------|------------------|-----------------------------------|----------------------------------------------------------------------------------------|------------------|
| 12. *Anacradium occidentale* | Leaves, stem bark | Anacardic acid, lectin            | Delays glucose absorption, reduces oxidative stress, inhibits α-glucosidase activity    | [16,267]         |
| 13. *Anemarrhena asphodeloides* | Rhizome         | Mangiferin, neomangiferin, sarsasapogenin | Reduces fasting blood glucose levels, improves glucose tolerance, reduces cholesterol and triglyceride levels, improves diabetic complications | [78,268–270]    |
| 14. *Annona salzmannii*  | Leaves, bark     | α-copaene, β-caryophyllene, δ-cadinene | Lowsers blood glucose levels, increases insulin secretion, improves glucose uptake, reduces glucose absorption, cholesterol, and triglyceride levels | [80,260]         |
| 15. *Annona squamosa*    | Leaves           | Rutin, quercetin, isoquercetin     | Lowsers blood glucose levels, increases insulin secretion, improves glucose tolerance, reduces glycosylated hemoglobin levels | [10,249,262,271] |
| 16. *Anogeissus latifolia* | Bark            | Ellagic acid, β-sitosterol, 3,4,3-tri-O-methylellagic acid | Lowsers plasma glucose and glycosylated hemoglobin levels, increases insulin levels, improves β-cell function | [250,272,273]    |
| 17. *Arachis hypogaea*   | Seeds            | Resveratrol, catechin, rutin, quercetin | Lowsers blood glucose levels, increases insulin secretion and glucose uptake, reduces oxidative stress, inhibits α-amyrase and α-glucosidase activity | [244,249,262,274] |
| 18. *Artemisia absinthium* | Rhizome         | α and β thujones, thujyl alcohol, azulene, cadinene | Lowsers blood glucose levels, activates adenosine monophosphate-activated protein kinase, increases insulin sensitivity | [16,275,276]    |
| 19. *Artocarpus heterophyllus* | Leaves, rhizome | Chrysin, silymarin, isoquercetin  | Lowsers blood glucose levels, improves β-cell function and glucose tolerance, increases insulin sensitivity, inhibits Pro-inflammatory cytokines | [78,271,277,278] |
| 20. *Asparagus racemosus* | Roots            | Asparagamine, asparagine, kaempferol, quercetin | Lowsers blood glucose levels, increases insulin secretion, improves glucose uptake and tolerance | [93,256,262]    |
| 21. *Atractylodes japonica* | Rhizome         | Atractans A, B, C, atractylenolide III | Lowsers blood glucose levels, decreases insulin resistance                               | [95,96,279]     |
| 22. *Azadirachta indica*  | Leaves           | Azadirachtin, nimbin, rutin, quercetin, campestrol | Lowsers blood glucose levels, improves β-cell function, increases insulin secretion, reduces cholesterol and triglyceride levels | [97,98,249,280] |
| Medicinal Plants            | Parts                | Phytoconstituents                                                                 | Pharmacological Effects                                                                 | References     |
|-----------------------------|----------------------|-----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|----------------|
| 23. *Balanites aegyptiaca*  | Fruit, seeds         | Balantin 1, 2, diosgenin, 3,4,6-tri-O-methyl-D-glucose, triethylphosphine         | Increases serum insulin and c-peptide levels, increases glucose metabolism, decreases gluconeogenesis | [16,281]       |
| 24. *Berberis vulgaris*     | Root bark            | Berberine, berbamine                                                              | Increases insulin secretion, improves insulin sensitivity, inhibits α-glucosidase and aldose reductase activity | [102,282,283] |
| 25. *Bidens pilosa*         | Roots                | Cytopiloyne, apigenin, luteolin, kaempferol, quercetin                           | Lowers blood glucose and glycosylated hemoglobin levels, increases insulin secretion and glucose uptake, improves glucose tolerance | [16,242,284–286] |
| 26. *Bougainvillea spectabilis* | Flowers, leaves | Pinitol, quercetin, β-sitosterol                                                   | Lowers fasting blood glucose and glycosylated hemoglobin levels, increases insulin secretion, improves glucose tolerance | [16,250,262,287] |
| 27. *Brassica juncea*       | Leaves, seeds        | Cinnamic acid, kaempferol, aniline                                                | Lowers blood glucose levels, increases insulin secretion and glucose uptake                | [16,256,288]   |
| 28. *Bridelia ferruginea*   | Leaves, stem bark    | Epigallocatechin, epigallocatechin gallate                                         | Lowers blood glucose levels, improves glucose tolerance, enhances insulin secretion, decreases gluconeogenesis | [16,289,290]   |
| 29. *Bunium persicum*       | Seeds                | Linoleic acid, palmitic acid, kaempferol, camphene, linalool                      | Lowers blood glucose levels, increases insulin levels in blood, improves insulin sensitivity, enhances glucose uptake and tolerance | [256,291–294] |
| 30. *Caesalpinia decapetala*| Leaves               | Quercitrin, kaempferol, astragalín, apigenin-7-rhamnoside                        | Decreases fasting blood glucose levels, increases insulin levels in blood, enhances antioxidant activity, improves glucose uptake, decreases nitric oxide | [16,256,295,296] |
| 31. *Calendula officinalis* | Leaves, bark         | Caffeic acid, quercetin, esculetin                                               | Lowers blood glucose levels and glycosylated hemoglobin levels, increases insulin secretion, reduces diabetic oxidative stress, increases GLUT4 expression in adipocytes, improves glucose utilization | [16,262,297,298] |
| 32. *Camellia sinensis*     | Leaves               | Rutin, quercitrin                                                                | Lowers blood glucose levels, improves β-cell function, increases insulin secretion, improves glucose tolerance | [117,249,295]  |
### Table 2. Cont.

| Medicinal Plants       | Parts          | Phytoconstituents                                                                                           | Pharmacological Effects                                                                                                                                                                                                 | References |
|------------------------|----------------|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| 33. Capsicum frutescens | Whole plant    | Capsaicin, β-carotene                                                                                       | Lowers blood glucose levels, increases insulin levels, improves glucose tolerance, inhibits pro-inflammatory cytokines                                                                                                   | [119,299,300] |
| 34. Carica papaya      | Fruit, leaves  | Chlorogenic acid, coumarin compounds                                                                         | Lowers blood glucose levels, stimulates insulin secretion, increases insulin sensitivity, inhibits α-amylase, α-glucosidase, glucose-6-phosphatase, and aldose reductase activity | [16,301,302] |
| 35. Cassia alata       | Leaves, seeds  | Emodin, kaempferol, β-sitosterol                                                                            | Lowers blood glucose levels, increases insulin secretion, enhances insulin sensitivity, inhibits phosphoenolpyruvate, carboxykinase, glucose-6-phosphatase activity | [16,250,256,266] |
| 36. Cassia fistula     | Stalk          | Lupeol, kaempferol, catechin, epicatechin                                                                   | Lowers blood glucose and glycosylated hemoglobin levels, increases insulin levels, reduces nitric oxide, improves glucose tolerance                                                                                     | [244,246,257,303] |
| 37. Catharanthus roseus| Leaves, roots  | Gallic acid, chlorogenic acid, vindoline I                                                                   | Lowers blood glucose levels, stimulates insulin secretion, improves glucose tolerance, decreases pro-inflammatory cytokines                                                                                             | [16,301,304,305] |
| 38. Cecropia obtusifolia| Root, bark     | Isoorientin, stigmast-4-en-3-one, chlorogenic acid, β-sitosterol                                               | Reduces blood glucose levels, improves insulin sensitivity, enhances glucose uptake, decreases cholesterol and triglyceride levels, inhibits glucose-6-phosphatase and hepatic glucose, improves glucose tolerance | [78,306,307] |
| 39. Cichorium intybus  | Bark, leaves   | Chlorogenic acid, chicoric acid, gallic acid, kaempferol, quercetin, β-sitosterol                             | Lowers blood glucose levels, stimulates insulin release, improves insulin sensitivity, inhibits α-amylase, α-glucosidase, glucose-6-phosphatase activity, prevents oxidative stress | [22,78,132,301,308] |
| 40. Cinnamomum zeylanicum| Bark          | Cinnamaldehyde, eugenol                                                                                      | Decreases blood glucose levels, reduces insulin resistance, inhibits α-glucosidase activity and formation of advanced glycated end products, inhibits sugar binding to albumin | [134,309,310] |
| 41. Citrus limon       | Fruit          | Diosmin, hesperetin                                                                                           | Lowers blood glucose levels, increases insulin secretion, enhances glucose utilization, stimulates β-endorphin secretion from adrenal glands, inhibits gluconeogenesis | [16,311,312] |
| Medicinal Plants          | Parts          | Phytoconstituents                                                                 | Pharmacological Effects                                                                 | References                      |
|--------------------------|----------------|----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|---------------------------------|
| 42. Citrus x aurantium   | Fruit          | Naringin, naringenin, epigallocatechin-3-gallate                                  | Decreases blood glucose levels, increases insulin secretion, improves glucose tolerance, increases GLUT4 translocation in skeletal muscles, decreases gluconeogenesis | [16,289,290,313]               |
| 43. Cola nitida          | Seeds          | D-catechin, L-epicatechin, naringenin, apigenin                                   | Lowers blood glucose levels, increases insulin sensitivity, decreases oxidative stress, inhibits α-amylase and α-glucosidase activity | [16,244,246]                   |
| 44. Coptis chinensis     | Rhizome        | Berberine, jatrhorrhizine                                                        | Lowers blood glucose levels, enhances aerobic glycolysis, inhibits gluconeogenesis, increases insulin secretion and insulin sensitivity | [33,282,314]                   |
| 45. Cornus officinalis   | Fruit, seeds   | Gymnemagenin, gymnemic acid, ursolic acid                                        | Lowers fasting blood glucose levels, increases insulin secretion, improves glucose uptake and tolerance, inhibits protein glycation | [143,279,315,316]              |
| 46. Curcuma longa        | Rhizome        | Curcumin, turmerin                                                               | Decreases fasting blood glucose, glycosylated hemoglobin, triglyceride, and cholesterol levels, inhibits α-amylase, α-glucosidase activity, and diabetic inflammatory processes | [78,317,318]                   |
| 47. Cudrania cochinchinensis | Bark, roots  | Kaempferol, vanillin, β-sitosterol                                                | Lowers blood glucose levels, increases insulin levels, decreases serum advanced glycation end products, improves glucose uptake, reduces insulin resistance | [250,256,319,320]              |
| 48. Cyamopsis tetragonoloba | Fruit         | Quercetin, kaempferol, gallic acid                                              | Lowers plasma glucose levels, increases insulin secretion, improves glucose tolerance, decreases triglyceride levels | [16,256,262,304]               |
| 49. Dalbergia sissoo     | Bark           | Biochanin A, tectorigenin, rhamnoglucoside, dalbergin, dalbergichromene          | Lowers blood glucose levels, improves insulin sensitivity and glucose tolerance, reduces insulin resistance | [321–323]                      |
| 50. Eriobotrya japonica  | Leaves, seeds  | Cinchonain-Ib, timosaponin, chlorogenic acid, epicatechin                         | Lowers blood glucose, total cholesterol, and triglyceride levels, enhances insulin secretion and sensitivity, improves glucose tolerance | [246,279,301,324,325]           |
| 51. Eucalyptus citriodora | Leaves        | Betulinic acid, gallic acid, quercitin, isoquercitrin, rhodomyrtosone E          | Lowers blood glucose levels, increases insulin secretion and sensitivity, improves glucose tolerance and antioxidant activity, decreases triglyceride levels | [155,295,304,326]              |
| Medicinal Plants       | Parts             | Phytoconstituents                          | Pharmacological Effects                                                                                     | References               |
|------------------------|-------------------|--------------------------------------------|------------------------------------------------------------------------------------------------------------|--------------------------|
| 52. *Eucalyptus globulus* | Leaves            | Eucalyptol, rutin, sesquiterpene           | Lowers blood glucose levels, improves β-cell function, increases insulin secretion, reduces oxidative stress | [157,249,327]            |
| 53. *Euclea undulata*   | Rootbark          | Botulin, lupeol, epicatechin               | Decreases serum glucose, increases insulin levels, improves insulin sensitivity, decreases glycosylated hemoglobin levels | [78,246,257]            |
| 54. *Eugenia jambolana* | Seeds             | Ellagic acid, gallic acid, chlorogenic acid | Lowers blood glucose levels, increases insulin sensitivity, improves β-cell function, improves glucose tolerance, inhibits α-amylase, α-glucosidase, and glucose-6-phosphatase activity | [11,272,301,304]         |
| 55. *Euphorbia hirta*   | Leaves            | Quercetin, kaempferol, gallic acid        | Lowers blood glucose levels, increases insulin secretion, improves glucose tolerance, decreases triglyceride levels, enhances glucose uptake | [162,256,262,304]        |
| 56. *Ficus benghalensis*| Bark, leaves      | Rutin, gallic acid, leucopelargonidin-3-O-α-rhamnopyranoside, lupeol, α-amyrin acetate | Decreases blood glucose levels, improve glucose tolerance and β-cell function, increases insulin secretion, | [249,328–330]            |
| 57. *Garcinia kola*     | Seeds             | Kolaviron, ascorbic acid                  | Decreases blood glucose level, stimulates insulin secretion, improves glucose utilization, inhibits glucose-6-phosphatase, exhibits free radical scavenging activity | [16,331,332]            |
| 58. *Glycine max*       | Seeds             | Kaempferol, soyasaponin, genistein, β-sitosterol | Lowers blood glucose and glycosylated hemoglobin levels, increases insulin levels in blood, decreases insulin resistance, improves glucose uptake, inhibits glucose absorption | [16,250,256]            |
| 59. *Glycyrrhiza glabra*| Roots             | Glycyrrhizin, glycyrrhetic acid, isoliquiritin | Lowers postprandial rise in blood glucose levels, decreases glycosylated hemoglobin levels                  | [333–335]               |
| 60. *Gymnema sylvestre* | Leaves            | Gymnemoside A,B,C,D,E,F, quercitol, lupeol, gymnemic acid | Lowers blood glucose and glycosylated hemoglobin levels, increases insulin secretion, inhibits glucose absorption in the small intestine | [149,257,315,336]       |
| 61. *Harungana madagascariensis* | Leaves | Harunganin, lupeol, betulinic acid, quercetin, β-sitosterol | Lowers blood glucose and glycosylated hemoglobin levels, increases insulin secretion, decreases insulin resistance, prevents diabetic nephropathy | [16,250,257,262,337,338] |
| Medicinal Plants | Parts | Phytoconstituents                                                                 | Pharmacological Effects                                                                                                                                                                                                 | References                  |
|------------------|-------|---------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| 62. *Helicteres isora* | Roots | Gallic acid, vanillin, *p*-coumaric acid                                         | Lowers blood glucose levels, increases insulin levels in blood, decreases triglyceride levels, reduces serum advanced glycation end products concentration, improves glucose tolerance | [175,304,319,339]            |
| 63. *Heritiera fomes*  | Bark  | Stigmasterol, *β*-sitosterol, epicatechin, procyanidins, proanthocyanidins, quercitrin | Decreases blood glucose and glycosylated hemoglobin levels, increases insulin levels, reduces insulin resistance, improves glucose uptake                                                                                      | [26,176,250,340]            |
| 64. *Hibiscus esculentus* | Roots, seeds | Isoquercitrin, quercetin-3-O-gentiobioside                                        | Decreases serum glucose levels, increases insulin secretion, improves glucose tolerance                                                                                                                                   | [16,341]                    |
| 65. *Hibiscus rosa-sinensis* | Leaves | Quercetin, cyanidin, thiamine, ascorbic acid, niacin                             | Decreases blood glucose concentration, increases insulin synthesis and secretion, reduces oxidative stress, improves endothelial functions, and reduces complications of type 2 diabetes mellitus | [179,262,342,343]            |
| 66. *Jatropha curcas*   | Leaves | Rhoifolin, isoorientin, isoquercitrin                                           | Decreases plasma glucose, cholesterol, and triglyceride levels, stimulates glucose uptake, inhibits DPP-IV activity                                                                                                  | [241,306]                   |
| 67. *Lantana camara*    | Leaves | Lantanoside, ferulic acid, oleanolic acid, caffeic acid                         | Lowers blood glucose levels, increases insulin secretion, improves glucose utilization, reduces oxidative stress                                                                                                   | [255,297,344]              |
| 68. *Linum usitatissimum* | Seeds | Caffeic acid, *p*-coumaric acid, ferulic acid                                   | Lowers blood glucose and glycosylated hemoglobin levels, increases insulin secretion, reduces diabetic oxidative stress, enhances antioxidant activity                                                                   | [297,339,344,345]          |
| 69. *Mangifera indica*  | Leaves, seeds | Mangiferin, gallic acid, kaempferol, curcumin                                  | Lowers fasting blood glucose levels, improves glucose tolerance, increases insulin secretion, reduces triglyceride and cholesterol levels, inhibits oxidative stress and diabetic inflammatory processes | [16,256,269,304,317]        |
| 70. *Momordica charantia* | Leaves, seeds | Charantin, vicine, momordicine II, oleanolic acid                             | Lowers blood glucose levels, stimulates insulin release, inhibits glucose-6-phosphatase and glucose transport in intestines                                                                                      | [22,134,255,336]           |
| 71. *Moringa oleifera*  | Leaves | Quercetin, kaempferol, vanillin, chlorogenic acid                              | Lowers plasma glucose levels, increases insulin secretion, improves glucose tolerance, decreases the concentration of serum advanced glycation end products                                                              | [16,22,189,256,319]      |
| Medicinal Plants | Parts       | Phytoconstituents                                      | Pharmacological Effects                                                                                                                                                                                                 | References         |
|------------------|-------------|-------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| 72. **Murraya koenigii** | Leaves      | Mahanimbine, isomahanine, ascorbic acid, kaempferol, quercetin | lowers blood glucose levels, reduces triglyceride levels, inhibits α-amylase and α-glucosidase activity, increases insulin secretion, improves glucose tolerance                                                                 | [78,191,346]       |
| 73. **Musa sapientum** | Flowers     | Rutin, delphinidin, syringin                           | lowers blood glucose levels, increases insulin secretion, reduces reactive oxygen species generation, prevents high glucose-induced cell proliferation                                                                 | [16,249,347]       |
| 74. **Nigella sativa** | Seeds       | Thymoquinone, thymol, α-pinene, oleic acid, linoleic acid | lowers blood glucose, glycosylated hemoglobin, total cholesterol, and triglyceride levels, promotes insulin secretion, reduces insulin resistance, decreases oxidative stress                                                                 | [291,348–350]      |
| 75. **Ocimum basilicum** | Leaves      | Linalool, linolen, eugenol, geraniol                  | lowers blood glucose levels, improves glucose uptake, inhibits advanced glycation end products generation and α-glucosidase activity                                                                                           | [196,197,310,351]  |
| 76. **Ocimum sanctum** | Leaves      | Eugenol, carvacrol, β-sitosterol, linalool            | lowers blood glucose levels, increases insulin secretion, decreases carbohydrate digestion and absorption, inhibits α-glucosidase activity, reduces insulin resistance                                                                 | [149,248,250,310]  |
| 77. **Olea europaea** | Leaves      | Oleuropein, oleanolic acid, luteolin                  | maintains blood glucose levels, promotes insulin secretion, improves insulin sensitivity, reduces oxidative stress, inhibits gluconeogenesis                                                                                           | [16,242,255,352]  |
| 78. **Panax ginseng** | Roots       | Ginsenoside Rb2, Rg2                                  | regenerates pancreatic beta cells, increases glucose uptake, reduces insulin resistance, and improves insulin sensitivity                                                                                                   | [248,279,353]      |
| 79. **Panda oleosa** | Stem bark   | Ginsenoside Rb2, protapananadiol/triol                | increases glucose uptake, reduces insulin resistance, and improves insulin sensitivity                                                                                                                                         | [204,353]          |
| 80. **Phaseolus vulgaris** | Seeds      | Hydroxycinnamic acid, rutin, quercetin, orientin, petunidin, catechin | lowers blood glucose and glycosylated hemoglobin levels, increases insulin secretion, improves glucose tolerance, reduces oxidative stress                                                                                         | [16,149,244,249,262] |
| 81. **Phyllanthus amarus** | Leaves      | Oleanolic acid, ursolic acid                          | lowers blood glucose levels, increases insulin secretion, improves glucose tolerance, inhibits oxidative stress-induced hepatic insulin resistance, inhibits gluconeogenesis                                                                 | [16,255,316]      |
| Medicinal Plants | Parts         | Phytoconstituents                      | Pharmacological Effects                                                                 | References          |
|------------------|---------------|----------------------------------------|------------------------------------------------------------------------------------------|---------------------|
| 82. *Plantago ovata* | Husk          | Kaempferol, catechin, myricetin, pinocembrin | Lowers blood glucose levels, increases insulin secretion, reduces insulin resistance, inhibits α-amylase and α-glucosidase activity | [208,244,256,354]   |
| 83. *Pterocarpus marsupium* | Bark         | Epicatechin, marsupin, carsupin, marsupol      | Lowers blood glucose levels, improves insulin sensitivity, enhaces insulin release, improves glucose uptake | [149,246]          |
| 84. *Punica granatum* | Flowers       | Gallic acid, rutin, nictoflorin           | Lowers blood glucose levels, improves β-cell function, increases insulin secretion, improves glucose tolerance, decreases triglyceride levels | [16,249,304]       |
| 85. *Rehmannia glutinosa* | Roots        | Catalpol, rehmannioside                  | Lowers blood glucose levels, prevents diabetic complications, promotes glucose utilization and glycogen synthesis, reduces oxidative stress | [214,279]          |
| 86. *Santalum album* | Bark          | Spirosantolol, α-santalene, α-santalol, β-santalol, α-bergamotol | Lowers blood glucose and glycosylated hemoglobin levels, decreases total cholesterol and triglyceride levels | [355]              |
| 87. *Selaginella bryopteris* | Leaves       | Gallic acid, rutin                       | Decreases plasma glucose and glycosylated hemoglobin levels, improves glucose tolerance, decreases triglyceride levels, inhibits inflammatory cytokines | [249,304,356]      |
| 88. *Sesamum indicum* | Seeds         | Pinoresinol, sesamin, sesaminol          | Lowers fasting blood glucose and glycosylated hemoglobin levels, inhibits α-glucosidase activity | [16,357,358]       |
| 89. *Solanum nigrum* | Leaves        | Gallic acid, catechin, epicatechin, rutin, naringenin | Lowers blood glucose levels, improves β-cell function and glucose tolerance, increases insulin secretion, reduces insulin resistance, inhibits α-amylase and α-glucosidase activity | [220,244,246,249,304,313] |
| 90. *Spirulina platensis* | Whole plant   | p-coumaric acid, catechin, β-carotene     | Lowers blood glucose levels, increases insulin levels, reduces insulin resistance, inhibits α-amylase and α-glucosidase activity, reduces oxidative stress and pro-inflammatory biomarkers | [222,244,300,339]  |
| 91. *Swertia chirayita* | Bark, leaves  | Swerchirin, mangiferin, swertiamarin, amarogentin | Lowers blood glucose levels, promotes insulin release, inhibits glucosidase and glucuronidase activity | [30,268,269,336]    |
| Medicinal Plants   | Parts            | Phytoconstituents                                      | Pharmacological Effects                                                                 | References                  |
|-------------------|------------------|--------------------------------------------------------|------------------------------------------------------------------------------------------|-----------------------------|
| 92. *Tamarindus indica* | Seeds            | Apigenin, naringenin, catechin, epicatechin, taxifolin   | Lowers blood glucose levels, increases insulin secretion, inhibits α-amylase and α-glucosidase activity, improves glucose tolerance, increases insulin sensitivity | [244,246,313,359]           |
| 93. *Terminalia arjuna* | Bark             | Arjungenin, arjunolone, ellagic acid, derivatives of arjunic acid | Lowers blood glucose levels, increases insulin sensitivity, decreases free radical damage | [29,360]                    |
| 94. *Terminalia chebula* | Fruit            | Chebulagic acid, gallic acid, ellagic acid, tannic acid  | Lowers blood glucose levels, improve glucose tolerance and lipid metabolism, stimulates glucose transport, decreases triglyceride levels | [245,304,360–362]           |
| 95. *Tinospora cordifolia* | Leaves, roots, stem | Tinosporaside, berberine, syringin                     | Lowers plasma glucose levels, stimulates insulin synthesis and secretion, decreases triglyceride levels, improves insulin sensitivity, inhibits gluconeogenesis | [149,282,363]               |
| 96. *Trigonella foenum-graecum* | Seeds           | Galactomannan, diosgenin, coumarin                      | Decreases blood glucose levels, stimulates insulin release, inhibits α-glucosidase and aldose reductase activity, increases insulin sensitivity | [16,302,364,365]            |
| 97. *Urtica dioica* | Leaves           | Quercetin, quercitrin, rutin                           | Lowers blood glucose and glycosylated hemoglobin levels, increases insulin secretion, reduces insulin resistance, improves antioxidant activity | [16,249,262,295]           |
| 98. *Vernonia amygdalina* | Leaves          | Sobrerol, vernoamyside E, luteolin, vitamin E          | Lowers blood glucose and glycosylated hemoglobin levels, increases insulin secretion, enhances insulin sensitivity, reduces oxidative stress | [16,235,242,366,367]        |
| 99. *Withania coagulans* | Fruit           | Withanolides, withacoagulin, withanosides, withaferin A | Lowers blood glucose levels, exhibits free radical scavenging activity, inhibits DPP-IV activity | [368,369]                   |
| 100. *Zingiber officinale* | Rhizome         | Gingerol, 6-paradol, 6-shogaol, camphene               | Lowers blood glucose levels, increases insulin levels, improves glucose tolerance and utilization, decreases cholesterol levels | [16,253,254,293]           |
Table 3. Antidiabetic phytoconstituents of medicinal plants and their chemical structures.

| Medicinal Plants   | Phytoconstituents | Chemical Structure |
|--------------------|-------------------|--------------------|
| 1. *Abrus precatorius* | Lupenone          | ![Lupenone](image) |
| 2. *Acacia arabica* | Quercetin         | ![Quercetin](image) |
| 3. *Acacia catechu* | Gallocatechin     | ![Gallocatechin](image) |
| 4. *Aegle marmelos* | Marmelosin       | ![Marmelosin](image) |
| 5. *Aframomum melegueta* | 6-paradol | ![6-paradol](image) |
| 6. *Ageratum conyzoides* | Kaempferol       | ![Kaempferol](image) |
| 7. *Albizia lebbeck* | Friedelin         | ![Friedelin](image) |
Table 3. Cont.

| Medicinal Plants         | Phytoconstituents | Chemical Structure |
|--------------------------|-------------------|--------------------|
| 8. *Albizia adianthifolia* | Viridiflorol      | ![Viridiflorol](image) |
| 9. *Allium cepa*          | Alliin            | ![Alliin](image)   |
| 10. *Allium sativum*      | Allicin           | ![Allicin](image)  |
| 11. *Aloe vera*           | Aloin             | ![Aloin](image)    |
| 12. *Anacradium occidentale* | Anacardic acid   | ![Anacardic acid](image) |
| 13. *Anemarrhena asphodeloides* | Sarsasapogenin | ![Sarsasapogenin](image) |
| 14. *Annona salzmannii*   | β-caryophyllene   | ![β-caryophyllene](image) |
### Table 3. Cont.

| Medicinal Plants     | Phytoconstituents | Chemical Structure |
|----------------------|-------------------|--------------------|
| 15. *Annona squamosa* | Rutin             | ![Rutin](image)    |
| 16. *Anogeissus latifolia* | β-sitosterol | ![β-sitosterol](image) |
| 17. *Arachis hypogaea* | Resveratrol       | ![Resveratrol](image) |
| 18. *Artemisia absinthium* | Azulene          | ![Azulene](image)   |
| 19. *Artocarpus heterophyllus* | Chrysin           | ![Chrysin](image)   |
| 20. *Asparagus racemosus* | Asparagine        | ![Asparagine](image) |
| 21. *Atractylodes japonica* | Atractylenolide III | ![Atractylenolide III](image) |
Table 3. Cont.

| Medicinal Plants          | Phytoconstituents | Chemical Structure |
|---------------------------|-------------------|--------------------|
| 22. Azadirachta indica    | Nimbin            | ![Nimbin](image)    |
| 23. Balanites aegyptiaca  | Diosgenin         | ![Diosgenin](image) |
| 24. Berberis vulgaris     | Berberine         | ![Berberine](image) |
| 25. Bidens pilosa         | Luteolin          | ![Luteolin](image)  |
| 26. Bougainvillea spectabilis | Pinitol     | ![Pinitol](image)   |
| 27. Brassica juncea       | Cinnamic acid     | ![Cinnamic acid](image) |
| Medicinal Plants          | Phytoconstituents          | Chemical Structure |
|--------------------------|----------------------------|--------------------|
| 28. Bridelia ferruginea  | Epigallocatechin gallate   | ![Epigallocatechin Gallate](image1.png) |
| 29. Bunium persicum      | Palmitic acid              | ![Palmitic Acid](image2.png)   |
| 30. Caesalpinia decapetala | Astragalin                | ![Astragalin](image3.png) |
| 31. Calendula officinalis | Esculetin                  | ![Esculetin](image4.png) |
| 32. Camellia sinensis    | Quercitrin                 | ![Quercitrin](image5.png) |
| 33. Capsicum frutescens  | Capsaicin                  | ![Capsaicin](image6.png) |
| Medicinal Plants     | Phytoconstituents | Chemical Structure |
|----------------------|-------------------|--------------------|
| 34. Carica papaya    | Coumarin          | ![Coumarin](image)  |
| 35. Cassia alata     | Emodin            | ![Emodin](image)   |
| 36. Cassia fistula   | Lupeol            | ![Lupeol](image)   |
| 37. Catharanthus roseus | Vindoline    | ![Vindoline](image) |
| 38. Cecropia obtusifolia | Isoorientin     | ![Isoorientin](image) |
| 39. Cichorium intybus | Chlorogenic acid  | ![Chlorogenic acid](image) |
| 40. Cinnamomum zeylanicum | Cinnamaldehyde | ![Cinnamaldehyde](image) |
Table 3. Cont.

| Medicinal Plants     | Phytoconstituents | Chemical Structure |
|----------------------|-------------------|--------------------|
| 41. *Citrus limon*   | Hesperetin        | ![Hesperetin](image) |
| 42. *Citrus x aurantium* | Naringin       | ![Naringin](image)  |
| 43. *Cola nitida*    | Apigenin          | ![Apigenin](image)  |
| 44. *Coptis chinensis* | Jatrorrhizine    | ![Jatrorrhizine](image) |
| 45. *Cornus officinalis* | Gymnemic acid    | ![Gymnemic acid](image) |
| 46. *Curcuma longa*  | Curcumin          | ![Curcumin](image)  |
Table 3. Cont.

| Medicinal Plants          | Phytoconstituents | Chemical Structure |
|---------------------------|-------------------|--------------------|
| 47. Cudrania cochinchinensis | Vanillin          | ![Vanillin chemical structure](image) |
| 48. Cyamopsis tetragonoloba | Quercetin         | ![Quercetin chemical structure](image) |
| 49. Dalbergia sissoo      | Biochanin A       | ![Biochanin A chemical structure](image) |
| 50. Eriobotrya japonica   | Cinchonain ib     | ![Cinchonain ib chemical structure](image) |
| 51. Eucalyptus citriodora | Rhodomyrtosone E  | ![Rhodomyrtosone E chemical structure](image) |
| 52. Eucalyptus globulus   | Eucalyptol        | ![Eucalyptol chemical structure](image) |
Table 3. Cont.

| Medicinal Plants | Phytoconstituents | Chemical Structure |
|------------------|-------------------|--------------------|
| 53. *Euclea undulata* | Epicatechin | ![Chemical Structure](image1) |
| 54. *Eugenia jambolana* | Ellagic acid | ![Chemical Structure](image2) |
| 55. *Euphorbia hirta* | Gallic acid | ![Chemical Structure](image3) |
| 56. *Ficus benghalensis* | α-amyrin acetate | ![Chemical Structure](image4) |
| 57. *Garcinia kola* | Kolaviron | ![Chemical Structure](image5) |
| 58. *Glycine max* | Genistein | ![Chemical Structure](image6) |
Table 3. Cont.

| Medicinal Plants       | Phytoconstituents | Chemical Structure |
|------------------------|-------------------|--------------------|
| 59. Glycyrrhiza glabra | Glycyrrhizin      | ![Glycyrrhizin](image) |
| 60. Gymnema sylvestre  | Gymnemic acid     | ![Gymnemic acid](image) |
| 61. Harungana madagascariensis | Harunganin | ![Harunganin](image) |
| 62. Helicteres isora  | p-coumaric acid  | ![p-coumaric acid](image) |
| 63. Heritiera fomes   | Stigmasterol     | ![Stigmasterol](image) |
| Medicinal Plants        | Phytoconstituents          | Chemical Structure |
|-------------------------|----------------------------|--------------------|
| 64. *Hibiscus esculentus* | Quercetin-3-O-gentiobioside | ![Quercetin-3-O-gentiobioside](image) |
| 65. *Hibiscus rosa-sinensis* | Ascorbic acid              | ![Ascorbic acid](image) |
| 66. *Jatropha curcas*    | Isoorientin                | ![Isoorientin](image) |
| 67. *Lantana camara*     | Caffeic acid               | ![Caffeic acid](image) |
| 68. *Linum usitatissimum* | Ferulic acid               | ![Ferulic acid](image) |
| 69. *Mangifera indica*   | Mangiferin                 | ![Mangiferin](image) |
| Medicinal Plants          | Phytoconstituents | Chemical Structure |
|---------------------------|-------------------|--------------------|
| 70. *Momordica charantia* | Vicine            | ![Vicine](image1)  |
| 71. *Moringa oleifera*   | Kaempferol        | ![Kaempferol](image2) |
| 72. *Murraya koenigii*   | Mahanimbine       | ![Mahanimbine](image3) |
| 73. *Musa sapientum*     | Delphinidin       | ![Delphinidin](image4) |
| 74. *Nigella sativa*     | Thymoquinone      | ![Thymoquinone](image5) |
| 75. *Ocimum basicillicum*| Linalool          | ![Linalool](image6) |
| 76. *Ocimum sanctum*     | Eugenol           | ![Eugenol](image7) |
Table 3. Cont.

| Medicinal Plants | Phytoconstituents | Chemical Structure |
|------------------|-------------------|--------------------|
| 77. *Olea europaea* | Oleanolic acid | ![Oleanolic acid](image1.png) |
| 78. *Panax ginseng* | Ginsenoside Rg2 | ![Ginsenoside Rg2](image2.png) |
| 79. *Panda oleosa* | Ginsenoside Rb2 | ![Ginsenoside Rb2](image3.png) |
| 80. *Phaseolus vulgaris* | Orientin | ![Orientin](image4.png) |
| Medicinal Plants         | Phytoconstituents | Chemical Structure |
|--------------------------|-------------------|--------------------|
| 81. *Phyllanthus amarus* | Ursolic acid      | ![Ursolic acid](image) |
| 83. *Pterocarpus marsupium* | Marsupin | ![Marsupin](image) |
| 84. *Punica granatum*   | Nictoflorin       | ![Nictoflorin](image) |
| 85. *Rehmannia glutinosa* | Catalpol          | ![Catalpol](image) |
| 86. *Santalum album*    | β-santalol        | ![β-santalol](image) |
| Medicinal Plants       | Phytoconstituents | Chemical Structure |
|------------------------|-------------------|--------------------|
| 87. *Selaginella bryopteris* | Gallic acid       | ![Gallic acid](image) |
| 88. *Sesamum indicum*   | Pinoresinol       | ![Pinoresinol](image) |
| 89. *Solanum nigrum*    | Naringenin        | ![Naringenin](image) |
| 90. *Spirulina platensis* | β-carotene       | ![β-carotene](image) |
| 91. *Swertia chirayita* | Swerchirin        | ![Swerchirin](image) |
| 92. *Tamarindus indica* | Taxifolin         | ![Taxifolin](image) |
| Medicinal Plants          | Phytoconstituents | Chemical Structure |
|---------------------------|-------------------|--------------------|
| **93. Terminalia arjuna** | Arjungenin        | ![Arjungenin](image) |
| **94. Terminalia chebula**| Tannic acid       | ![Tannic acid](image) |
| **95. Tinospora cordifolia** | Syringin         | ![Syringin](image)   |
| **96. Trigonella foenum-graecum** | Galactomannan   | ![Galactomannan](image) |
Table 3. Cont.

| Medicinal Plants     | Phytoconstituents | Chemical Structure |
|----------------------|-------------------|--------------------|
| 97. *Urtica dioica*  | Quercitrin        | ![Quercitrin](image) |
| 98. *Vernonia amygdalina* | Sobrerol         | ![Sobrerol](image)  |
| 99. *Withania coagulans* | Withaferin A     | ![Withaferin A](image) |
| 100. *Zingiber officinale* | Gingerol         | ![Gingerol](image)   |

7. Plant-Based Drug Formulations Available on the Market and Their Role in Diabetes

For the past few decades, there has been an increasingly growing trend in many European countries to develop and sell plant-based medicines [370]. The latter are known as herbal formulations or phytomedicines. These preparations have been standardized and confirmed for their safety profile and effectiveness in the treatment of various diseases. Similar to any other allopathic medicine, herbal formulations can also be prepared as diverse formulations such as tablets, capsules, elixirs, suspensions, solutions, emulsions, and powders [371]. Phytomedicines can either be single herb- or polyherbal formulations [35]. Several phytomedicines have been marketed worldwide for the control and management of diabetes. These include Antibetic, Diabetics, Diabetica, Diabet, Diasol, Diabecon, Diashis, GlucoCare, GlycoNase,
Glyoherb, Karmin Plus, SugarMax, and Sugar Loss [35,372]. These products comprise a combination of individual constituents from several antidiabetic plants. Many of these preparations are sold with directions about diet, rest, and physical activities to enhance their effectiveness [35,372].

8. The Future of Plant-Based Antidiabetic Medicines

Nearly 75% of the globally used herbal medicines have been developed based on traditional medicine practitioners [24]. Medicinal plants will continue to be used for their natural safety and potency in many remedies, as well as cosmetics, perfumes, and in the food and beverages industry [373]. Biologically active components derived from traditional medicinal plants have yielded several clinically used drugs and still play a key role in the discovery of new medicines. Thus, it is reasonable to assume that plants used in folk medicine can be used as a potential source for the discovery of new drugs to treat diabetes. The most frequently recommended synthetic drug, metformin, has blood glucose-lowering properties in Type 2 diabetes and the search for many such drugs persists [370]. Moreover, any plant-derived antidiabetic drug with a novel mode of action compared to existing antidiabetic agents has a high potential to be used in clinics [374]. Although the use of plant-based medicines is widespread in developing countries, recently, developed countries have also shown interest in using herbal drugs and therapies. With the rise in the incidence of diabetes mellitus, the demand for plant-based antidiabetic medicines is increasing worldwide. It is expected that countries such as China, India, and Japan, which have an abundance of medicinal plant species and are the greatest exporters of medicinal plants worldwide, will be the most sought [375]. More studies are required regarding the pharmacokinetics/pharmacodynamics of different phytoconstituents in laboratory animals and in clinical use to establish the benefits and mode(s) of action of these compounds in the treatment and management of diabetes. Extensive investigations into the pharmacology, toxicology, metabolism, and tissue distribution of medicinal plants and their phytomolecules are necessary for the development of new potent antidiabetic drugs [376].

9. Conclusions

Diabetes mellitus has risen as a major public health crisis, particularly in underdeveloped countries. Thus, recent research efforts have been centered on the discovery of new natural sources of antidiabetic therapies for the treatment and management of diabetes. As traditional medicinal plants with antidiabetic activity may be considered potential candidates for diabetes management in the long run, they are being extensively researched for novel targets, mechanisms of action, and routes of administration. Plant-based antidiabetic medicines are inexpensive, readily available, and hold low risks of side effects. This makes them promising new antidiabetic agents. With the progression of medicinal plant-based research, scientists and physicians have started to develop newer classes of antidiabetic drugs based on the pharmacology of the phytochemicals isolated from these plants. However, more studies are required for in-depth investigation of these newly discovered antidiabetic drugs at the molecular, therapeutic, and physiological levels in order to control and manage diabetes mellitus worldwide.

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Abbreviations

- AMPK: 5′ adenosine monophosphate-activated protein kinase
- cAMP: cyclic Adenosine monophosphate
- DPP-IV: Dipeptidyl peptidase-4
- G6Pase: Glucose-6-phosphatase
- GLP-1: Glucagon-like peptide-1
- GLUT-2: Glucose transporter-2
- GLUT-4: Glucose transporter-4
- HbA1c: Hemoglobin A1c
- IDF: International Diabetes Federation
- KATP: Adenosine triphosphate-sensitive potassium channel
- PEPCK: Phosphoenolpyruvate carboxykinase
- PI3K/AKT: Phosphoinositide 3-kinase/protein kinase B
- PKA: Protein kinase A
- PPAR-γ: Peroxisome proliferator-activated receptor-γ
- SGLT: Sodium–glucose linked transporter

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