



Vol. 12(1), Pp. 1-8, January 2025,

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<https://journals.directresearchpublisher.org/index.php/drjhp/issue/archive>

Review Article
ISSN: 2449-0814

THE TREATMENT OF DIABETES MELLITUS WITH TRADITIONAL HERBAL MEDICINE: CURE OR MYTH?

Ajuma Fatima Sule^{1*}, James Omale², and Eniola Joseph Olajide³

¹Department of Biochemistry, Prince Abubakar Audu University, PMB 1008, Anyigba, Kogi State, Nigeria.

²Department of Biochemistry, Prince Abubakar Audu University, PMB 1008, Anyigba, Kogi State, Nigeria.

³Department of Biochemistry, Prince Abubakar Audu University, PMB 1008, Anyigba, Kogi State, Nigeria.

Corresponding author email: sulefatima@gmail.com

ABSTRACT

Millions of individuals around the world are diagnosed with diabetes mellitus. Poor management of elevated level of blood glucose can result in complications that can impact vision, the heart, kidneys and nerves. The cost of purchase and side effects affiliated with the use of oral anti-diabetic drugs makes herbal medicine an attractive therapeutic alternative for diabetic patients. Furthermore, there is wide spread belief that use of herbs has more therapeutic effects than allopathic medicine. This review aims to ascertain the potency of indigenous medicine in the cure or management of diabetes mellitus by utilizing relevant scientific literatures. A number of databases including Google scholar, Scopus, PubMed, Research gate etc. were searched for pertinent literature reports. The output from the review identified some plants with glucose lowering ability. Examples of such medicinal plants include *Moringa oleifera*, *Azadirachta indica*, *Allium sativum*, *Ginkgo biloba*, *Momordica charantia* etc. The anti-diabetic effect of these medicinal plants is attributed to the presence of bioactive principles called phytochemicals which may reduce elevated blood glucose by various mechanisms such as enhancing the cells' sensitivity to insulin, preventing the β cells of the pancreas from degenerating and inactivating some key enzymes involved in carbohydrate metabolism. In conclusion, there is no scientific evidence to prove that herbal medicine cures diabetes mellitus. Rather, the reported mechanisms of actions of the bioactive principles in these medicinal plants makes them likely candidates in the control of elevated blood sugar.

Keywords: Diabetes Mellitus, Medicinal Plants, Phytochemicals, Cure, Myth, Indigenous medicine

Article information

Received 8 November 2024;

Accepted 29 December 2024;

Published 3 January 2025

DOI: <https://doi.org/10.26765/DRJHP61881042>

Citation: Sule, A. F., Omale, J., and Olajide, E. J. (2025). THE TREATMENT OF DIABETES MELLITUS WITH TRADITIONAL HERBAL MEDICINE: CURE OR MYTH?. Vol. 12(1), Pp. 1-8. This article is published under the terms of the Creative Commons Attribution License 4.0.

INTRODUCTION

Elevation of blood level of glucose above the normal threshold depicts diabetes mellitus (Kumar *et al.*, 2013). Type I diabetes, Type II diabetes and Gestational diabetes are the three primary categories of diabetes mellitus. The β cells of the pancreas are attacked and destroyed by the immune system of an individual resulting in insulin shortage and type I diabetes mellitus. Cells in the body, including those found in the muscle and liver, are less sensitive to insulin when an individual has type II diabetes

mellitus. Pregnant women can develop gestational diabetes mellitus (Sonia *et al.*, 2018). The actual etiology of gestational diabetes is not known although, several theories indicates that hormones such as human placental lactogen, cortisol and estrogen secreted by the placenta during pregnancy can lower the responsive ability of the body to insulin adequately thereby leading to insulin resistance in pregnant women (Plows *et al.*, 2018). International Diabetes Federation (2021) stated that an

estimated 537 million individuals around the world are diabetic. A lot of these cases are observed in developing countries and due to poor diet and sedentary lifestyle in these regions, the estimation of diabetic people is projected to rise to about 783 million by the end of the year 2045 (Hossain *et al.*, 2024). Diabetes mellitus diminishes general living condition by causing emotional distress and even physical disabilities such as impaired vision and amputation due to impairment to the retina, nerves and feet. The current management strategies for diabetes mellitus involves keeping fit, eating healthy, use of insulin for type I diabetes and oral hypoglycemic drugs for type II diabetes mellitus (Gupta *et al.*, 2021). These medications can be expensive for patients to purchase more also, there are several reported side effects associated with the use of oral hypoglycemic drugs such as gastrointestinal issues, liver dysfunction, skin rash etc. Due to these challenges, a lot of patients have resorted to the use of herbal medicine as alternative therapeutic approach for treatment of diabetes mellitus. This is because these herbal medicines are readily available, cost effective and they are believed to have little or no side effects (Lema *et al.*, 2024). Majority of people living in developing nations rely on the use of indigenous medicine for the treatment of diabetes mellitus and other conditions. In Nigeria, the prevalence rate of the use of herbal medicine for the treatment of diabetes and other chronic ailments within the populace is estimated to be about 24 – 83% (Awodele *et al.*, 2014). Various scientific reports have highlighted the potential of some traditional herbal medicines in the management of diabetes mellitus. The widely used oral anti-diabetic drug metformin was isolated from the medicinal plant *Galega officinalis* (Kifle *et al.*, 2021). Furthermore, the World Health Organization (WHO) has encouraged the incorporation of herbal plants into the diet of diabetic individuals (Yedjou *et al.*, 2023). As a result of this, there is an increased focus on the use of indigenous medicine for the treatment of diabetes mellitus with so much claim on achieving a cure to this metabolic disorder through the use of herbs. Hence, this review paper aims at addressing this belief by providing an overview of the mechanisms of action of these anti-diabetic medicinal plants and highlighting demerits associated with the co-administration of herbal medicines with allopathic medicine.

METHODOLOGY

To achieve the objectives of this review, authors obtained relevant information from scientific reports published in reputable journal collections from scientific databases such as Scopus, Google scholar, and Research gate, PubMed central, Web of Science and Medline.

TRADITIONAL HERBAL MEDICINE

Herbal preparations made from plant parts like the leaves,

fruits, stem and roots are used in traditional medical practice to treat a variety of ailments (Nontokozi and Mthokozisi, 2018). Depending on the location and culture, this herbal remedy is prepared differently. According to Hira *et al.* (2017), the various parts of the plants may be used freshly prepared or they may be dried and administered in the form of concoction, decoction or infusion.

A lot of research reports the presence of biologically active ingredients in herbal formulations. These active principles enhance the taste, appearance and aroma of plants while shielding them against harm and illnesses. Scientifically, these biologically active ingredients are referred to as phytochemicals and they comprise a number of classes including glycosides, saponins, terpenoids, alkaloids, tannins and flavonoids. These phytochemicals are also responsible for the therapeutic potentials of these plants (Saxena *et al.*, 2013). Herbal remedies are used globally particularly in developing nations in South America, Asia and Africa (Anoka, 2012).

Many contemporary pharmaceuticals are synthesized from these bioactive compounds in these therapeutic plants. For example; the active principle of aspirin is salicylic acid obtained from the bark of *Salix alba* (white willow) and the meadowsweet plant, *Filipendula ulmaria* (Klessig *et al.*, 2016); the anti-malarial medication artemisinin and quinine are synthesized from the leaves of *Artemisia annua* (sweet wormwood plant) and the bark of *Cinchona pubescens* respectively (Zhao *et al.*, 2022). *Catharanthus roseus*, also known as Madagascar periwinkle, is the source of the anticancer medications vinblastine and vincristine, which are used to treat leukemia. While digoxin, a cardiac glycoside, is derived from the leaves of *Digitalis purpurea* (foxglove plant) is used in the treatment of heart failure (Awuchi and Amagwula, 2020). A lot of plants with therapeutic effects can be combined and used as medications to treat numerous ailments. This herbal preparation is termed a Polyherbal mixture. More than one herb is combined in trado-medical practice with the aim of strengthening the therapeutic capacity of the formulation (Dubey and Dixit, 2023).

TRADITIONAL HERBAL MEDICINES UTILIZED IN TREATMENT OF DIABETES MELLITUS

Since natural products gained prominence in experimental studies, a lot of plants such as *Bauhinia forficata*, *Cecropia obtusifolia*, *Kalanchoe pinnata* and *Punica granatum* have been used in the regulation of blood glucose levels (Yueng *et al.*, 2021). Due to the fact that natural products typically differ by nation and culture, their use in treating diabetes mellitus has a significant indigenous specificity (Table 1). This is demonstrated by the fact that *Senna auriculata* (L.) is commonly used in Sri Lanka and *Bauhinia forficata* is more common in Latin America. Anti-diabetic plants

Table 1: Names of medicinal plants use in treatment of diabetes

Botanical Name	Family	Plant Parts used	Mechanism of Action	References
<i>Allium sativum</i>	Alliaceae	Bulbs	Regulating metabolism of hepatic glucose	Xie <i>et al.</i> , 2023
<i>Curcuma longa</i>	Zingiberaceae	Rhizomes	Activation of Peroxisome Proliferator-activated Receptor - γ (PPAR- γ)	Pivari <i>et al.</i> , 2019
<i>Panax quinquefolius</i> L.	Araliaceae	Rhizomes	Regulate the uptake of glucose and improve insulin secretion.	Chen <i>et al.</i> , 2019
<i>Medicago sativa</i>	Fabaceae	Leaf	Stimulates the secretion of insulin	Farsani <i>et al.</i> , 2016
<i>Gingko biloba</i>	Gingkoaceae	Leaf	Improves the sensitivity of the cells to insulin	Zou <i>et al.</i> , 2024
<i>Moringa oleifera</i>	Moringaceae	Leaf, Seeds	Improves the sensitivity of the cells to insulin, Ameliorates oxidative stress	Dwomoh <i>et al.</i> , 2024
<i>Azadirachta indica</i>	Meliaceae	Leaf	Increase in the expression of insulin receptor, Inhibition of α -amylase and α -glucosidase activities	Zanzabil <i>et al.</i> , 2023
<i>Achyranthes aspera</i>	Amaranthaceae	Seeds	Lowering glucose absorption from the gut	Vijayaraj <i>et al.</i> , 2016
<i>Senna auriculata</i>	Caesalpinioidae	Bark, Seeds, Roots, Leaf	Stimulates the proliferation of pancreatic β -cells, Improves the sensitivity of the cells to insulin.	Salehi <i>et al.</i> , 2020; Nille <i>et al.</i> , 2021
<i>Bauhinia forficata</i>	Fabaceae	Leaf	Anti-inflammatory effects and decreasing the levels of glycated haemoglobin	Souza <i>et al.</i> , 2020
<i>Tamarindus indica</i>	Fabaceae	Seeds	Insulin mimetic effects, Stimulating the expression of glucose transporter genes, Stimulates expression of the pancreatic β cells.	Zanzabil <i>et al.</i> , 2023
<i>Mangifera indica</i>	Anacardiaceae	Peels, Stem bark, Leaf	Inhibition of α -amylase and α -glucosidase activities, Improves the sensitivity of the cells to insulin. Improve the uptake of glucose into the cells	Zaravand <i>et al.</i> , 2023
<i>Annona squamosa</i>	Annonaceae	Leaf	Inhibit the digestion of starch and delay the uptake of glucose into the cells	Ansari <i>et al.</i> , 2020
<i>Momordica charantia</i>	Curcubitaceae	Fruits, Leaf	Induce the synthesis of insulin	Oyelere <i>et al.</i> , 2022
<i>Kalanchoe pinnata</i>	Crassulaceae	Leaf	Combats oxidative stress, Inhibition of α -amylase and α -glucosidase activities, Enhance the uptake of glucose into the cells	George <i>et al.</i> , 2019
<i>Punica granatum</i>	Lythraceae	Flowers	Activation of Peroxisome Proliferator-activated Receptor - γ (PPAR- γ), Improves the sensitivity of the cells to insulin	Gharib and Khouari, 2019
<i>Nelumbo nucifera</i>	Nelumbonaceae	Leaf, Seeds	Stimulates the secretion of insulin from the pancreatic β cells	Sharma <i>et al.</i> , 2016
<i>Wedelia chinensis</i>	Asteraceae	Leaf	Antioxidant effects, Inhibition of α -amylase and α -glucosidase activities	Zanzabil <i>et al.</i> , 2023
<i>Ficus racemose</i>	Moraceae	Fruits, Leaf, Bark	Inhibition of α -amylase and α -glucosidase activities, Facilitates the transport of glucose across cell membranes.	Zanzabil <i>et al.</i> , 2023
<i>Coccinia cordifolia</i>	Curcubitaceae	Leaf	Enhances the regeneration of the pancreatic β cells, Insulin mimetic effect, Inhibition of α -amylase and α -glucosidase activities	Putra <i>et al.</i> , 2021
<i>Bryophyllum pinnatum</i>	Crassulaceae	Leaf	Inhibition of α -amylase and α -glucosidase activities	Ibitoye <i>et al.</i> , 2018

customary and routinely used in Africa include *Panax quinquefolius* L. (ginseng), *Curcuma longa* (turmeric), *Medicago sativa* (alfalfa), *Gingko biloba* and *Moringa oleifera* (Patle *et al.*, 2021).

OVERVIEW OF PLANTS SECONDARY METABOLITES WITH ANTI-DIABETIC PROPERTIES

Flavonoids

The free radical scavenging ability of flavonoids and their capacity to alter cell signaling contributes to their anti-diabetic effects. Fruits,

vegetables and some plants are dietary sources of flavonoids (Ramachandran and Baojun, 2015). Rutin is a dietary flavonoid and its anti-diabetic effects includes lowering the rate of absorption of carbohydrates from the small intestine, promoting the uptake of glucose into the cells, promoting insulin secretion and preventing further deterioration of the pancreatic β cells. Furthermore, rutin improves antioxidant status and reduces the synthesis of advanced glycation end products (Ghorbani, 2017). Isoflavones have been reported to exert stimulatory effects on the pancreatic β cells to ensure adequate insulin secretion (Vinayagam and Xu, 2015). Cyanidins

exert their anti-diabetic effects by inhibiting the activities of α -glucosidase and α -amylase thereby lowering post prandial glucose levels. Additionally, cyanidins have been reported to reverse degenerative changes in the pancreatic β cells of streptozotocin induced diabetic rats (Al-Ishaq *et al.*, 2019).

Alkaloids

Berberine, an alkaloid of benzoyl tetra isoquinoline, has been shown to have anti-diabetic properties in rats with type 2 diabetes induced by streptozotocin-nicotinamide.

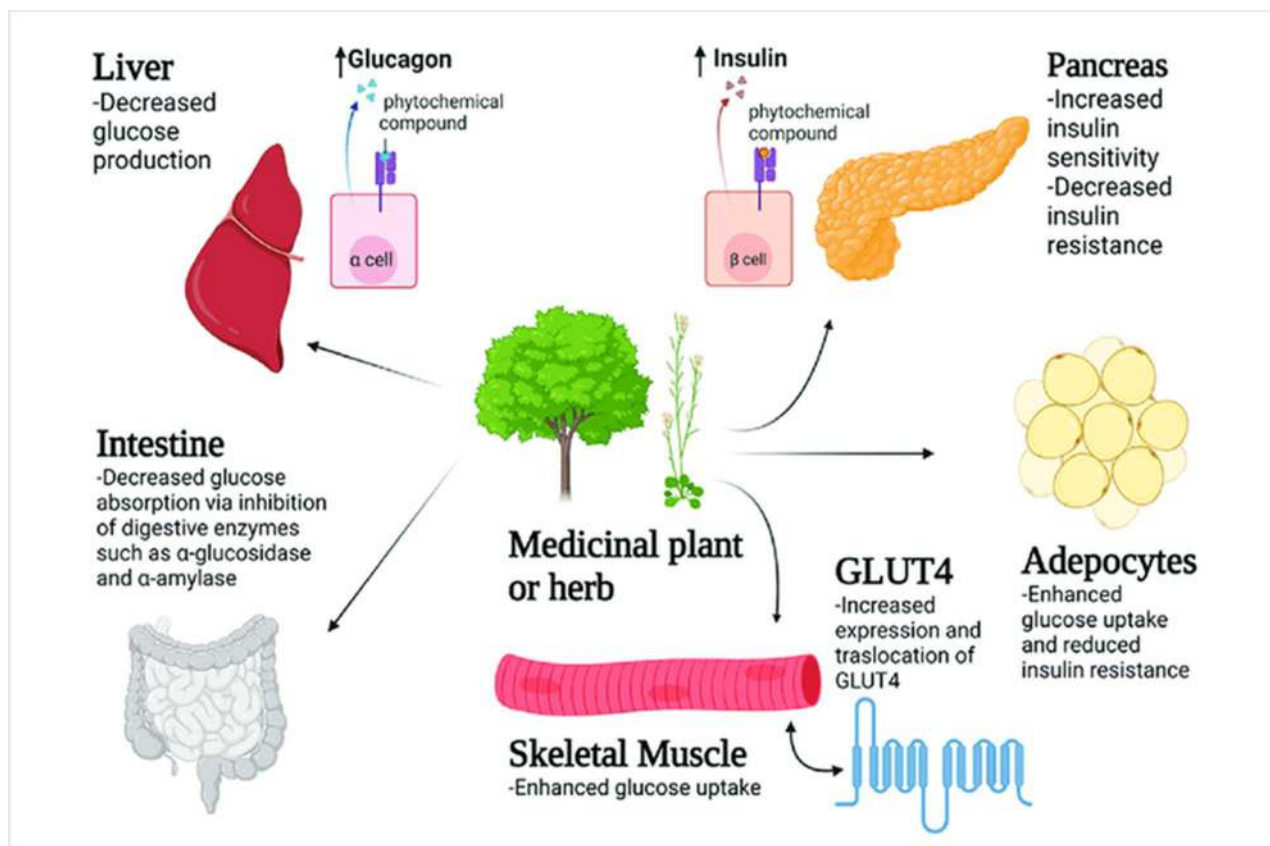


Figure 1: Anti-diabetic Effect of Medicinal Plants (Source: Usai *et al.*, 2022).

When the alkaloid was administered to diabetic rats, oxidative stress parameters were lowered, high lipids were decreased, hemoglobin glycosylation was improved and antioxidant status was enhanced. At the same time, gluconeogenic enzyme activities were decreased (Patrick and Isaac, 2018). The imidazoline alkaloids harmaline and nor-harmaline have been reported to improve insulin secretion in the pancreatic β cells. Furthermore, the three alkaloids piperumbellactam A, B and C exert inhibitory effect on the activities of the enzymes; aldose reductase, maltase – glucoamylase and α -glucosidase (Behl *et al.*, 2022).

Tannins

The tannins found in plants can be categorized as hydrolysable and condensed types. One of the major attributes of tannins is their free radical scavenging capacity. Uncontrolled blood glucose level is associated with oxidative stress due to impairment of the antioxidant status of the diabetic patient (Figure 1). Tannins have the capacity to impair damage caused by oxidative stress due to their antioxidant effects (Kumari and Jain, 2012). Furthermore, tannins have been reported to have insulin –

like effects and also help lower post prandial glucose levels by inhibiting some key enzymes that participate in metabolism of carbohydrate (Sieniawska, 2015). In an experiment conducted using *in vitro* model of human starch digestion, hydrolysable tannins such as vesicalagin and acutissimin exerted an inhibitory effect on the digestive function of α -amylase (Tong *et al.*, 2014). More also, proanthocyanidins an example of condensed tannins has been reported to inhibit the digestive functions of α -glucosidase (Ou-Yang *et al.*, 2020).

Saponins

Saponins are a class of secondary metabolites that are recognized for their glucose lowering effects. The class of saponins consists of terpenoids and steroidal types (Figure 1). Anti-diabetic plants that have been identified as sources of saponins include; *Momordica charantia*, *Garcinia kola*, *Trigonella foenum-graecum* and *Berberis vulgaris* (El-Barky *et al.*, 2017). Saponins have been reported to elicit glucose lowering effect through various mechanisms such as improving the secretion of insulin by the pancreatic β cells, improving the glycogen reserve in the liver, lowering the rate of gluconeogenesis by inhibiting

the catalytic activity of two important enzymes in the gluconeogenic pathway, promoting the synthesis of new pancreatic β cells and improving expression of Glucose Transporters (GLUT) – 4 (Perumal *et al.*, 2014; El-Barky *et al.*, 2017).

COMPONENTS OF SOME POLYHERBAL MIXTURES USED IN TREATING DIABETES MELLITUS

Ruzu bitters: *Uvarie chamae* (bush banana), *Curculigo Pilosa* (squirrel groundnut) and *Citrullis colocythis* (bitter apple) (Obasi and Ogugua, 2021).

Yoyo bitters: *Acinos arvensis*, *Chenopodium murale*, *Citrus aurantifolia*, *Aloe Vera* and *Cinnamomum aromaticum* (Paula-Peace, 2021).

Oroki herbal mixture: *Sorghum bicolor*, *Khaya grandifolia*, *Cassia sieberiana*, *Staudtia stipitate*, *Alstonia cognesis*, *Ocimum basillicum*, *Mangifera indica*, *Cythula prostrate*, *Securidaca longepedunculata*, *Saccharum officinarum* and water (Adeyemi and Owoseni, 2015).

Fijk flusher: *Cassia alata*, *Citrus medica*, *Aloe barbaris*, *Aloe vera* and *Cassia angustifolia* (Adeyemi and Owoseni, 2015).

Vegies Detox: Detox tea made from dark green leafy vegetables such as spinach, collards and kale. A plain cup of green tea from a steeped bag contains zero (0) calories according to U.S. department of Agriculture nutrition data. When an individual lose weight, there will be an increase in insulin sensitivity which will lead to a lower blood sugar level (Rena, 2018).

EFFICACY OF HERBAL MEDICINE IN TREATMENT OF DIABETES MELLITUS: TRUTH OR MYTH?

A lot of anti-diabetic herbal plants are usually prescribed by the traditional healers or are self-prescribed by the patients. Due to the claims of the anti-diabetic potential of these plants, they have received several scientific interest and evaluation to verify their effectiveness. From various scientific studies, the glucose lowering ability of some therapeutic plants have been verified using animal models and *in vitro* experiments (Usai *et al.*, 2022). The development of a well-known oral glucose lowering drug metformin whose active ingredient is synthesized from the plant *Galega officinalis* justifies the possibility of developing other anti-diabetic medications from plants (Kifle *et al.*, 2021).

One of the myths surrounding the use of plants in management of diabetes mellitus is that, it is completely free of harm when consumed because it is a product of nature. However, this belief is false because, despite the fact that products of nature may be regarded as

unadulterated and safe; the use of these herbal preparations is affiliated with problems of contamination and a lot of unidentified herb-drug interactions or herb-herb interactions. A significant number of patients are completely unaware of the components of the herbal preparations they are ingesting. These are concerning factors that can lead to detrimental side effects in diabetes management (Emmanuel *et al.*, 2023).

The use of some of these antidiabetic plants has been associated with several reported side effects. For example; the risk associated with the long-term use of *Panax quinquefolius* (ginseng) includes low levels of blood sugar, anxiety, tenderness of the breast and inability to fall asleep (insomnia). Furthermore, ginseng may interact with certain drugs when co-administered. Some medications that could interact negatively with ginseng are warfarin, statins and anti-hypertensive medications (Chen *et al.*, 2019). Hypoglycemia is one of the side effects associated with use of *Trigonella foenum-graecum* (fenugreek) in the treatment of diabetes mellitus. Fenugreek also causes itching, gastrointestinal problems, light-headedness and headache. More also due to its mucilage content, it lowers the contact of drugs with the intestinal mucosa thereby impairing their absorption (Somdatta *et al.*, 2023). *Azadirachta indica* (neem) has also been reported to lower the bioavailability and decrease the effectiveness of the oral anti-diabetic medication glipizide (Chaudhari *et al.*, 2019). A polyherbal combination or single use of parts of *Ocimum gratissimum*, *Moringa oleifera*, *Vernonia amygdalina* and *Picralima nitida* seeds holds significant importance in a lot of homes for the treatment of diabetes mellitus in Africa. The efficiency of these plants in lowering blood sugar has been proven in many documented research reports however, there is dearth of information on the interaction of these herbs with allopathic medicine. Therefore, despite the efficacy of herbal plants in managing diabetes mellitus there some demerits associated with the use of these plants.

Currently, there is no scientific study to prove that plants with therapeutic effects cures diabetes particularly, type 1 diabetes mellitus. However, research has indicated the potential of some medicinal plants to lower blood glucose level by several mechanisms which include improving the response of cells to insulin (Usai *et al.*, 2022). Therefore, such plants are valuable in managing type 2 diabetes mellitus but the drawbacks associated with the prolonged use of these plants should not be neglected.

CHALLENGES ASSOCIATED WITH THE USE OF HERBAL MEDICINE FOR DIABETES MANAGEMENT.

Non-standardization of herbal products is one of the biggest challenges facing the use of herbal medicine in the management of diabetes and other ailments. Standardization involves the development of an industrial

standard governing the use of a product which is developed based on the agreement of various stake holders, standard organizations and the government (Goel *et al.*, 2023). The composition and quality of most of these herbal preparations being marketed are unknown. More also there is scarcity of data regarding accepted methodologies needed for proper laboratory evaluation of these products (Sissi and Iris, 2011). Additionally, the processes involved in isolating the active ingredients from these herbal preparations is highly cost implicative for the manufacturers. This in turn deter the zeal and pursuit for standardization of these products (Eruaga *et al.*, 2024).

Lack of quality control by regulatory bodies is another challenge associated with the use of herbal medicines. Most of these herbal preparations prescribed at home by traditional healers or the products branded, marketed and sold in the markets are not certified by regulatory bodies. These products are at great risk of being contaminated and toxic therefore posing great health danger to the consumers and even death (Onyeaka *et al.*, 2024). Ekor (2010) conducted a toxicity assessment of the polyherbal blend yoyo bitters and the research was evoked by the unpublished case of a young man who self-medicated with this herbal product and was hospitalized for liver failure. This polyherbal blend is promoted and widely accepted among Nigeria's populace. Ogoun *et al.* (2015) reported that prolonged administration of yoyo bitters has renal toxic effects as observed in experimental rats. Examples of some regulatory bodies in Nigeria include: Standard Organization of Nigeria (SON) and National Agency for Food Drug Administration and Control (NAFDAC) (Mathew *et al.*, 2022).

Co-administration of different herbs or co-administration of herbs with allopathic medicine can lead to detrimental side effects. The research conducted by Ekor *et al.* (2023) indicated that a lot of patients combine the use of herbal medicine with conventional anti-diabetic drugs (35.4 – 88.4% of the population) and majority of these patients do not disclose the use of traditional herbal medicine to their health experts (63.8 – 91.3%). Herb-drug interactions is capable of causing antagonistic effects among the components of the herbs. This could lead to decrease in the efficacy of the herb or toxicity to the organs (Ramesh *et al.*, 2017).

Anti-diabetic drugs such as glimepiride, glipizide, rosiglitazone and glibenclamide acts as substrates of Cytochrome (CYP) - P450 isoenzyme family. The medicinal plant *Hypericum perforatum* (St. John's wort) have been reported to inhibit the activity of CYP2C and CYP3A. Furthermore, *Gingko biloba* inhibits CYP3A4, CYP2C9 and CYP2C19 (Nasri and Rafieian-Kopaei, 2015).

CONCLUSION

This review indicates that, remission is not the same as a

cure and traditional herbal medicine does not cure any type of diabetes as claimed. Rather, scientific evidences have shown that the presence of some bioactive constituents in some of these plants makes them potential candidates in the management of diabetes mellitus. Unless there are changes to the regulation, standardization and funding of research on herbal products, it is unlikely that they will become a major alternative to allopathic medicine in the foreseeable future.

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