

Review Article

Indigenous Antidiabetic Medicinal Plants used in Nigeria: A Review

Abstract

The most prevalent endocrine illness and leading cause of morbidity and mortality is diabetes mellitus. There are numerous natural treatments for both the prevention and treatment of diabetes mellitus used by traditional medical systems. Reviewing published Nigerian plants with putative anti-diabetic properties was the goal of this work. The databases of Google Scholar, Elsevier, African Journals online, Medline, Web of Science, SCOPUS, PubMed, and ResearchGate were searched for articles that described the medicinal plants used to treat and manage diabetes in Nigeria. Only 35 research articles based on data published between June 2000 and August 2023 were included in this review, out of a total of 120 literature references examined. This review offers relevant information and the most recent scientific findings on the plants used to treat and manage diabetes in Nigeria. The cellular mechanisms through which these natural agents exert their protective and therapeutic effects on diabetes mellitus may be; antioxidative stress, restricting the breakdown of glycogen, pancreatic β -cell regeneration, gluconeogenesis, anti-inflammatory and intracellular signals transduction pathways. Finally, it can be said that indigenous medicinal herbs utilized in Nigerian have the potential to treat diabetes mellitus and its complications; and may even be the source for potential drug discovery.

Keywords: Diabetes, Medicinal plant, Nigeria, Traditional, Hyperglycemia

1. Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by either inadequate insulin secretion, inadequate cellular action of the insulin, or both [1]. Long-term hyperglycemia results in remodeling of the vessel wall in the retinal and renal circulations, which leads to retinopathy with a potential for vision loss and nephropathy [2]. These conditions are caused by inadequate insulin action on target tissues, which results in abnormal metabolism of carbohydrates, lipids, and proteins [1]. One of the root causes of diabetes is the environment, which includes obesity, diet, physical activity, lifestyle, and an increase in the number of senior individuals [3]. While type 2 diabetes (T2D) is the most common form of diabetes, type 1 diabetes (T1D) is characterized by the β -cells' inability to release insulin and/or the cells' inability to utilize the insulin secreted by the pancreatic β -cells [4]. Gestational diabetes mellitus (GDM), is characterized as a state of hyperglycemia that is discovered during pregnancy. GDM affects over 15% of pregnancies globally, resulting in almost 18 million births each year [5].

Comment [JJ1]: What are the species of plants used in it treatment? How many plants are used? what are the IUCN status of these species? What families?

Comment [JJ2]: Give a summary of this in this section, but good for your method

The prevalence of diabetes is projected to rise globally by 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045 [6]. By 2035, there will be 41.5 million cases of diabetes in the Africa Region [7]. All regions of Nigeria have seen a considerable rise in the frequency of DM, with the south-south geopolitical zone seeing the highest prevalence [8]. Diabetes mellitus is treated with insulin, dietary changes, and oral hypoglycemic medications; however, the high cost of diabetes medications and their associated side effects have made it difficult to treat and manage diabetes mellitus in modern times [9]. Because oral hypoglycemic medications are expensive and associated with a number of side effects, most people tends to use herbal therapy as an alternative for the treatment of diabetes [10]. According to reports, out of the 1355 novel medications that were approved between 1981 and 2010, 26% were from natural sources [11,12].

Furthermore, herbs are a fundamental component of African systems, approximately 80% of people worldwide rely on herbs for treatment, maintenance, and prevention of disease [13]. Numerous medicinal plants have been identified for the treatment of diabetes in Nigeria, and the efficacy of folkloric claims of these plants has been validated by several studies; linking their therapeutic effects to their phytochemical composition. Hence, it is pertinent to identify some of these plants that have antidiabetic properties.

2. Method

2.1 Lecture search process

The review was conducted using English keywords to search on the internet; using Google Scholar, African Journal Online, Elsevier, SCOPUS, Medline, Science Direct, Web of Science, PubMed and ResearchGate on the use of plants in Nigerian traditional medicine for the treatment and management of diabetes. The search terms utilized were 'diabetes in Nigeria', 'hypoglycemic plants in Nigeria', 'Nigerian plants with anti-diabetic potential' and 'anti-diabetic medicinal plants in Nigeria'. This review only includes articles that were published. English language articles were included after language restriction was taken into account. Scientific names of plants, traditional use of the plant to treat illness, plant parts, plant extract, phytochemical components (if stated), diabetes type, and animal mode for in vivo and in vitro research were all extracted from the included papers. A total of 414 articles were found and subsequently assessed for their applicability to the topic of interest. 120 papers were deemed relevant to the subject of this evaluation, however we only looked at 35 of Nigeria's most well-known plants used to treat diabetes.

Sterculia tragacantha

Sterculia tragacantha (family: *Sterculiaceae*). It is referred to as 'Abalo' (Igbo) and 'Uhobo' (Yoruba). It is frequently used to treat common cold, infectious disorders, gout, diarrhea, edema, and diabetes [14]. In vivo research on the leaf demonstrated hypoglycemic effects, improvements in body weight and antioxidant status, and mitigated streptozotocin (STZ)-induced dysregulations of Na⁺-K⁺-ATPase, cholinesterases, and neurotransmitters in experimental rats' brain tissue [15]. Additionally, it controls the anti-inflammatory response by blocking the cyclooxygenase-2/ nitric oxide (COX-2/NO) signaling axis in diabetic rats' brains. Epicatechin and procyanidin B2, bioactive components from *S. tragacantha*, docked well to the binding cavities of acetylcholinesterase, butyrylcholinesterase, -amylase, and -glucosidase with binding affinities, suggesting that these compounds are the bioactive component that may be accountable for the antidiabetic and neuroprotective activities of *S. tragacantha* [15]

Comment [JJ3]: Authority

Comment [JJ4]: Apply scientific principle please

Comment [JJ5]: Ditto

Comment [JJ6]: Where is the result for this review?

Hunteria umbellata K. Schum

Hunteria umbellata K. Schum (family: *Apocynaceae*). It is known as ‘erin’ (Yoruba) and ‘nkpokiri’ (Ibo). *Hunteria umbellata* is used to treat diabetes, obesity, fever, leprosy sores, menstrual pain, infertility, yaws, intestinal worms, abdominal discomfort, and stomach aches [16]. The plant phytochemicals identified are saponin, flavonoids, glycosides, steroids, tannins, volatile oils, phenols, and a significant amount of alkaloids [17]. The STZ-induced diabetic rats were treated with water extract of *H. umbellata* seed. The extract significantly ($P = .05$) decreased blood glucose, serum total protein, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), bilirubin levels, and glycated hemoglobin levels while increasing hemoglobin (Hb), Red blood cell count (RBC), neutrophil, lymphocyte counts and liver glycogen levels [18,19]. Similar studies showed increase in catalase (CAT), Glutathione S-Transferase (GST) and reduced malondialdehyde (MDA) levels; hence, extract ability to lower blood glucose may be by inhibition of intestinal glucose absorption and increased glycogenesis [20].

Comment [JJ7]: spelling

Newbouldia laevis

Newbouldia laevis (family: *Bignoniaceae*), its local names are ‘Ogirisi’ (Igbo), ‘Akoko’ (Yoruba) and ‘Aduruku’ (Hausa). The plant is used to treat and manage diseases like diabetes, hypertension, inflammation, skin diseases, ulcer, tumors, constipation, pains, infectious diseases, tooth ache, dysentery, impotency, sore feet, wound healing, orchitis, anaemia, ulcer, epilepsy, convulsion, arthritis, migraine, eye problems, snake bites, and rheumatism [21]. Glycosides, anthraquinolones, steroids, volatile oils, tannins, terpenoids, alkaloids, flavonoids, proteins, oil, saponins, carbohydrates, resins, sterols, reducing sugar and acidic compounds are some of the phytochemical components of the plant [21,23]. When *Newbouldia laevis* leaf extract was administered to alloxan-induced diabetic rats, the blood glucose level, platelet count, and white blood cells (WBC) all decreased significantly ($P = .05$). Significantly ($P = .05$) lowered were the activities of ALT, AST, ALP, total bilirubin, urea, and creatinine. There was also an increase in serum total protein, total antioxidant status (TAS), RBC and its indicators [24].

Comment [JJ8]: Scientific authority please

Vitex doniana

Vitex doniana (family: *Verbenaceae*), it is known as ‘Dinya’ (Hausa), ‘Oori-nla’ (Yoruba), and ‘Uchakoro’ (Igbo). Leprosy, dysentery, diarrhea, anemia, jaundice, gonorrhoea, backaches and diabetes are among the conditions that are historically treated using *Vitex doniana* leaves [25]. Flavonoids, tannins, saponins, anthraquinones, balsam, sugars, resin, cardiac glycosides, and alkaloids are among the phytochemicals found in the plant [26]. Alloxan-induced diabetic rats were treated with *Vitex doniana*, which dramatically decreased serum blood glucose and MDA concentrations while considerably increasing body weight, superoxide dismutase SOD, CAT, GST, and ascorbic acid concentrations ($P = .05$). Histological studies of the diabetic rats administered aqueous and ethanolic leaves of *Vitex doniana* in streptozotocin-induced diabetic rats showed increase; in the volume density of islets, percentage of β -cells and size of islet, which suggested regeneration of β -cells. Furthermore, there was a significant decrease ($P = .05$) in ALT, AST and ALP [27].

Comment [JJ9]: Ditto

Solanum anomalum

The *Solanum anomalum* Thonn. ex Schumacher (family; *Solanaceae*), the plant is utilized to treat conditions including diabetes, gastrointestinal disorders, infections, inflammation, and aches [28,29]. *Solanum anomalum* was shown to include phytochemicals like steroidal saponins, steroidal alkaloids, flavonoids, phenolic compounds and coumarins [29]. Alloxan-induced

Comment [JJ10]: Ditto

Comment [JJ11]: Move this authority to where the species was first mentioned.

hyperglycemia in rats was tested using *Solanum anomalum* leaf extract and hydroethanolic fractions; fasting blood glucose, glycosylated hemoglobin, triglycerides, LDL and VLDL cholesterol levels were significantly ($P = .05$) lowered. While insulin and HDL cholesterol were increased [30]. Additionally, the leaf extract significantly increased the levels SOD, CAT, Glutathione peroxidase (GPx), and GSH. There was a decreased in total and direct bilirubin, ALT, AST, and ALP [31].

Ficus exasperata

Ficus exasperata (Vahl) (family *Moraceae*), it is known as 'Ewe Ipin' (Yoruba), 'Baure' (Hausa), and 'Asesa' (Igbo). The plant is used as a stimulant; used to treat stomach pains, ulcers, arrest bleeding and diabetes mellitus [32]. The phytochemicals present are alkaloids, flavonoids, tannins, cyanogenic glycosides, saponins, and polyphenolic substances [33]. STZ was administered intraperitoneally many times at modest doses to produce Type 1 Diabetes Mellitus. When aqueous *Ficus exasperata* leaf extract was administered; blood glucose, blood pressure, and lipid profiles were all reduced, and the blood vessel microanatomy was nearly restored to normal [32]. The animals' body weight, packed cell volume (PCV), Hb concentration, and RBC all improved after treatment with the plant extract [34].

Comment [JJ12]: Move to where species was first mentioned

***Gongronema latifolium* Benth**

Gongronema latifolium (family: *Asclepiadaceae*), it is known as "arokeke" (Yoruba) and "utazi" (Igbo). The leaves are used to treat diabetes, hypertension, intestinal worms, colic, diarrhea, nausea, anorexia, and malaria [35]. It has phytochemicals like glycosides, alkaloids, flavonoids, saponins, saponins, tannins, essential oils, and total phenols [36]. Alloxan-induced diabetic rats received *Gongronema latifolium* leaf extract, which significantly reversed the changes in fasting blood glucose (FBG) levels. With an increase in CAT, SOD, and GPx activity in the kidneys and brains. The MDA, NO, acetylcholinesterase (AChE), butyrylcholinesterase (BChE), dopamine (DOPA), serotonin, epinephrine, nor-epinephrine, cyclooxygenase (COX-2) activity levels were decreased. Antioxidant protection against oxidative stress was strengthened and the brain's neurotransmitters are modulated as a result of *Gongronema latifolium* neuroprotective action [37]. Similar studies have found that *Gongronema latifolium* effectively increases the liver glycogen content, antioxidant enzyme activities, levels of glucose transporters (GLUT-2 and GLUT-4) and relative hexokinase gene expression. It's possible that an increase in insulin secretion is what causes the observed elevations in GLUT 2 and GLUT 4 levels [38].

Comment [JJ13]: Should not be italicized

Ocimum gratissimum

Ocimum gratissimum (family: *Lamiaceae*), it is called 'Effirin-na' (Yoruba), 'Nchanwu' (Igbo), and 'Daidoya' (Hausa). *Ocimum gratissimum* has historically been used to treat diabetes mellitus, kidney infections, warts, headaches, and diarrhoea [39]. Flavonoids, saponins, polyphenols, glycosides, alkaloids, tannins, steroids, terpenoids, and carbohydrates are among the phytochemicals present in *Ocimum gratissimum* [40]. In STZ-induced diabetes, treatment with fractions (n-hexane, chloroform, ethyl-acetate, n-butanol, and water) of *Ocimum gratissimum* increased body weight, glucose tolerance, available blood insulin, insulin sensitivity; and decreased FBG (40). Similar research revealed significantly ($P = .05$) decreased TC, LDL, and VLDL levels and higher HDL levels [41].

Comment [JJ14]: Scientific authority??

Dacryodes edulis

Comment [JJ15]: Ditto

Dacryodes edulis L (family: *Burseraceae*), it is known as "Ube Igbo" (Igbo) and "Eleme" (Yoruba). The plant is used to treat fever, diabetes, leprosy, malaria, diarrhea, hypertension, skin illnesses, labor pain, retarded growth, oral and ear ailments [42, 43]. Flavonoids, alkaloids, glycosides, tannins, saponins, steroids, reducing sugars, hydrogen cyanide and soluble carbohydrates are among the phytochemicals found in *Dacryodes edulis* [42]. Fruit extract from *Dacryodes edulis* was used to treat alloxan-induced diabetic rats; it lowered the blood glucose, total cholesterol, triglycerides, LDL-C, ALT, and ALP levels. However, the levels of HDL-C significantly increased. The pancreatic histology was nearly restored to normal, with clearly defined islets [42]. A significant ($P = .05$) increase in the levels of insulin, GSH, SOD, CAT, and decrease in MDA, and concurrent inhibition of α -amylase and α -glucosidase activities [44]. Another study using fructose-STZ-induced diabetic rats, found that pancreatic morphology and β -cell function were considerably enhanced in rats treated with the butanol fraction of the plant extract and there was repair of the pancreatic capillary networks. Along with lowering the expression of Nrf2, there was a significant ($P = .05$) suppression of the activities of glycogen phosphorylase, fructose 1,6 biphosphatase, glucose 6 phosphatase, and acetylcholinesterase [45].

Raffia palm (Raphia hookeri)

Comment [JJ16]: Ditto

Raffia palm (*Raphia hookeri*) wine (RPW) is one of the natural products from plants. It is known by the common names 'palmy', 'oguro', 'emu', 'tombo', 'nkwu ocha' and 'nkwu enu'. Ascorbic acid, B-vitamin complex, notably thiamine, potassium, magnesium, calcium, sodium, phosphorus, and nitrogen have all been identified as being present in palm wine. For sweetness, it also contains sucrose, glucose, xylose, raffinose, and lactose [46, 47]. It is used alone or in combination with other medicinal herbs to treat diabetes mellitus, digestive health, and the overall welfare of breastfeeding women [48]. When administered to STZ-induced diabetic rats; RPW produced significant ($P = .05$) increase in insulin, GSH, SOD, catalase, ATPase and HDL-c, whereas the blood glucose, fructosamine, ALT, uric acid, triglycerides, LDL-c, MDA, NO and myeloperoxidase activity were reduced. The activities of fructose 1, 6-bisphosphatase, glucose-6-phosphatase, and acetylcholinesterase were also reduced. RPW restored the shape and capillary networks of beta-cells while enhancing pancreatic beta-cell function. RPW controls glucose homeostasis by increasing insulin secretion and preventing redox imbalance in diabetes [49].

Comment [JJ17]: Which plants???

Comment [JJ18]: What are these other medicinal herbs? Are they not plants that are used in treating diabetes mellitus? They should be included in this article if the topic can be effectively treated

Azadirachta indica

Comment [JJ19]: Ditto

Azadirachta indica (family: *Meliaceae*), is known as 'Maina' (Hausa), 'Ogwu-akom' (Igbo), and 'Dogonyaro' (Yoruba). It is used to treat diabetes mellitus, malaria, headaches, stomach ulcers, jaundice, anemia, dental issues, bacterial, fungal, and viral infections [50, 51]. Alkaloids, cardiac glycosides, flavonoids, oxalate, phenol, phytate, saponin, steroid, tannin, and triterpenoids are among the phytochemicals found in *Azadirachta indica* leaves [52]. The effect of aqueous extract of *Azadirachta indica* leaf on STZ-induced diabetes revealed an enhanced Hb concentration, PCV, RBC, platelet count and an increase in HDL-c. The total cholesterol, LDL-c, triglycerides, and VLDL were all significantly ($P = .05$) decreased. Additionally, pancreatic islet regeneration was demonstrated by histological studies [53].

Terminalia catappa

Comment [JJ20]: Ditto

Terminalia catappa (family: *Combretaceae*), it goes by the Yoruba name 'Furutu' and is referred to as 'fruit' by other tribes in Nigeria. Rheumatism, diarrhea, dysentery, diabetes, gonorrhea, stomach pains, headache, sexual dysfunction, anti-diabetic, itching, anti-indigestion, skin conditions, arthritis and colic are all treated with all parts of the plant [54]. The plant phytochemicals includes vitamins, carotenoids, alkaloids, tannins, flavonoids, terpenoids, saponins, phenols and steroids [55]. High-fat diet and low dose STZ induced diabetic rats were treated with aqueous root bark and flower extracts of *Terminalia catappa*; the blood glucose, total cholesterol, triglyceride, LDL, serum liver marker enzyme, kidney indicators, and bilirubin levels significantly ($P = .05$) decreased, while albumin, total protein, electrolytes, certain haematological markers and antioxidants showed a significant ($P = .05$) increase and there was an improved β -cell function and insulin resistance indices. The microanatomy of the pancreas was also enhanced [56]. The expression of the mRNA for the glucose transporter isoform 4 (GLUT-4), protein kinase B (AKT), phosphatidylinositol 3-kinase (PI3K), and insulin receptor substrate 1 (IRS-1) were unaffected. Therefore, *Terminalia catappa* reverses insulin resistance, enhances glucose transport, and activates PI3K/AKT signaling to provide its antidiabetic activities [57].

Syzygium cumini

Comment [JJ21]: Ditto

Syzygium cumini Linn (family: *Myrtaceae*), it is called 'Ori' (Yoruba) and 'Malmoo' (Hausa). The plant is used to treat diabetes, hypertension, fever, diarrhea, abdominal aches, and strengthening of the teeth and gums [58]. The phytochemical screening identified the presence of sterols, phlobatanins, volatile oil, saponins, tannins, terpenes, and flavonoids [58]. In alloxan-induced diabetes, treatment with *Syzygium cumini* leaf extract decreased fasting blood glucose, glycated hemoglobin levels (HbA1C), MDA, glucose-6-phosphatase activity. Additionally, there was a significant ($P = .05$) increase in the levels of GLUT 2, the pancreatic beta-cell scores, SOD, CAT, and GPx, and hexokinase activities [59].

Comment [JJ22]: Move to first citation please

***Solanum macrocarpon* Linn**

Comment [JJ23]: Remove italics please

Solanum macrocarpon Linn (family: *Solanaceae*), it is called 'gbagba pupa' (Yoruba), 'aara' (Igbo), and 'Ganyen Gauta' (Hausa). The plant is used in lowering blood cholesterol levels, controlling high blood pressure, losing weight, possessing anti-haemorrhoidal and anti-glaucoma characteristics [60]. It contains phytochemicals such as tannin, phenol, saponins, cardiac glycoside, flavonoid, alkaloid, reducing sugar, terpenoids, phytates and cyanides [61]. The effect of aqueous extract of *Solanum macrocarpon* leaf on alloxan-induced rat model of diabetes showed a significant ($P = .05$) decreased in FBG levels, glycated Hb, serum lipid profiles, lipid peroxidation, and glucose-6-phosphatase. Hexokinase activity, liver glycogen level, antioxidant enzyme activities, and the expression of the GLUT-2 and GLUT-4 glucose transporter genes all increased significantly ($P = .05$) [62]. Similar findings reported a significantly reduced levels of neurotransmitters, cholinesterases, cyclooxygenase-2 and nitric oxide in the brain of an alloxan-induced rat model of diabetes. *Solanum macrocarpon* leaf aqueous extract may be helpful in the treatment of diabetic neuropathy [63].

Chrysophyllum albidum

Comment [JJ24]: Ditto

Chrysophyllum albidum (family: *Sapotaceae*), its common names include 'Agbalumo' (Yoruba), 'udara' (Igbo), and 'Agwaliba' (Hausa). The plant is used for treating skin eruptions, stomach ache, diarrhea, diabetes, sleeping sickness, yellow fever, and malaria [64]. Among the phytochemicals found are tannins, alkaloids, terpenoids, flavonoids, saponins, reducing sugar, steroids, and cardiac glycosides [65]. *Chrysophyllum albidum* leaf extract was utilized to treat STZ induced diabetes. The body weight, SOD, CAT, glutathione, HDL, and insulin levels significantly ($P = .05$) increased, while the MDA, LDL, triglycerides, and total cholesterol levels were significantly ($P = .05$) decreased. Histologically there was a recovery of damaged islets and an improvement in the number of islet cells [66, 67].

Petersianthus macrocarpus

Comment [JJ25]: Ditto

Petersianthus macrocarpus (family: *Lecythidaceae*), the Igbo's call it 'Ogbu Onya'. It is used to relieve pain and fever associated with malaria, headaches, "recurrent" fever, constipation, hemorrhoids, and venereal illnesses. It also works as an abortifacient and has hypotensive effects [68]. Alkaloids, saponins, tannins, phenols, flavonoids, cardiac glycosides, steroids, terpenoids, anthocyanins, and anthraquinones were all detected during phytochemical screening [68]. Treating STZ-induced diabetes with *Petersianthus macrocarpus* resulted in a significantly lower blood glucose levels and histologically there was evidence of a granulated and conspicuous pancreatic islet of Langerhans. [69].

Costus aferker-gawli

Comment [JJ26]: Ditto

Costus aferker-gawl (family: *Costaceae*), it is known as 'tete-egun' (Yoruba), 'Okpete' or 'Okpoto' (Igbo), and 'Kakizawa' (Hausa). It is used to treat malaria, diabetes mellitus, measles, arthritis, sore throats, headache, stomach disorders, coughs, urethral discharges, venereal infections, jaundice, miscarriage, and respiratory issues [70]. Alkaloids, flavonoids, tannins, phenols, glycosides, terpenoids, steroidal saponins, and saponins are among the phytochemicals present in the plant [71]. Ethanolic leaves extract of *Costus aferker-gawl* was used to treat alloxan-induced diabetes, the result showed a significant ($P = .05$) decrease in blood glucose levels. Histologically, the islets of Langerhans were restored [72].

Senecio biafrae

Comment [JJ27]: Ditto

Senecio biafrae (family *Asteraceae*), is known locally as 'worowo' (Yoruba) and 'Ota eke' (Igbo). It is used to treat cases of infertility in women, diabetes, pulmonary defects, cough, bleeding from cuts, sore eyes, rheumatic pain, and localized oedemas [73, 74]. Alkaloids, saponin, glycosides, tannin, phlobatannin, phenol, flavonoids, steroids and chalcones are among the phytochemicals present in *Senecio biafrae* [75]. Studies on the effects of aqueous leaf extract of *Senecio biafrae* on alloxan-induced diabetic rats revealed a significant reduction ($P < 0.05$) in blood glucose, total cholesterol, triglycerides, LDL-c and VLDL levels and an increase in HDL levels, Hb, RBC, platelets, PCV, WBC, Mean corpuscular haemoglobin concentration, mean corpuscular volume, and mean corpuscular haemoglobin [76,77].

Xylopiya aethiopia

Comment [JJ28]: Ditto

Xylopiya aethiopia (family: *Annonaceae*), the fruit is called 'uda' (Igbo), 'Kimba' (Hausa), and 'euru' (Yoruba). It can be used as an abortifacient; and used to treat diabetes, dysentery, diarrhea, stomach disorders, menstrual irregularities, naso-pharyngeal infections, arthritis, rheumatism and infections [78]. Phytochemical analysis shows the presence of alkaloids, saponins, flavonoids, tannins, terpenes, steroids, and cardiac glycosides [78]. A near-normal islet of Langerhans was

observed during histological analysis of the pancreas in STZ-induced diabetic rats treated with an aqueous leaf extract of *Xylopia aethiopica*. There was more pronounced insulin staining, also a significant ($P = .05$) increase in the proportion of immunolabelled surface area was observed. Hence, the extract can cause β -cells to release insulin [79]. Similar research revealed a significantly decreased levels of blood glucose, fructosamine, LDH, serum lipids and increase serum insulin, β -cell function (HOMA-) and glucose tolerance ability [80].

Carica papaya

Comment [JJ29]: Ditto

Carica papaya (family: *Caricaceae*), the plant is known as 'Ibepe' (Yoruba) 'Gwanda' (Hausa) and 'Okwere' (Igbo) in the Yoruba, Hausa, The plant is used to treat diabetes, obesity, infections, dengue fever, jaundice, stomach pain and malaria [81]. Phytochemical analyses revealed the presence of alkaloids, flavonoids, saponins, tannins, anthraquinones, anthocyanosides, and reducing sugars [81]. Diabetic rats induced with STZ received oral administration of *Carica papaya* seed extracts. The extract significantly lowered blood glucose, inhibit α -amylase and α -glucosidase enzymes [82]. In alloxan-induced diabetes, the *Carica papaya* extract significantly decreased plasma total cholesterol, triglycerides, LDL-C and increase plasma HDL-C [83].

Spondias mombin

Spondias mombin (Linn) (family: *Anacardiaceae*), it is called 'Iyeye' (Yoruba), 'Ngulungwu' (Igbo) and 'isada' (Hausa). *Spondias mombin* is used to treat gonorrhoea, diabetes, diarrhea, and the placenta ejection in goats and women [23]. Phenolic acids, flavonoids, tannins, triterpenes, steroids, reducing sugar, alkaloids, anthraquinone, and saponins are among the phytochemicals present in *Spondias mombin* [84]. *Spondias mombin* was used to treat STZ induced diabetic rats; there was a significant decrease in the levels of blood glucose, ALT, ALP, total bilirubin, urea, creatinine, total serum cholesterol, triglyceride, LDL-C, VLDL, and there was an increased in plasma insulin, total protein, albumin, globulin and HDL-C (84). Similar report was observed in treating alloxan induced diabetic rats with *Spondias mombin*. The extract exhibited significant blood glucose lowering effect in the oral glucose tolerance test [85].

Comment [JJ30]: Moved to first citation

Anacardium occidentale

Comment [JJ31]: Ditto

Anacardium occidentale, (family: *Anacardiaceae*), it is called 'Kash' (Hausa), 'Okpokpo' (Ibo), and 'Kaju' (Yoruba). Diarrhoea, diabetes, dysentery, colonic pain, malaria, asthma, leprosy, internal worm infections, constipation, warts, and sore throat are all conditions that the plant is used to treat [86]. Phytochemicals present includes; saponin, phenolics, tannins, flavonoids, coumarins, terpenoids, glycoside, oxalate, phytate, quercetin, vitamins, and selenium [87]. Treatment of STZ-induced diabetes with the leave extract of *Anacardium occidental* resulted in significant decrease in fasting blood sugar ($P = .05$) and regeneration of beta cells [86]. Similar study was reported on aqueous and methanolic *A. occidentale* stem-bark extracts, which significantly reduced ($P < 0.001$) basal blood glucose concentrations of fasted normal and fasted STZ- induced diabetic rats.

Eucalyptus globulus

Comment [JJ32]: Ditto

Eucalyptus globulus (family: *Myrtaceae*), commonly referred to as Tasmanian Blue Gum. Fresh leaves of the plant are traditionally used to treat conditions like cough, lung problems, diabetes, catarrh, inflammation, flu, and liver infections [88]. Phytochemicals present includes; cardiac glycosides, alkaloids, tannins, terpenoids saponins, steroids, and phenolic compounds [89]. The effects of *Eucalyptus globules* leaves on alloxan-induced diabetic rats showed a significantly

reduced fasting glucose level, MDA, HC03-, and liver enzymes. There was a significantly (P = .05) increased in serum levels of xantine oxidase and CAT [90].

Phyllanthus amarus

Comment [JJ33]: Ditto

Phyllanthus amarus (family: *Euphorbiaceae*), it is called 'Iyin-Olobe' (Yoruba) and 'ngwu' (Igbo). It is used to treat liver diseases, renal stone diseases, diabetes mellitus, menstrual disorders, infections, inflammation, pain, skin ulcers, typhoid fever, hyperlipidemia, hypertension and anemia [91]. Alkaloids, tannins, saponins, anthraquinones, cardiac glycosides, and flavonoids are among the phytochemicals present in *Phyllanthus amarus* [92]. Diabetes was induced in rats using alloxan and it was treated with aqueous leaf extract of *Phyllanthus amarus*; there was a significant reduction in fasting blood glucose. Histologically, the architecture of the pancreas appeared intact [93].

Phyllanthus niruri

Phyllanthus niruri L (family: *Euphorbiaceae*), it is known as 'enyikwonwa and ngwu' (Igbo); 'geeron-tsuntsaaayee' (Hausa) and 'ehin olobe' or 'yin-olobe.' (Yoruba). It is used as a diuretic, laxative, dysentery and to treat tumors, kidney stones, fever, diabetes, constipation, tuberculosis, jaundice, hepatitis B, syphilis, gonorrhoea [94]. Flavonoids, alkaloids, terpenoids, polyphenols, tannins, coumarins, and saponins are the active phytochemicals present in *Phyllanthus niruri* [95]. The methanol extract of aerial parts of *Phyllanthus niruri* was used to treat alloxan induced-diabetic rats. *Phyllanthus niruri* significantly (P = .05) reduced fasting blood sugar and suppressed the postprandial rise in blood glucose. There was a decrease total cholesterol and triglycerides levels. Additionally, *Phyllanthus niruri* treated had increased body weight and the histological studies showed that the pancreas architecture was restored [94]. Okoli et al [96] reported a decreased in Hb glycation and increased in the liver glycogen levels; in vitro, the extract also inhibited α -amylase and α -glucosidase activities. Hence, *Phyllanthus niruri* may owe their blood glucose lowering properties to inhibition of glucose absorption and enhancement of glucose storage [96].

Comment [JJ34]: Move to the first citation??

Parkia biglobosa

Comment [JJ35]: Ditto

Parkia biglobosa (family: *Fabaceae*), it is called 'Dawadawa' (Hausa), 'Ogiri' (Igbo), and 'iru' (Yoruba). *Parkia biglobosa* is used to treat diabetes mellitus, infections, malaria, and inflammatory diseases [97]. The plant is reported to contain phenols, flavonoids, sugars, tannins, terpenoids, steroids, saponins, alkaloid, glycosides, alkaloids, and phenols [98]. The hydromethanol extract from *Parkia biglobosa* stem bark significantly attenuated serum glucose level and glycosylated Hb in fructose-STZ induced type 2 diabetic. There was also increase in the hepatic hexokinase activity and glycogen level; increase pancreatic SOD, CAT and decreased in MDA level. The seed extract of *Parkia biglobosa* also decrease the blood glucose levels in glucose-loaded and alloxan-induced diabetic rats [99].

Persea Americana

Comment [JJ36]: Ditto

Persea americana (family: *Lauraceae*), it local names are ''Ewé pia' (Yoruba), 'Akukwo Ube oyibo' (Igbo), and 'Ganyen piya' (Hausa). The leaves have been used as an effective antihypertensive, antidiabetic, anti-inflammatory remedies, analgesic, and for treating malaria [100]. The phytochemicals present includes; flavonoids, tannins, alkaloid, saponins, glycosides,

phenolic, and triterpenoid [101]. The aqueous extract of *Persea americana* seeds was used to treat alloxan induced diabetes, the in vitro analyses showed the potency of the extract against free radicals and its enzyme inhibitory potential. *Persea americana* seeds showed a marked decrease in FBG, TG, LDL-c, G6P, F-1, 6-BP, MDA, IL-6, TNF- α , and NF- κ B and increased in liver glycogen, hexokinase, and HDL-c. The HPLC revealed luteolin and myricetin to be the phytochemicals that were present in the highest concentration in the extract. Hence, *Persea americana* seeds can promote the activation of the phosphatidylinositol 3-kinase - PI3K/Akt pathway and the inhibition of β -cell death, which may be the primary mechanism by which *Persea americana* seeds promotes insulin sensitivity and regulates glycolipid metabolism [102].

Annona muricata

Annona muricata L (family: *Annonaceae*), it is called 'ebo' or 'apekan' (Yoruba), 'fasadarur' or 'tuwon biri' (Hausa), and 'sawansop' (Ibo). it is used as a laxative, purgative; used to treat fever, wound healing, skin diseases, diabetes, internal and external parasites [103,104]. The presence of the following phytochemical were detected in *Annona muricata*; flavonoids, alkaloids, terpenoids, tannins, carbohydrates, saponins, cardiac glycosides, phytosterols, and proteins [104]. Alloxan induced diabetic rats treated with *Annona muricata* peel inhibited α -amylase and α -glucosidase enzymes and reduced FBG levels, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), glucose 6-phosphatase (G6P), fructose 1,6-bisphosphatase (F-1,6-BP), MDA, TG, TC, IL-6, TNF- α , and NF-Kb. Furthermore, *Annona muricata* improved serum insulin levels, homeostasis model assessment of β -cell function (HOMA- β), hexokinase, CAT, GST, and HDL-c. *Annona muricata* significantly up-regulated expression of AKT and Bcl2 in the liver and pancreatic tissue [103].

Comment [JJ37]: Ditto

Ocimum basilicum

Ocimum basilicum (family: *Lamiaceae*), it is called 'Effirin' (Yoruba), 'Nchanwu' (Igbo), 'Dodoya' (Hausa). It is used to treat headaches, coughs, diabetes, diarrhea, constipation, digestive problems, warts, worms, tooth decay, kidney malfunction and inflammation [105]. Phytochemicals presents in the plant are terpenoids, alkaloids, flavonoids, tannins, saponin glycoside, and ascorbic acid [106]. The treatment with the extract of *Ocimum basilicum* on alloxan induced diabetes rats significantly ($P = .05$) reduced FBG concentration, ALT, AST, serum cholesterol and triglycerides and slightly increased mean body weight. Also, oral glucose tolerance was significantly ($P = .05$) improved. The extract increase liver glycogen content and produce significant ($P < 0.001$) inhibition of α -glucosidase and α amylase [107].

Comment [JJ38]: Ditto

Vernonia amygdalina

Vernonia amygdalina (family: *Compositae*), it is called 'ewuro' (Yoruba), 'Onugbu' (Igbo), 'doki' (Hausa). The plant act as a remedy against diabetes, bacterial infection, GIT disorders, kidney problems, liver diseases, malaria, infertility, helminthic diseases, nausea and hypertension [108]. Phytochemicals present are saponins, alkaloids, terpenes, flavonoids, steroids, phenolic acids and coumarins [108]. The chloroform fraction of *Vernonia amygdalina* was administered to STZ-induced diabetic rats. There was a significant decrease ($P = .05$) in the expression of the gluconeogenic enzymes; F-1,6-BP, phosphoenol pyruvate carboxykinase and G6P in the liver and muscle. The extract also significantly increased glucose oxidation via the pentose phosphate pathway (PPP) i.e. increased expression of the glucose 6-phosphate dehydrogenase (G6PDH) gene ($P = .05$) in the liver. Conversely, the expression of the G6PDH in the muscle and adipose

Comment [JJ39]: Ditto

tissues significantly decreased ($P = .05$), suggesting enhanced utilization of NADPH and ribose in the clearance of reactive oxygen species (ROS) and for expression of other relevant genes respectively. Also, transcription of the cell proliferation regulatory enzyme, PI3K increased in the liver. The extract also caused a decrease in the expression of key enzymes of glycolysis namely hexokinase and PFK, suggestive of a glucose sparing for ribose and NADPH production in PPP [109].

Dennettia tripetala

Dennettia tripetala (family: *Annonaceae*), It is called 'Mmimi' (Igbo), 'Ata igbere' (Yoruba). It is used as a remedy for diabetes, cough, fever, toothache, and nausea [110]. The phytochemicals constituents of *Dennettia tripetala* includes; tannins, alkaloids, steroids, flavonoids, cardiac, glycosides, saponins, terpenoids proteins, carbohydrates [110]. The fractions (methanol, n-hexane, ethyl acetate, butanol and water) of *Dennettia tripetala* leaves extract in treating alloxan-induced diabetic rats, showed significantly ($P = .05$) decreased in FBG levels, serum triglyceride, serum cholesterol and LDL and a significant ($P = .05$) increase in HDL levels. The body weight gain was moderate. Also there was marked rejuvenation of the pancreatic β cells [111].

Comment [JJ40]: Ditto

Murraya koenigii

Murraya koenigii (family: *Rutaceae*), it is called 'efirin oso' (Yoruba), 'marugbo sanyan' (Hausa), 'akwukwo curry' (Igbo). *Murraya koenigii* is used as tonics for inducing digestion and flatulence, reducing fever, treating diabetes, manage renal pains, analgesic, body heat reducer, thirst quencher, reducing inflammation, managing blood disorders, cure dysentery, treating piles, itching, fresh cuts, dysentery, bruises, edema, itching [112]. Alkaloids, tannins, flavonoids, phenols, reducing sugars, saponins, and terpenoids are present in *Murraya koenigii* [113]. Aqueous and ethanolic leaf extracts of *Murraya koenigii* was used to treat alloxan induced diabetic rats. Significant decrease ($P = .05$) in the blood glucose levels was observed (114)

Comment [JJ41]: Ditto

Telfairia occidentalis

Telfairia occidentalis (family: *Cucurbitaceae*), it is called 'ugu' (Igbo), 'iroko' or "apiroko" (Yoruba), 'kabewa' (Hausa). The plant is useful in the management of diabetes, cholesterolemia, anaemia, malaria, chronic fatigue, liver problems, impaired defense immune systems, has potential to regenerate testicular damage and also increase spermatogenesis [115,116]. The phytochemical screening revealed the presence of alkaloid, flavonoids, phenol, tannins, saponins, steroids, terpenes and balsam [117]. The blood glucose lowering effect of the extract of the seed of *Telfairia occidentalis* on alloxan-diabetic rats showed a reduced blood glucose concentration [118]. Similar report showed significant ($P = .05$) decrease in the FBG in alloxan induced diabetic rats, and also, lowering of FBG in normal (non-diabetic) [119].

Comment [JJ42]: Ditto

Citrus paradisi Macfad

Citrus paradisi Macfad (family: *Rutaceae*), it is called 'Abefa' (Yoruba) and 'Kalgo' (Hausa). *Citrus paradisi Macfad* is reputed for the management of anemia, diabetes mellitus and obesity; it decreases the symptoms of cold, relieves the symptoms of rheumatoid arthritis, asthma, and decreases the risk of heart attack [120]. Phytochemical present are alkaloids, saponin, flavonoids, tannins and cardiac glycosides [121]. The seed extract of *Citrus paradisi Macfad* was used to

Comment [JJ43]: Ditto

treat alloxan-induced diabetic rats; the extract showed a significant ($P = .05$) reductions in FBG, TG, TC, LDL-c, VLDL-c. The extract also caused significant ($P = .05$) increase in HDL-c [121].

Aloe vera (Aloe barbadensis)

Aloe vera (Aloe barbadensis) (family: *Liliaceae*), it is called 'aloe' (Igbo). Therapeutic claims of *Aloe vera* include teeth and gum treatment, constipation, diabetes, induced foot ulcers, antimicrobial and antioxidant properties and protection from irradiation. *Aloe vera* is also used commercially as an ingredient in yogurts, beverages, and some deserts [123]. The phytochemical constituents of *aloe vera* leaf include saponin, alkaloids, flavonoids, glycosides, phenol and tannins [124]. Treatment with *Aloe barbadensis* leave extract on STZ induced - diabetic rats showed a decrease in blood glucose, an increased SOD activities and significantly reduced MDA [123].

Conclusion

Numerous Nigerian medicinal herbs have glucose lowering abilities that can help manage diabetes and its repercussions. About 35 medicinal plants used to treat diabetes are listed in this study. This review provides basic knowledge on various kinds of plants that could be used as antidiabetics in Nigeria. However, many of the plants mentioned require more pharmacological and clinical research in order to prove any successful plant remedies for diabetes.

Comment [JJ44]: These are no conclusions for this review, please redo it properly

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Comment [JJ46]: Ditto

Comment [JJ47]: Old

Comment [JJ48]: Ditto

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Comment [JJ49]: Ditto

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Comment [JJ50]: Ditto

Comment [JJ51]: Ditto

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Comment [JJ52]: Ditto

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