Review Article

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A Comprehensive Review of Medicinal Plants with Antidiabetic Potential

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ABSTRACT

Diabetes is one of the most common chronic diseases and its incidence and prevalence have been increasing in recent years. Moreover, many comorbidities can be observed in addition to diabetes. For this reason, medicinal plants have been an important complementary treatment option for individuals with diabetes from past to present. However, as in every disease, the correct use of medicinal plants in diabetes is important. Failure to do so may worsen the course of the disease, cause side/adverse effects and lead to herb-drug interactions. This review aimed to identify antidiabetic medicinal plants comprehensively and to describe the most commonly used ones in detail. When the studies in the literature were evaluated, it was determined that many medicinal plants with antidiabetic effects have been used from past to present, but the potential mechanism of activity, positive/negative effects, dosages, and plant-drug interactions of many of them have not been fully revealed. Further research is needed, as the incorrect and unknowing use of these medicinal plants can worsen the course of the disease.

Keywords: Antidiabetic, diabetes, medicinal plants

1. Introduction

Diabetes mellitus (DM), a condition that occurs when the pancreas does not produce enough insulin or the body cannot use the insulin it does produce effectively, is one of the world's most common chronic diseases [1-3]. In the last 40 years, more people have been diagnosed with DM. Today, more than 460 million people are affected [3, 4]. Ten years after being diagnosed, approximately 60% of patients are thought to suffer from three or more comorbidities, which directly contribute 6.7 million deaths annually [5]. DM is a chronic disease that occurs when blood glucose levels are too high. Glucose in the blood is the main source of energy for the human body, controlled by pancreatic cells. There are three types of diabetes: type 1 diabetes (T1DM), type 2 diabetes (T2DM) and gestational diabetes (GDM).

People with T1DM are unable to produce enough insulin or any insulin at all, so the sugar stays in the blood and does not reach the cells. In people with DM, the pancreatic beta (β) cells responsible for producing insulin are damaged by a faulty immune system and cannot produce insulin. Can occur at any age, mostly in children and adolescents. T2DM is linked to varying degrees of insulin resistance and impaired β-cell function, which can be influenced by multiple risk factors (genetic/metabolic/environmental). In addition, people with high blood glucose levels and a high risk of developing T2DM are those with factors such as ageing, family history of T2DM, obesity, hypertension and pre-diabetes. In addition, GDM may be the most common cause of T2DM in some women who are pregnant [1, 2, 4-8]. GDM shares many pathological similarities with T2DM and is a type of DM associated with hyperglycaemia in pregnant women. It is usually diagnosed in the 2nd or 3rd trimester of pregnancy with a prevalence of 2-4%. In 2017, there were reports that approximately one in seven pregnant women worldwide had GDM. Maternal insulin resistance in GDM raises fetal glucose levels, boosting fetal growth. GDM usually resolves after the baby is born, but both mother and baby are at risk of developing T2DM later in life [9-11]. The global prevalence of GDM ranges from 5-25.5%, depending on race, ethnicity, age and gender. Hyperglycaemia affected 16.7% of all pregnancies worldwide, of which 80.3% were due to GDM, according to the International Diabetes Federation (IDF) 2021 Diabetes Atlas [11].

DM can be measured by analysing blood glucose levels. The fasting blood glucose level in a healthy person is 80 mg/dl. After a meal, this level can rise to 160 mg/dl. Different tests used to diagnose DM in the laboratory are finger stick blood glucose test, fasting blood glucose, glucose tolerance test and glycohaemoglobin [9]. Although there are many ways to diagnose DM, there is no complete cure for DM and, due to its increasing prevalence worldwide, scientists are constantly searching for different approaches to the treatment and prevention of DM [2, 9]. The IDF estimates that there will be approximately 463 million adults with DM in 2019 and that this number will increase to 578 million by 2030 and 700 million by 2045 [7]. Moreover, the greatest concern about this observation is the development of chronic complications associated with the disease [2, 9]. The main goal in a person with DM is to improve metabolic factors associated with complications. The primary strategy is to achieve recommended targets for blood pressure, lipids and glycaemia. This strategy consists of combining lifestyle and dietary changes and increased physical activity with pharmacological intervention from several classes of agents [2, 12]. Pharmacological treatment strategies for DM have improved over the last few decades. There are several categories of antidiabetic drugs on the market. These include insulin analogues, sulfonylureas, biguanides, dipeptidyl peptidase-4 inhibitors, thiazolidiones, α-glucosidase inhibitors, etc., and the mechanism to counteract the increased glucose level is different for each category [9, 12]. However, antidiabetic drugs have serious effects such as hypoglycaemic coma and liver and kidney damage [7]. Also traditional and complementary medicine is one of the approaches used by people with DM in addition to pharmacological treatment, especially in recent years. WHO defines the term of "traditional and complementary medicine" as the total knowledge of health practices and skills based on local beliefs and experiences, while just "complementary medicine" is defined as various health practices that are not part of the tradition or traditional medicine of the country [13].

The WHO recommends using herbal supplements to help treat DM [7, 13-15]. For many years, plants have been widely used by people with DM. At least 4 billion people in developing countries use medicinal plants to treat metabolic diseases such as DM [7]. Therefore, antihyperglycaemic medicinal plants have continued to play an important role in managing DM.

Recent pharmacological studies have revealed the antidiabetic properties of medicinal plants, including antihyperglycaemic, anti-lipidaemic, hypoglycaemic and insulin mimicking properties [16, 17]. This property has been attributed to a number of phytochemical constituents that are present in medicinal plants and have anti-diabetic properties. Phenolics, glycosides, alkaloids, terpenoids, flavonoids and carotenoids are known to be the major groups of these phytochemicals [18]. Although many of these medicinal plants have antihyperglycaemic effects, there is not enough evidence to support the routine use of plants to improve blood glucose control in people with DM. From the patient's perspective, medicinal plants/herbal products are accepted as part of medical intervention There is a lack of precise and consistent data on the positive/negative effects, information on their mechanisms of medicinal plants used in DM. Evidence on antidiabetic medicinal plants/herbal products should be studied further, especially given the positive impact on a specific mechanism. In this context, this review aims to comprehensively identify antidiabetic medicinal plants from past to present and to explain in detail the most commonly used ones.

2. Materials and Methods

In this study, a literature search has been conducted in the Google Scholar, PubMed, Science Direct, Web of Science, Scopus and ULAKBIM databases in order to identify in detail the medicinal plants used in preparations for their antidiabetic activities and their proven effects in the world and in our country, from 2007-2024 years. Scientific studies (experimental studies, meta-analysis studies and systematic reviews) considered appropriate for the subject were analysed to ensure the scientific integrity of the subject.

3. Results and Discussions

As a result of a comprehensive literature review in databases, medicinal plants with antidiabetic effects are listed in Table 1.

Table 1. Medicinal plants with antidiabetic effect.

Latin Name	Family	Parts Used	Literature
Acacia catechu (L. f.) P. J. H. Hurter & Mabb.	Fabaceae	Cortex	[12, 21]
Aegle marmelos Corr. ex Roxb.	Rutaceae	Fructus, Folia, Semen	[9, 12-21]
Aerva lanata (L.) Kuntze	Amaranthaceae	Herba	[12]
Allium cepa L.	Liliaceae	Bulbus	[9, 20, 21]
Allium sativum L.	Liliaceae	Bulbus	[7-9, 21]
Aloe vera (L.) Burm. f.	Asphodeloideae	Folia	[9, 22-25, 26]
Andrographis paniculata Nees. L	Acanthaceae	Herba	[25, 26-29]
Annona squamosa L.	Annonaceae	Folia	[9, 27]
Anoectochilus roxburghii Wall. (Lindl.)	Orchidaceae	No data	[22]
Apium graveolens L.	Apiaceae	Herba	[26]
Artemisia dracunculus L.	Asteraceae	Folia	[2]
Astragalus membranaceus Bunge	Fabaceae	Radix	[22, 23]
Atriplex halimus L.	Amaranthaceae	Folia	[26]
Azadirachta indica A. Juss.	Meliaceae	Folia	[9, 12, 21, 29]
Bambusa arundinaceae (Retz.) Willd.	Poaceae	Folia	[12]
Berberis integerrima Bunge	Berberidaceae	Radix	[27]
Beta vulgaris L.	Amaranthaceae	Fructus, Radix	[8, 21, 22]
Bidens pilosa L.	Asteraceae	No data	[22]

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Table 1 (*continue*). Medicinal plants with antidiabetic effect

Latin Name	Family	Parts Used	Literature
Brassica juncea (L.) Czern.	Brassicaceae	Semen	[9]
Cajanus cajan (L.) Huth	Fabaceae	Folia	[9, 12]
Callistephus chinensis (L.) Nees.	Asteraceae	Flos	[12]
Camellia sinensis (L.) Kuntze	Theaceae	Folia	[8, 21, 23, 26]
Capparis decidua (Forssk.) Edgew.	Capparaceae	Fructus	[21]
Carica papaya L.	Caricaceae	Semen	[9, 22]
Carthamus tinctorius Mohler, Roth, Schmidt & Boudreaux	Asteraceae	Flos	[23]
Carum carvi L.	Apiaceae	Semen	[9]
Catharanthus roseus (L.) G. Don	Apocynaceae	Semen, Herba	[9, 25]
Centarium erythraea Rafn.	Gentianaceae	Herba	[21]
Centella asiatica L.	Apiaceae	Folia	[27]
Ceratonia siliqua L.	Fabaceae	Folia	[21]
Cinnamomum cassia (L.) J. Presl.	Lauraceae	Cortex	[9, 21-22]
Cinnamomum verum L.	Lauraceae	Cortex	[12, 22, 23]
Citrullus colocynthis (L.) Schrad.	Cucurbitaceae	Fructus	[21, 26]
Citrus limon (L.) Osbeck	Rutaceae	Fructus	[21]
Coccinia grandis (L.) Voight	Cucurbitaceae	Folia	[12]
Coffea canephora Pierre ex A. Froehner	Rubiaceae	Semen	[21]

Table 1 (*continue*). Medicinal plants with antidiabetic effect

Latin Name	Family	Parts Used	Literature
Convolvulus arvensis L.	Convolvulaceae	Herba	[21]
Cucurbita pepo L.	Cucurbitaceae	Fructus	[21]
Coptis chinensis Franch.	Ranunculaceae	Rhizoma	[12]
Corchorus olitorius L.	Malvaceae	Folia	[12]
Coriandrum sativum L.	Apiaceae	Herba	[9]
Crocus sativa L.	Iridaceae	Stigma	[26]
Curcuma longa L.	Zingiberaceae	Rhizoma	[9, 22, 29]
Cynara cardunculus L.	Asteraceae	Herba	[21]
Cynara scolymus L.	Asteraceae	Folia	[26]
Eugenia jambolana (Lam.) Willd.	Myrtaceae	Bulbus, Fructus	[9, 21]
Ficus carica L.	Moraceae	Folia	[21]
Ficus deltoidea Jack	Moraceae	Flos, Folia	[12]
Ficus hispida L. f.	Moraceae	Folia	[9]
Garcinia indica Choisy.	Clusiaceae	Fructus, Semen	[12]
Ginkgo biloba L.	Ginkgoaceae	Folia	[26, 28]
Globularia alypum L.	Plantaginaceae	Folia	[21]
Glycine max (L.) Merrill	Fabaceae	Semen	[12, 22]
Gymnema sylvestre (Retz.) R.Br. ex Sm.	Apocynaceae	Folia, Cortex	[20-22, 27-29]

Table 1 (*continue*). Medicinal plants with antidiabetic effect

Latin Name	Family	Parts Used	Literature
Helicterus isora L.	Sterculiaceae	Radix	[29]
Hemidesmus indicus (L.) R. Br.	Apocynaceae	Rhizoma	[21]
Hibiscus sabdariffa L.	Malvaceae	Flos, Calyx	[7, 21]
Holarhena antidysenterica (L.) Wall. ex G. Don	Apocynaceae	Semen	[12]
Laurus nobilis L.	Lauraceae	Folia	[21]
Lonicera japonica Thunb.	Caprifoliaceae	Flos	[22]
Malus domestica L.	Rosaceae	Fructus	[8]
Mangifera indica L.	Anacardiaceae	Semen, Folia	[9, 21]
Marrubium vulgare L.	Lamiaceae	Herba	[8]
Mentha piperita L.	Lamiaceae	Herba	[8]
Momordica charantia L.	Cucurbitaceae	Fructus	[7, 20, 23, 26, 28, 29]
Moringa oleifera Lam.	Moringaceae	Radix	[25]
Morus nigra L.	Moraceae	Folia	[27]
Murrya koenigii (L.) Spreng.	Rutaceae	Folia	[12, 21]
Musa paradisiacal L.	Musaceae	Flos, Fructus, Semen	[9, 29]
Nigella sativa L.	Ranunculaceae	Semen	[12, 23]
Ocimum basilicum L.	Lamiaceae	Herba	[8, 12]
Ocimum sanctum L.	Lamiaceae	Herba	[9, 20, 21, 29]

Table 1 (*continue*). Medicinal plants with antidiabetic effect

Latin Name	Family	Parts Used	Literature
Olea europaea L.	Oleaceae	Folia	[8, 12, 23, 26]
Opuntia ficus-indica (L.) Mill.	Cactaceae	Fructus, Herba	[21, 27]
Panax spp.	Araliaceae	Fructus	[9, 20, 22, 25, 27]
Papaver rhoeas L.	Papaveraceae	Herba	[8]
Petroselinum crispum (Mill.) Fuss	Apiaceae	Herba	[8]
Phyllanthus emblica L.	Phyllanthaceae	Fructus, Folia	[9]
Phyllanthus niruri L.	Phyllanthaceae	Aerial parts	[29]
Phyllanthus urinaria L.	Phyllanthaceae	Folia	[12]
Picrorhiza kurroa Royle ex Benth.	Plantaginaceae	Rhizoma	[12]
Piper methysticum L.	Piperaceae	Radix	[29]
Pistacia lentiscus L.	Anacardiaceae	Folia	[8]
Prunus dulcis (Mill.) D.A. Webb	Rosaceae	Fructus	[8]
Prunus persica (L.) Batsch.	Rosaceae	Folia	[8]
Pterocarpus marsupium Roxb.	Fabaceae	Radix	[12, 21, 29]
Pterocarpus santalinus L. F.	Fabaceae	Radix	[29]
Punica granatum L.	Lythraceae	Folia, Semen	[8, 9]
Rhamnus alaternus L.	Rhamnaceae	Herba	[8]
Rosmarinus officinalis L.	Lamiaceae	Folia	[8]

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Table 1 (*continue*). Medicinal plants with antidiabetic effect

Latin Name	Family	Parts Used	Literature
Rubus fruticosus L.	Rosaceae	Fructus	[8]
Ruta graveolens L.	Rutaceae	Radix	[8]
Salacia oblonga Wall. ex Wight & Arn.	Celastraceae	Radix, Fructus	[26, 29]
Salacia reticulata Wight	Celastraceae	Radix, Fructus	[20, 21]
Salvia officinalis L.	Lamiaceae	Herba	[8, 26]
Satureja khuzestanica Jamzad	Lamiaceae	Folia	[29]
Scoparia dulcis L.	Plantaginaceae	No data	[29]
Silybum marianum (L.) Gaertn.	Asteraceae	Semen	[20, 22, 26]
Stevia rabudiana (Bertoni) Bertoni	Asteraceae	Folia	[29]
Strychnos potatorum L. f.	Loganiaceae	Semen	[12]
Swertia chirata (Roxb. ex Flem) Karsten.	Gentianaeae	Semen, Herba	[9, 12]
Syzygium cumini (L.) Skeels	Myrtaceae	Semen	[29]
Syzygium polyanthum (Wight) Walp.	Myrtaceae	Folia	[27]
Tamarindus indica L.	Fabaceae	Semen	[12]
Terminalia bellirica (Gaertn) Roxb.	Combretaceae	Fructus	[12]
Terminalia catappa L.	Combretaceae	Fructus	[9]
Terminalia chebula Retz.	Combretaceae	Fructus	[12]
Terminelia arjuna (Roxb. ex DC.) Wight & Arn.	Combretaceae	Semen	[9]

Table 1 (*continue*). Medicinal plants with antidiabetic effect

Latin Name	Family	Parts Used	Literature
Teucrium polium L.	Lamiaceae	Herba	[8, 26]
Thymus serpyllum L.	Lamiaceae	Herba	[8]
Tinospora cordifolia (Giloy)	Menispermaceae	Radix	[9, 21, 29]
Trigonella foenum-graecum L.	Fabaceae	Semen	[9, 20, 22-26]
Urtica dioica L.	Urticaceae	Herba	[8, 23]
Uvaria chamae P. Beauv.	Annonaceae	Radix	[12]
Vetiveria zizanioides (L.) Nash	Poaceae	Radix	[12]
Zingiber officinale Roscoe	Zingiberaceae	Rhizoma	[7-9, 22]

Detailed information about the medicinal plants (*Allium sativum* L., *Aloe vera* (L.) Burm. F., *Artemisia dracunculus* L., *Cinnamomum verum* L., *Gymnema sylvestre* R. Br., *Momordica charantia* L., *Trigonella foenum-graecum* L., *Zingiber officinale* Roscoe,) most commonly used for antidiabetic purposes is given below, in alphabetical order.

Allium sativum L.

Allium sativum L. is the common name of "Garlic", is a plant in the Liliaceae family. Garlic is one of the most fascinating medicinal plants used throughout history. Garlic is known to have antihypertensive, immunomodulatory, cardioprotective, hypolipidae-

mic, hypoglycaemic antiinflammatory, antioxidant, antimicrobial, and anticancer. Researchs have suggested that garlic may help lower blood glucose level and improve insulin sensitivity, which may be beneficial for diabetes. Clinical studies have shown that garlic supplementation with standard antidiabetic medications effectively reduces insulin resistance, lipid profile, and glycaemic parameters, including fasting plasma glucose and HbA1c, particularly for T2DM. These effects are thought to be due to sulphur compounds such as diallyl disulphide and diallyl trisulphide in its structure. These compounds act as hydrogen sulphide donors that control T2DM [2, 7, 30-35].

Aloe vera (L.) Burm. f.

Aloe vera (L.) Burm. F. is a medicinal plant belonging to the Liliaceae family, distributed in the hot and dry regions of North Africa, the Middle East of Asia, the Southern Mediterranean and the Canary Islands, and used in the treatment of diabetes in India and the Arabian Peninsula. The inner leaf gel contains the hypoglycaemic and insulin-sensitising water-soluble fibre glucomannan. Although studies have shown inconsistent results, clinical trials have shown that *A. vera* extract provides an improvement, particularly in fasting blood glucose levels. *A. vera* has also been shown to have a potential effect on glycaemic control, reducing hyperglycaemia and hypercholesterolaemia in people with DM. Aloeresin-A, an active compound of *A. vera*, inhibits α-glucosidase activity and reduces α-glucosidase and intestinal glucose absorption [36-41].

Artemisia dracunculus L.

Artemisia dracunculus L., which belongs to the Asteraceae family and is known as "Russian Tarragon", has recently been shown to possess antidiabetic properties. It has long been part of traditional medicine in Asian countries and is a popular spice in Europe. It is used for gastrointestinal problems, as an anaesthetic, hypnotic and anti-epileptic, and as an effective treatment for inflammation, fever and helminthiasis. Furthermore, antibacterial, antifungal, antidepressant, analgesic, hepatoprotective, antiprotozoal, and hypoglycaemic effects have been reported lately. *A. dracunculus*, containing 4,5-di-O-caffeolquinic acid, 6-demethoxycapillerisone, davidigenin, and 2', 4'-dihydroxy-4-methoxydihydrochalcone, sacuranetin, has been shown to inhibit hepatocellular phosphoenolpyruvate carboxykinase (PEPCK) gene expression, thereby contributing to glucose homeostasis, positively influencing insulin signalling in muscle, and increasing insulin sensitivity compared to baseline [2, 42-44]. The FDA has listed *A. dracunculus* and its derivatives as safe [45]. Although more research is needed on use and dosage.

Cinnamomum verum L.

Cinnamomum verum L., also known as "Ceylon cinnamon", is an important spice of the Lauraceae family that is rich in phytochemicals, particularly in China and Sri Lanka [46]. Cinnamon has been shown to be effective in helping to manage T2DM. Cinnamon was shown to be effective in lowering blood glucose levels in patients with T2DM. However, the results of cinnamon supplements in people with DM have been inconsistent and contradictory. Potential antidiabetic properties have been shown by a number of cinnamon-derived phytochemicals. Cinnamaldehyde, a water-soluble polyphenol, is one such compound. Polyphenolic compounds also have antiinflammatory properties by regulating interleukin-1 and -6 (IL-1 and -6), C-reactive protein (CRP) and tumour necrosis factor (TNF)-alpha [47]. Cinnamon polyphenols are known to increase the synthesis and accumulation of glycogen by increasing the levels of GLUT4 proteins and insulin receptor-β, decreasing the activity of glycogen synthase kinase-3 β (GSK3β) and increasing the levels of tristetraprolin protein. A proanthocyanidin from the cinnamon stem facilitates the activation of β-subunit phosphorylation on various insulin receptors. This increases insulin signalling and improves insulin sensitivity. Through its ability to transport GLUT4 via the MPK pathway, it has also been shown to improve T2DM. Cinnamon has been shown to improve DM by increasing glycogen synthesis, increasing glucose uptake, regulating insulin sensitivity and response, inhibiting gastrointestinal enzyme activity and gluconeogenesis [2, 46-49]. Considering the studies in the literature, it is concluded that Cinnamon is promising for DM and insulin resistance, more research should be done for the prevention and management of DM and the dose-response relationship should be determined.

Gymnema sylvestre R. Br.

Gymnema sylvestre R. Br. is a medicinal plant of the Apocynaceae family, known as "Gurmar", native to Africa, the Middle East and India, which has been

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used historically in the treatment of DM. *G. sylvestre* is considered to be most important herbal products used in Ayurveda for the treatment of DM and is also listed in the Indian Pharmacopoeia as a plant with antidiabetic properties. It has broad therapeutic potential, including hypoglycaemic, antioxidant and anti-cancer activities. The antidiabetic properties of the plant are attributed to its gymnemic acids, gymnemosides, and gurmarin. *G. sylvestre* affects carbohydrate metabolism by improving glucose uptake and increasing insulin and β-cell numbers. Besides systemic hypoglycaemic activity, other studies have reported that *Gymnema* preparations suppress sweet taste, reduce small intestinal glucose uptake, improve glucose metabolism, reduce HbA1c, insulin secretion and dyslipidaemia [2, 50-54]. However, there are no definitive clinical trials to give clear guidance on efficacy and safety. Furthermore, using *Gymnema*-based dietary supplements with (or instead of) approved antidiabetic drugs may carry risks if used without medical supervision. Uncertainties about Gymnema composition and herb-drug interactions/hypoglycaemic effects [54]. Clearly, well-designed clinical trials are needed to support *G. sylvestre*'s antidiabetic effects.

Momordica charantia L.

Momordica charantia L., known as "Bitter melon/pomegranate", is a medicinal plant of the Cucurbitaceae family that is widely used in complementary therapies to treat DM in both developing and developed countries, including Vietnam, India, China, East Africa, South-North Asia, and Central-South America. Improves insulin sensitivity and reduces hepatic glucose production, regulating and lowering glucose levels with DM [2, 7, 19, 55, 56]. Some plants increase the secretion of insulin, improve the uptake of glucose and inhibit the absorption and production of glucose [57-60], effective glucose lowering, especially in T2DM patients [61]. In addition, bitter melon has a hypoglycaemic effect, stimulating glucose uptake into skeletal muscle cells and increasing insulin secretion [62-64]. Several bioactive secondary metabolites have been attributed to the mechanism by which *M. charantia* acts on DM, including. Specifically, polypeptide-p has been reported to have a structure similar to animal insulin and therefore hypoglycaemic [65]. In addition, the fruits and seeds of *M. charantia* have antioxidant, anti-inflammatory, immunomodulatory, hypolipidaemic and anti-hyperglycaemic activity. These parts stimulate glucose uptake by activating the action of glucose-6-phosphatase dehydrogenase in the pentose phosphate pathway, owing to phenols, phytosterols, saponins and tannins [66]. However, the compounds that are responsible for the observed antidiabetic effects are poorly characterised [56]. Furthermore, *M. charantia* fruit aqueous extract has been shown to protect pancreatic β-cells by downregulating MAPKs and NF-κB to reduce impaired insulin signalling. *M. charantia* upregulates the expression of the peroxisome proliferator-activated receptor gamma (PPAR-γ) gene. This gene is involved in glucose metabolism [64-66]. In particular, modulating "Protein Tyrosine Phosphatase 1B (PTP1B)" acts as a negative regulator of the insulin signalling pathway and also contributes to the hypoglycaemic effect. By transporting GLUT4 across the cell membrane, it stimulates insulin secretion from pancreatic β-cells and increases glucose uptake [66]. When evaluating the side effects of *M. charantia*, there are no significant toxic effects. However, there are many reports showing its negative effects. There are also reports of increased risk of inflammatory diseases and acute intoxication symptoms such as seizures, neurological disorders and respiratory distress. Furthermore, *M. charantia* has been reported to have dose-dependent antifertility effects by significantly reducing estrogen and progesterone levels, with abortive and teratogenic properties *in vivo* [55]. The clinical results of *M. charantia* are inconsistent when these studies are evaluated in the literature.

Trigonella foenum-graecum L.

Trigonella foenum-graecum L., known as "Fenugreek", has a long medicinal history and is used worldwide to treat DM. Native to the Mediterranean region, Asia and Europe, and cultivated in India and Northern Africa, plant of the Fabaceae family. Seeds used as food or spice, high in protein and fibre [2,67]. Both *in vivo* and clinical studies have reported hypoglycaemic and hypocholesterolaemic effects of fenugreek [68-70]. The clinical effects of fenugreek, particularly its hypoglycaemic effects, are attributed to its dietary fibre content, which may have an effect on gastric emptying and a decrease in postprandial blood glucose levels [68]. In particular, active antidiabetic compounds in fenugreek have been identified as diosgenin, galactomannan, trigoneosides and 4-hydroxyisoleucine. The mechanisms of these com-

pounds, however, are poorly understood [8]. Fenugreek alkaloids' hypoglycaemic effect is also due to antioxidant activity. The antioxidant effect is due to the inhibition of reactive oxygen species (ROS) and proinflammatory cytokines, which can be the cause of insulin resistance. By regulating insulin secretion, the dietary fibre in fenugreek seed also contributes to the hypoglycaemic effect. It also contributes to its antidiabetic properties by delaying gastric emptying to slow intestinal glucose absorption. Another mode of action of fenugreek in controlling hyperglycaemia is the regeneration of pancreatic beta cells to increase insulin secretion. Fenugreek also improves glucose utilisation by increasing glucose uptake by fat and muscle tissue and by increasing glucose-6-phosphate dehydrogenase activity. However, fenugreek seed powder has been reported to have a positive effect on glycaemic index and glucose tolerance. It has also been found to lead to improvements in fasting glucose and dyslipidaemia [68-70]. Additionally, it has been reported that the use of 10 g of fenugreek as a dietary supplement in patients with pre-diabetes is associated with a reduction in conversion to DM without adverse effects and is probably beneficial because it reduces insulin resistance [71]. As fenugreek is consumed in the diet, it is thought to be safe; however, it is noted that this effect is dose-dependent. It has been found that fenugreek has minimal side effects of 0.2-1 g per/kg for up to 7 days, and it has been reported that fenugreek seeds should not be consumed during pregnancy due to its estrogenic activity as it may affect fetal development [67]. Although studies in the literature suggest that it may be a safe and effective treatment for people with DM, more needs to be done to determine how it affects DM.

Zingiber officinale Roscoe

Zingiber officinale Roscoe (Ginger), is a spice from India, China, Nigeria, Indonesia, Bangladesh, Australia, Jamaica and Nepal. The effects of ginger include antiinflammatory, immunomodulatory, antioxidant, hypolipidaemic, hypoglycaemic, antiemetic, antihypertensive and antidiabetic. These effects have been attributed to phenolic compounds such as gingerols, shogaols, paradols and non-volatile compounds such as zingiberone, zingiberole and zingiberene [72]. Many preclinical and clinical studies have shown that ginger is a promising hypoglycaemic dietary supplement, particularly for the treatment of T2DM. Ginger regulates insulin, promoting glucose removal from insulin-responsive tissues and helping to maintain blood sugar balance. Specifically, 6-gingerol in its structure has been found to increase glucose uptake in insulin-responsive adipocytes, and insulin-responsive glucose uptake increases and ameliorates DM in cells treated with gingerol. Ginger rhizomes have been reported to prevent the development of insulin resistance, particularly by regulating "Peroxisome Proliferator–Activated Receptors" (PPARs). It was reported that the consumption of 30 g of ginger powder per day for 3 days significantly reduced blood glucose levels in patients with T2DM. Gingerol has been shown to attenuate sodium arsenite-induced T2DM. This attenuation protects islet cells and activates insulin receptors [73-77].

4. Conclusion

Many medicinal plants have been used in the past and present for their antidiabetic effects. Although there is a wide range of medicinal plants for this purpose, there are questions that need to be clarified about the mechanism of action, dosage, clinical/side effects, and plant-drug interactions of these medicinal plants. As a result of the studies to be carried out in this direction, our belief is that medicinal plants with antidiabetic activity can help prevent the disease and improve its symptoms.

Conflict of Interest

The authors has no conflicts of interest, financial or otherwise, to declare.

Statement of Contribution of Researchers

Concept – E.B., G.E.C.; Design – E.B., G.E.C.; Supervision – G.E.C.; Resources – E.B.; Materials – E.B.; Data Collection and/or Processing – E.B., G.E.C.; Analysis and/or Interpretation– E.B., G.E.C.; Literature Search – E.B.; Writing – E.B., G.E.C.; Critical Reviews – E.B., G.E.C.

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