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Review

Uses of African Plants and Associated Indigenous Knowledge for the Management of Diabetes Mellitus

John Awungnjia Asong [1,*], Peter Tshepiso Ndhlovu [2], Ahmed Olatunde [3] and Adeyemi Oladapo Aremu [4,5,*]

1 Unit for Environmental Sciences and Management, Faculty of Natural and Agricultural Sciences, Private Bag X6001, North-West University, Potchefstroom 2520, South Africa
2 School of Biology and Environmental Sciences, Faculty of Agriculture and Natural Sciences, University of Mpumalanga, Private Bag X11283, Mbombela 1200, South Africa; tshepiso.ndhlovu@ump.ac.za
3 Department of Medical Biochemistry, Abubakar Tafawa Balewa University, Bauchi 740272, Nigeria; olatundebch@gmail.com or aolatunde@atbu.edu.ng
4 Indigenous Knowledge Systems Centre, Faculty of Natural and Agricultural Sciences, North-West University, Private Bag X2046, Mmabatho 2745, South Africa
5 School of Life Sciences, College of Agriculture, Engineering and Science, University of KwaZulu-Natal, Durban 4001, South Africa
* Correspondence: asong.asong@nwu.ac.za (J.A.A.); oladapo.aremu@nwu.ac.za (A.O.A.); Tel.: +27-18-389-2573 (A.O.A.)

Abstract: Diabetes mellitus (DM) is a common non-communicable and chronic metabolic disorder regarded as a global epidemic with high morbidity and mortality. Although, conventional medicines are available for the management of DM, Indigenous knowledge, including the use of botanicals, has contributed to the management of this life-threatening disease in Africa. This is due to the perceived effectiveness and minimal side effects associated with plants and plant-derived compounds as an affordable remedy against DM. This review focuses on the contribution of Indigenous African plants to the management of DM. Relevant literatures were reviewed from online scientific databases, such as PubMed, ScienceDirect, and Google Scholar, using keywords singly and in combination. The review revealed that Indigenous health practitioners use several medicinal plants in the management of DM, with a range of 14–255 botanicals recorded. Approximately 80 compounds with antidiabetic potency have been isolated from different parts of African medicinal plants, with the majority belonging to flavonoids and terpenoids. Particularly, compounds such as apigenin, combretin B, convallatoxin, kaempferol, and quercetin remain the most promising antidiabetic compounds isolated from African medicinal plants. Limited clinical trials have been conducted on these compounds despite these milestones. There is, therefore, the need for further investigations to explain their antidiabetic effects, particularly under clinical conditions. Plants from which these compounds were isolated were selected based on ethnopharmacological knowledge. With these developments, medicinal plants and Indigenous knowledge remain an integral part of the global strategy to combat DM.

Keywords: Asteraceae; biodiversity; fabaceae; enzyme inhibition; medicinal plants; phytochemicals

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1. Introduction

Humans, in their daily interactions, have adopted certain habits and lifestyles, which, in some cases, have led to the development of certain ailments commonly referred to as lifestyle or non-communicable diseases. Often, the unhealthy behaviours and diminished consciousness of physical well-being of people in a sedentary routine have led to serious health issues with life-threatening consequences [1–3]. These diseases, which are often chronic, are long-term and may be linked to a combination of causes, including genetic, physiological, environmental, and behavioural factors [4]. Diabetes mellitus (DM) is among the leading causes of death globally and causes more deaths than all other diseases put together, with more mortalities occurring in low- and middle-income countries [5]. It is estimated that these diseases lead to about 35–40 million deaths annually [1,5,6], with DM responsible for approximately 1.6 million cases [1]. DM is recognised as a significant factor in both mortality and morbidity globally, affecting various demographics regardless of geographic location, age group, or gender [7]. Current data indicate that DM can be caused by lifestyle risk factors, including an unhealthy diet, inadequate physical activity, tobacco usage, alcoholism, the intake of a high-fat diet, and the inadequate consumption of fruits and vegetables in one's diet [1,5,8].

DM is a rapidly increasing health issue [9]. Globally, the prevalence of this disorder has exponentially increased due to environmental and lifestyle changes in low- and middle-income countries, which are more prone to mortality [10]. These behavioural risk factors are gradually pushing families and communities to the threshold of poverty, which may continue to increase if necessary measures are not put in place, as it creates a vicious cycle of risk [1]. According to the World Health Organisation, 7 of the 10 leading causes of death in 2019 were as a result of DM [11]. Given the above statistics, it is a serious health challenge that affects many individuals and contributes to the global financial health burden [12]. DM is a chronic heterogeneous metabolic disorder with multiple etiologies and is characterised by persistent hyperglycemia due to defective insulin secretion or action or both, resulting in derangements in the metabolism of biological macromolecules, specifically carbohydrates, lipids, and proteins [13,14].

The American Diabetes Association classifies diabetes into type 1, type 2, and gestational DM [14]. Type 1 DM is characterised by the absolute deficiency of insulin production and release from the pancreatic β-cells, resulting in a lack of the hormone in blood fluids, with the subsequent formation of hyperglycemia. On the other hand, type 2 DM is associated with partially dysfunctional pancreatic β-cells and insulin resistance. Moreover, type 2 DM is considered the most predominant type of the disease and accounts for more than 90% of reported cases. On the other hand, gestational DM occurs during pregnancy. In most cases, gestational DM resolves after birth, but its occurrence could serve as a risk factor for the development of type 2 DM in later stage of life. Reports indicate that long-term or untreated DM (whether type 1 or type 2) could lead to the development of DM micro- and macro-vascular complications, such as retinopathy, nephropathy, neuropathy, diabetic foot ulcers, stroke, and hypertension, among others. Due to these complications, persons with DM usually experience a lesser quality and expectancy of life, irrespective of age [15].

1.1. Prevalence of Diabetes Mellitus

From the prevalence perspective, DM affected 537 million persons aged 20 and 79 years in 2021, and if urgent measures are not taken to curtail its negative effects on health, the figure is expected to rise to 643 and 783 million by 2030 and 2045, respectively [16–19]. It is the 9th leading cause of death globally in lower-middle-income countries and the 10th cause of mortality in high-income countries [11]. Thus, DM is among the leading causes of health burden in the world, especially in Africa. Approximately 4.3% (14 million) of the adult population in Africa suffered from DM in 2012 and 4.7% (19.4 million) in 2019, and the disease accounted for more than 500,000 deaths [16–18]. In Africa, current estimated data reveal that 24 million people, a ratio of about 1:22 adults, are living with DM. Recently, DM accounted for about 416,000 deaths in 2021 [19]. Furthermore, it is projected that by 2045, 55 million adults in Africa will be living with DM [19] if drastic action is not taken. In 2019, South Africa had an estimated value of 4.6 million individuals affected by DM, more than double the estimated number of 2 million people reported to be living with the disorder in 2014 [20]. West Africa was the most affected region in Africa in 2014, with the highest number of adults living with DM. Nigeria (3.2 million) and Côte d'Ivoire (421,023) were the most affected countries in West Africa, while Kenya and Cameroon were the most affected countries in the Eastern and Central regions of the continent, respectively [21].

1.2. Global Burden of Diabetes Mellitus

The disease burden is causing the world an estimated USD 966 billion annually [19]. Low–middle-income countries that are more affected by DM are already experiencing economic turmoil; thus, there is a need for a cost-effective solution to minimise the rising effects of this global health burden. Current treatment regimens available to manage DM rely, to a greater proportion, on synthetic antidiabetic drugs, such as insulin injection, insulin secretagogues, dipeptidyl peptidase inhibitors, and alpha glucosidases inhibitors, alongside lifestyle modification [22]. However, synthetic antidiabetic agents have characteristic side effects, including weight gain, nausea, liver and heart failure, gastrointestinal discomfort, hypoglycaemia, and diarrhoea [23,24]. In addition, the phobia of insulin injections and inconsistency in dietary and lifestyle modification have appeared as challenges in the control of DM. In addition to these challenges, conventional drugs do not completely cure the disorder and are taken throughout life, which could be a challenge to diabetic individuals. Furthermore, the high cost of synthetic drugs for managing the metabolic disease has made it impossible for a greater proportion of African populations and other low–middle-income populations to procure these agents. Based on all these limitations, coupled with the constant increase in the prevalence of DM, there has been a paradigm shift to Indigenous approaches as interventions to manage DM, especially in low- and medium-income regions. These Indigenous approaches depend highly on medicinal plants due to their affordability, accessibility, efficacy, and safety [25,26]. There has been a steady rise in the number of scientific publications on the efficacy of medicinal plants in the management of DM over the years (Figure 1). Based on the data analysed, using ScienceDirect, as an example of a reliable search engine/tool, publications on African plants have consistently contributed 16–20% of global outputs. Thus, this review provides an appraisal of the contribution of Indigenous knowledge systems through ethnopharmacology in the management of DM in Africa. Indigenous methods of diagnosis for DM, preparation of medicinal plant remedies and isolated compounds used against the disease were examined in this review.

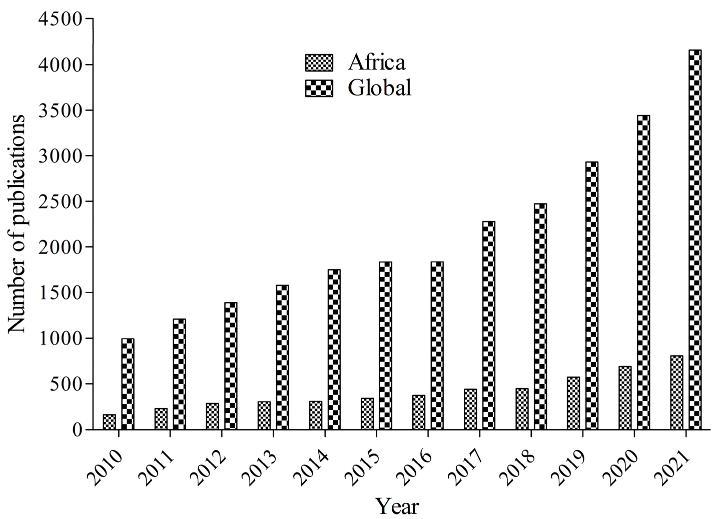


Figure 1. Overview of publications that focus on plants used in managing diabetes mellitus from 2010 to 2021.

2. Indigenous Methods of Diagnosing Diabetes Mellitus

In most African countries, DM is named according to the most prevalent symptom. With many dialects in the continent, different names are used to refer to DM. For example, in the Bafut Kingdom of the North West region of Cameroon, it is referred to as '*Nighoni-shugar*' (sugar sickness) [27], and '*isifo sikashukela*' by the Zulus of South Africa [28].

Traditional health practitioners have been at the forefront of the management of DM, especially where access to modern medicine is hindered by socio-economic factors. The diagnosis is usually the first step of the management process, especially if the patient has not been previously exposed to scientific laboratory testing or where primary healthcare facilities are not well equipped to diagnose DM; in such cases, people often turn to traditional diagnostic methods [27]. Diagnosis by Indigenous health practitioners (IHPs) depends solely on the phenotypic, psychological, and social signs or symptoms displayed by the patient at the time of diagnosis [29]. In some situations, herbal formulation, which changes colour after contact with urine containing glucose, is used as a diagnostic test. The patient pours his/her urine on the formulation, which is kept for 4–7 days, and a colour change is observed [24]. In some cases, patients are asked to taste their urine if it is sugary. Based on available data, the diagnostic test used by IHP is classified as major or minor, depending on the frequency of the symptoms presented by patients. The higher the frequency of a symptom (the number of patients diagnosed with that symptom), IHPs consider it as a more major symptom, and vice versa. The most encountered symptoms by IHPs are frequent urination; erectile dysfunction (for men); copious sweating during observation periods by traditional healers; weakness and fatigue; blurred vision; excessive hunger; sudden weight loss or gain; tingling or numbness in legs, feet, or fingers; and drowsiness. Difficulties in the treatment and healing of wounds are considered by IHPs as major symptoms while sweating, vomiting, fatigue, swelling of legs and feet, obesity, nausea, itchy skin, and fruity breath are considered minor signs due to their lower frequency. In some cases, IHPs use incantations or diagnosis by divination [28,30,31].

Traditional diagnosis occurs within a traditional religious supernatural context and acts as a medium with ancestral shades [32]. Differential diagnosis of DM is often challenging because of its association with multiple underlying pathophysiological mechanisms, diseases, and treatment options [33]. Traditional health practitioners have identified clinical manifestations of DM to include swollen tummies, tiredness, weakness, oversleeping, overweight, painful body parts, sexual dysfunction, and brown eyes.

Traditional treatments in local communities have largely disappeared, but some are prescribed by alternative medical practitioners or taken as supplements to conventional therapy [34]. Traditional methods for detecting DM complications have limitations [35], such as establishing the type or stages of DM compared to other tests—for example, the glycated haemoglobin (HbA1c) test. Moreover, HbA1c, and oral glucose tolerance test assist doctors in detecting type 2 DM, pre-diabetes, and gestational DM [36,37]. The prevalence of DM complications in newly diagnosed patients underscores the need for more robust and early detection methods. Therefore, more advanced techniques are needed to improve the early identification of DM complications.

3. Botanical Overview, Preparation, and Administration of Plants Used in Managing Diabetes Mellitus

3.1. Families, Life Forms, and Plant Parts

African Indigenous knowledge has relied heavily on medicinal plants for the management of DM across all sub-regions of the continent (Table 1). Prior to 2014, over 185 medicinal plants across the continent, belonging to 75 plant families, had been explored by IHP and other categories of knowledge holders, with about 52% of plants originating from the West African region, 21.91% from North Africa, 13% from Southern Africa, 8% from East Africa, and 6% from Central Africa. The most representative families were Asteraceae, Lamiaceae, Fabaceae, Cucurbitaceae, Apocynaceae, Anarcardiaceae, Rutaceae, Rubiaceae, Combretaceae, and Caesalpiniaceae, and all had more than 5% distribution of the total number of plants explored for the management of DM by IHPs [24,31]. The dominance of the families cited above is not new, as several ethnobotanical studies have revealed at least one of the above families as the dominant family in studies involving DM or other diseases, pointing out an aspect of the holism of African medicine [38–40].

The most common life forms of plants used in preparing remedies consist of trees, followed by shrubs and herbs, while grasses are sparingly used. Trees and shrubs are available all year round, whereas grasses and herbs are available during particular seasons.

This difference in availability has been cited as the main reason why most IHPs prefer them (trees and shrubs) for the management of DM across the continent [41,42]. In African traditional medicine, roots (47%), stems (23%), leaves (17%), and other parts (consisting of aerial parts, tubers, and stem bark < 10%) have been used by IHPs for the treatment of the disease [31,43].

Table 1. Overview of literature documenting the use of medicinal plants in the management and treatment of diabetics across Africa.

Authors	Title of the Review	Number of Plants
Abouzekry et al. [44]	Phytotherapy for diabetes mellitus; A review of Middle Eastern and North African folk medicinal plants	14
Balogun et al. [38]	Antidiabetic medicinal plants used by the Basotho Tribe of Eastern Free State: A review	26
Chukwuma et al. [45]	Medicinal plants with concomitant anti-diabetic and anti-hypertensive effects as potential sources of dual acting therapies against diabetes and hypertension: A review	102
Idm'hand et al. [2]	Ethnopharmacological review of medicinal plants used to manage diabetes in Morocco	255
Mohammed et al. [24]	African medicinal plants with antidiabetic potentials: A review	185
Mohammed and Tajuddeen [43]	Antidiabetic compounds from medicinal plants traditionally used for the treatment of diabetes in Africa: A review update (2015–2020)	24
Seetaloo et al. [46]	Potential of traditionally consumed medicinal herbs, spices, and food plants to inhibit key digestive enzymes geared towards diabetes mellitus management—A systematic review	94
Semenya and Maroyi [47]	A review of plants used against diabetes mellitus by Bapedi and Vhavenda ethnic groups in the Limpopo Province, South Africa	61

3.2. Preparation and Administration of Plant-Based Remedies

Among the reported studies, the highest number of medicinal plants were compiled by Idm'hand et al. [2] and Mohammed et al. [24]. Although the methods were not the same, there is a need for methodological harmony to ensure feasible reporting of outcomes and quality standards [48]. The studies revealed that medicinal plants, common to several countries, were used to manage DM treatment (Table 2). Among the common plants, *Allium sativum* was prominent across the continent [2,39,49–55]. This indicates that the plant is likely effective against DM, and certain communities share the same knowledge about this medicinal plant.

IHPs use various methods to prepare remedies for the treatment of DM in African communities (Table 2). The choice of method is, sometimes, based on the complexity or simplicity of the method of the remedy to be prepared and the number of plants needed for single-dose preparation [56]. The available data indicate that the most widely used methods of preparation include decoctions, infusions, maceration, and cooking/boiling [43,57,58]; other methods include soaking as tea and powdering dry plant parts. A couple of factors associated with the preparation method may affect the potency of the remedy being prepared. These factors include the state of the material (fresh or dry), the type of solvent used, the boiling duration, and the amount of water used for boiling [31]. The quantity of plant materials to be used to prepare remedies for DM, as reported, also depends on the age of the patient and the severity or degree of symptoms.

Table 2. Ethno-botanical information of popular African medicinal plants used for the management of diabetes mellitus in multiple countries. The botanical names of the plants were verified using The World flora online (http://www.worldfloraonline.org/, accessed on 31 January 2024).

Scientific Name and Family	Plant Part and Method of Preparation	Life Form	Countries	Reference
Aloe ferox Mill. Xanthorrhoeaceae	The liquid from the leaves is boiled to powder and soaked in water, and ½ of a cup of decoction is taken orally.	Shrub	South Africa and Mauritius	[39,46,59]
Aloe vera Xanthorrhoeaceae	Excision and incision wounds and the wounds were treated with extract of *A. vera* for specific days.	Shrub	South Africa, Kenya, Senegal, and Madagascar	[3,39,49,53]
Allium sativum L. Amaryllidaceae	A fresh plant is crushed and boiled, and ½ of a cup of decoction is taken orally.	Herb	Benin, South Africa, Morocco, Kenya, Sudan, Nigeria Togo, Senegal, and Ethiopia	[2,39,49–55]
Ajuga remota Benth. Lamiaceae	Leaves and whole plant; decoction.	Herb	Kenya and Ethiopia	[53,60]
Olea europaea L. Oleaceae	Roots and bark; decoction.	Shrub	Kenya and Morocco	[2,53]
Cassia singueana Delile. syn. *Senna singueana* Caesalpiniaceae	Plant part is boiled and consumed orally.	Tree	Nigeria and Kenya	[53,61]
Khaya senegalensis A. Juss. Meliaceae	Decoction made of *K. senegalensis* stem bark and garlic is taken orally.	Tree	Togo and Nigeria	[52,62]
Parkia biglobosa (Jacq.) G. Don. Fabaceae	Decoction made of *P. biglobosa* leaf and garlic is taken orally.	Tree	Togo and Nigeria	[52,62]
Mangifera indica Lam. Moringaceae	Leaves are infused and orally taken.	Tree	Guinea, Senegal, and Nigeria	[49,63,64]
Sclerocarya birrea A. Rich. Hochst. Anacardiaceae	Leaves and bark.	Tree	Senegal, South Africa, and Cameroon	[49,65,66]

4. Ethnopharmacological Insights into African Medicinal Plants in the Management of Diabetes Mellitus

The documentation of plant inventory used for the disease among knowledge holders is logically followed by in vitro and in vivo inhibition studies for their anti-diabetic activity. This is often assessed using enzymes actively involved in the breakdown of carbohydrates. Examples of these enzymes are α-glucosidase and α-amylase, and plant extracts are evaluated for their ability to serve as enzyme inhibitors [43]. According to available data, over 80 bioactive compounds with antidiabetic potency have been isolated from 24 medicinal plants from different regions of the continent (Ethiopia, Ghana, Guinea, Kenya, Mauritius, Madagascar, Morocco, Namibia, Nigeria, South Africa, Tanzania, and Togo). Out of this number, 19 have been used by IHPs to treat DM (Figure 2). Most of the bioactive molecules belong to the terpenoid and flavonoid families. Notwithstanding the large numbers, apigenin (**1**), combretin B (**2**), kaempferol (**3**), quercetin (**4**), and convallatoxin (**5**) are said to be the most promising antidiabetic compounds (Table 3). As of 2020, ten (10) different mechanistic actions have been established to be exhibited by medicinal plants used by IHPs to treat DM, including the inhibition of intestinal glucose uptake (α-glucosidase and α-amylase), stimulation of glucose muscle uptake via glucose transporters, inhibition of adipogenesis, inhibition of protein tyrosine phosphate 1B (PTP 1B), improvement in pancreatic β-cell integrity, interactions with peroxisome proliferator-activated receptors (PPARs), and interactions with glucose-metabolising enzymes [67,68].

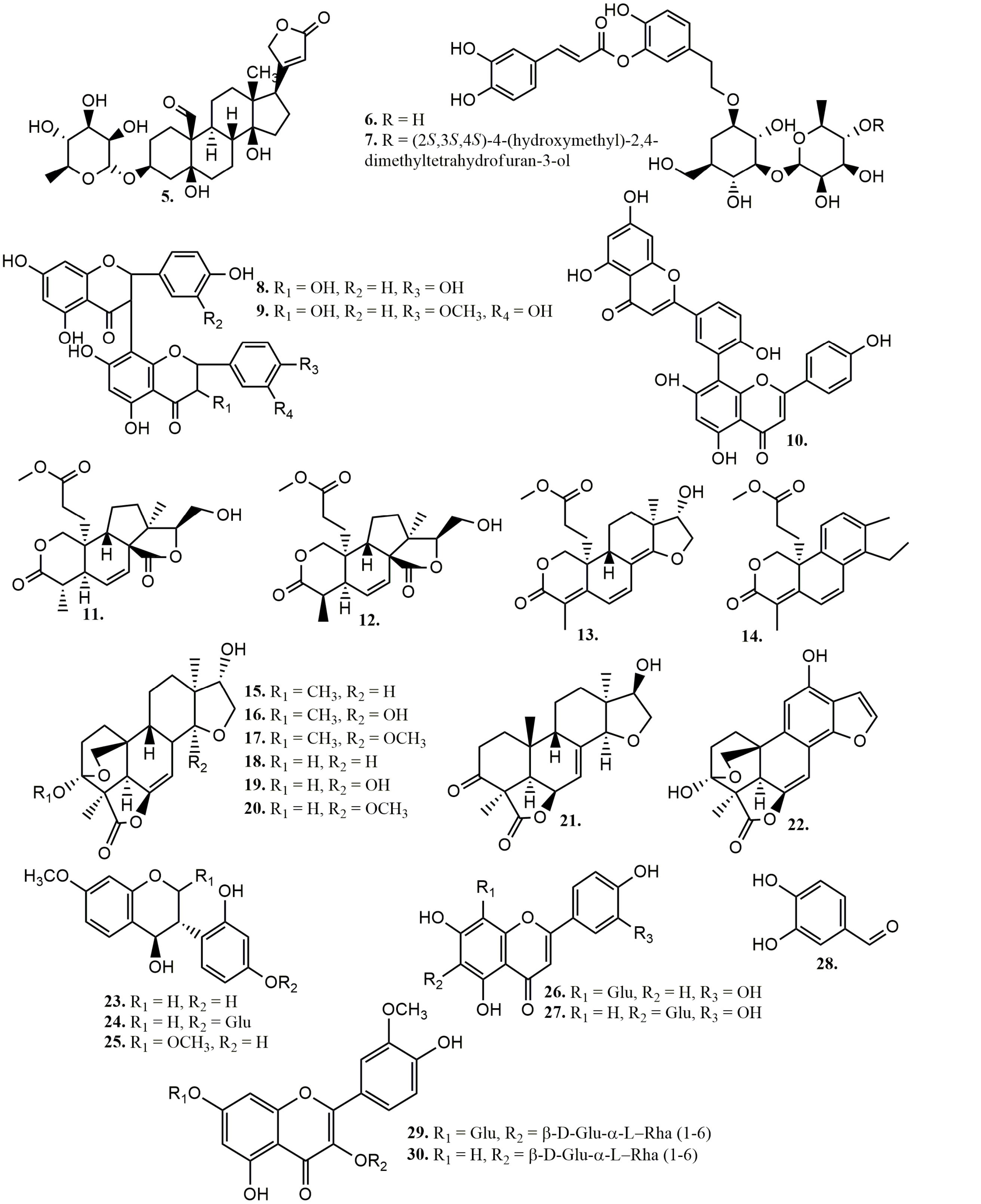
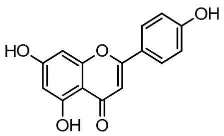
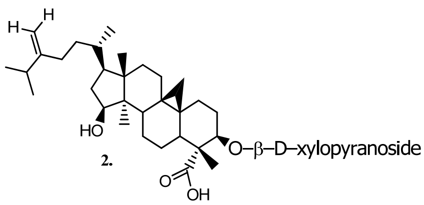
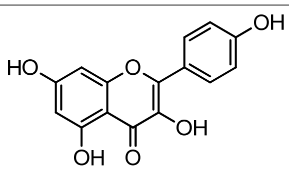
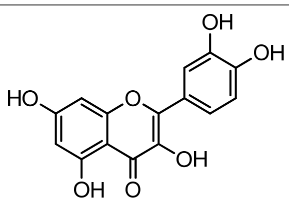


Figure 2. Chemical structures of antidiabetic compounds found in African medicinal plants.

4.1. Carbohydrate Digestive Enzyme-Inhibitory Activity of African Medicinal Plants

Several African medicinal plants are known to inhibit the uptake of intestinal glucose into the systemic circulation, which then increases blood glucose [69]. The inhibition of α-amylase and α-glucosidase is one of the strategies used for the management of DM. These enzymes play a vital role in the degradation of carbohydrates in diets into simpler forms (usually monosaccharides, mainly glucose) [70]. The inhibition of α-amylase and α-glucosidase activities prolongs the total digestion of carbohydrates by elevating the digestion time, leading to a decrease in the absorption rate of intestinal glucose, thus reducing postprandial blood glucose [43,71]. Many compounds have been obtained from African medicinal plants, indicating significant inhibition of α-amylase and α-glucosidase activities. *Newbouldia laevis* (P. Beauv.) Seem. ex Bureau (Bignoniaceae) leaf infusion is used to manage DM in the southern region of Nigeria [72]. Scientific evidence shows that ethanol extract from leaves decreases fasting blood glucose in diabetic animals [73]. Thereafter, two compounds, caffeic acid glycosides, newboulasides A (**6**) and B (**7**), were obtained from ethanol extract and discovered to display potent inhibitory activities against α-amylase. Newboulaside A (**6**) and B (**7**) showed IC_{50} values of 8 and 5.8 μM, respectively, which was comparable with the IC_{50} value (2.61 μM) of acarbose, used as standard [74]. Another important medicinal plant used in African settings to manage DM is *Garcinia kola* Heckel, usually referred to as *bitter cola*. The seed is used to treat DM in Southern Nigeria and has been found to contain several bioactive compounds, such as kolaviron (**8**), kolaflavanone (**9**), and bioflavonoids, among others, which are responsible for in vivo and in vitro antidiabetic activities [75–81]. Kolaviron (**8**), an important compound isolated from *bitter kola*, inhibited the activities of α-glucosidase and α-amylase, with IC_{50} values of 31.1 and 24.6 μM, respectively [82].

Table 3. Examples of promising anti-diabetic compounds isolated from African medicinal plants.

Name of Compound	Chemical Structure	Plant, Plant Part	Biological Assay and Response	Reference
Apigenin (**1**)	 **1.**	*Agave americana* L. leaves	α-amylase	Sahnoun et al. [67]
Combretin B (**2**)	 **2.**	*Combretum fragans* F. Hoffm leaves	α-glucosidase Antihyperglycemic Antioxidant	Dawé et al. [83]
Kaempferol (**3**)	 **3.**	*Bryophyllum pinnatum* (Lam.) Oken. leaves	α-Glucosidase α-Amylase Antihyperlipidemic, Antioxidant	Ibitoye et al. [84]
Quercetin (**4**)	 **4.**	*Bryophyllum pinnatum* (Lam.) Oken. Leaves	α-amylase α-glucosidase	Ibitoye et al. [84]

4.2. Dipeptidyl Peptidase IV-Inhibitory Potential of African Medicinal Plants

Dipeptidyl peptidase (DPP)-IV inhibitors are agents that activate the degradation of endogenous incretin hormones (glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1) and then stimulate pancreatic glucose-dependent insulin secretion [85]. African medicinal plant extracts and their phytomolecules display strong action against DPP-IV activity. *Antidesma madagascariense* Lam. (Phyllanthaceae) stem bark and leaf decoctions are used in Madagascar traditional medicine to treat DM [86,87]. From a phytochemistry perspective, amentoflavone (**10**) (biflavonoid), which was formed by phenol oxidative reaction of two apigenin (**1**) molecules via C3′ and C8′, was obtained from ethyl acetate extract of *A. madagascariense* leaves [68]. Amentoflavone (**10**) and the extract inhibited the activity of DPP-IV with IC_{50} values of 3.9 and 79.2 μg/mL, respectively [70]. Thus, the compound and extract of *A. madagascariense* enhanced insulin sensitivity to peripheral tissues, and it is claimed that amentoflavone (**10**) is a vital inhibitor of DPP-IV activity in the extract [43,68].

4.3. Protein Tyrosine Phosphatase IB-Inhibitory Activity of African Medicinal Plants

Another important target for African medicinal plants and their chemical constituents is PTP 1B. It is a negative modulator of insulin receptor signal transduction cascade. PTP 1B inhibitors stimulate the phosphorylation of cellular substrates of insulin receptor kinase, which then activates phosphoinositide-3-kinase (PI3K) and a reduction in the expression of protein kinase B [88,89]. PI3K stimulation and protein kinase B downstream expression then stimulate the glucose transporter 4 protein's translocation from vesicles in cells to the plasma membrane and thus enhance glucose uptake into the cells for cellular respiration [88,89]. African medicinal plants and associated compounds have shown some interesting results against PTP 1B activity. In Central and West Africa, *Icacina oliviformis* (Poir.). J Raynal, belonging to the Icacinaceae family, is used in the preparation of food [90]. The ethyl acetate fraction of the tubers contains several compounds, such as oliviformislactone A (**11**) and B (**12**), secopimaranlactone A (**13**), secocleistanthone A (**14**), 3-*O*-methylhumirianthol (**15**), 3-*O*-methyl-14-hydroxy-humirianthol (**16**), 3-*O*-methyl-14-methoxyhumirianthol (**17**), humirianthol (**18**), Icacinol (**19**), 14a-methoxyhumirianthol (**20**), icacinlactone I (**21**), and 12-hydroxyIcacinlactone A (**22**) [91]. Among these bioactive compounds, secocleistanthone A (**14**), secopimaranlactone A (**13**), and oliviformislactone A (**11**) exerted PTP 1B-inhibitory activity, with IC_{50} values ranging from 3.24 to 32.2 μM, and were reported to have a δ-lactone group as their ring A [91], which plays a significant role in the antidiabetic activity of the compounds.

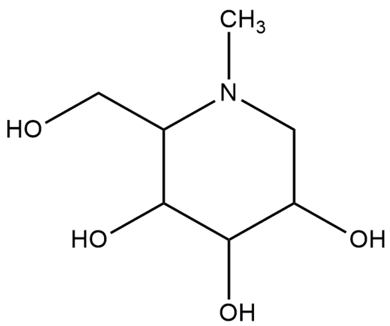
4.4. Effect of African Medicinal Plants on Peroxisome Proliferator-Activated Receptors

PPARs are groups of ligand-stimulated transcription factors that play a vital role in inflammation, cell proliferation, and energy metabolism [92]. Activators of PPARs, in most cases PPARγ, enhance insulin sensitivity and lipid and glucose uptake in target tissues through elevation of glucose transporters' expression, activation of muscle lipogenesis, and liver glycogenesis [93]. The ethyl acetate fraction of *Trigonella stellate* Forssk. (Fabaceae) stimulates both PPARγ and PPARα by 1.8-fold (50 μg/mL) and 1.5-fold (50 μg/mL), respectively [94]. Following purification using the chromatographic technique, butanol and ethyl acetate fractions of the roots and aerial parts of *T. stellate* contain several compounds. From the plant, (3*S*,4*R*)-4,2′,4′-trihydroxy-7-methoxyisoflavan (**23**), (3*R*,4*S*)-4,2′,4′-trihydroxy-7-methoxy-4′-*O*-β-D-glucopyranosylisoflavan (**24**), and (2*S*,3*R*,4*R*)-4,2′,4′-trihydroxy-2,7-dimethoxyisoflavan (**25**) activate PPARγ activity, whereas the activity of PPARα is stimulated by (3*R*,4*S*)-4,2′,4′-trihydroxy-7-methoxy-4′-*O*-β-D-glucopyranosylisoflavan (**24**) [94].

4.5. Effects of African Medicinal Plants on Metabolic Tissues

The biosynthesis of glycogen and breakdown of glucose are vital in the treatment of high blood glucose in DM. Defective stimulation of glycogen synthase and glucose-6-phosphate inhibition elevates the risk of development of type 2 DM [95]. These two enzymes play important roles in the storage of glucose in the liver and gluconeogenesis, and targeting their actions is a valid process in the regulation of DM [43]. Hexane and ethyl acetate fractions of *Myrianthus arboreus* can potently decrease the production of glucose in the liver by reducing glucose-6-phosphatase activity and elevating the storage of glucose by elevating the activity of glycogen synthase [96]. Among the several compounds found in the ethyl acetate fraction of the plant, isoorientin (**26**), orientin (**27**), and 3,4-dihydroxybenzaldehdye (**28**) stimulate the activity of glycogen synthase in HepG2 cells and reduce glucose-6-phosphatase activity in H4IIE cells [97].

The impaired actions of fat tissues, such as excessive fat cell differentiation, may increase the risk of DM and associated metabolic diseases [98]. The accumulation of defective fats due to impaired adipose tissue action induces adipocyte hypertrophy and insulin resistance, along with impaired insulin secretion from the β-cells of the pancreas and, subsequently, into DM [99]. Medicinal plants from Africa inhibit the defective accumulation of fats. For instance, methanol extract of *Aulacopilum glaucum* subsp. *glaucum* leaves obtained from the Tunisian Sahara Desert inhibited adipogenesis in 3T3-L1 cells. Two compounds, isorhamnetin-3-*O*-[apiosyl(1→6)]glucosyl-7-*O*-rhamnoside (**29**) and isorhamnetin-3-*O*-rutinoside (**30**), isolated from the extracts through Bioassay-guided purification, inhibited adipogenesis in 3T3-L1 cells [100]. These bioactive phytocompounds were proposed to be responsible for the antidiabetic property of the plant and their potential to inhibit adipogenesis, providing credence to the traditional use of the Sahara Desert plant in the management of DM [43]. In another study, 1-deoxynojirimycin (**31**) (Figure 3), which can be obtained from both plants, such as *Morus alba* and *Commelina communis* and microorganisms like *Bacillus subtilis* MORI, was reported to stimulate the levels of adiponectin and its receptors in 3T3-L1 adipose cells, with a subsequent significant reduction in the levels of blood glucose and stimulating insulin sensitivity [99]. In addition to the effects of 1-deoxynojirimycin, the compound elevated the phosphorylation of 5′ adenosine monophosphate-activated protein kinase in a remarkable fashion. 1-deoxynojirimycin (**31**) elevated the expression of glucose transporter 4 mRNA. Hence, it is concluded that the compound's blood glucose-lowering effects are linked to high levels of glucose transporter 4 [99].



31.

Figure 3. Chemical structure of 1-deoxynojirimycin.

Furthermore, medicinal plants in Africa show antidiabetic properties through other mechanisms, such as stimulation of glucose uptake in skeletal muscles, enhancing the integrity of β-cells in the pancreas, and other possible actions. Overall, African medicinal plants and their chemical constituents hold great potential in alleviating DM and its complications through the various mechanisms mentioned above.

5. Conclusions

In the search for long-lasting solutions to the treatment and management of DM, it is critical for both Indigenous-based medicine systems and orthodox or conventional medicine to work together. It is ascertained in this study that ethnopharmacological knowledge can contribute to the management of DM in particular. It is a serious heterogeneous metabolic disorder that results in life-threatening conditions when left untreated. The current synthetic antidiabetic agents present serious challenges of safety, cost, accessibility, and availability. The search for alternative therapy to synthetic antidiabetic drugs was extended to medicinal plants due to their availability, efficacy, and safety. Also, this study has shown that African medicinal plants are huge repositories of chemical compounds that can become lead candidates in the search for antidiabetic drugs since they have shown promising antidiabetic potency in in vitro and in vivo studies. Thus, there is a need to further investigate these compounds using other parameters beyond the already evaluated models as well as their subjection to clinical trials, which is critical in the process of drug discovery and development.

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