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Review

# The use of plants in the traditional management of diabetes in Nigeria: Pharmacological and toxicological considerations

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ABSTRACT

*Ethnopharmacological relevance:* The prevalence of diabetes is on a steady increase worldwide and it is now identified as one of the main threats to human health in the 21st century. In Nigeria, the use of herbal medicine alone or alongside prescription drugs for its management is quite common. We hereby carry out a review of medicinal plants traditionally used for diabetes management in Nigeria. Based on the available evidence on the species' pharmacology and safety, we highlight ways in which their therapeutic potential can be properly harnessed for possible integration into the country's healthcare system.

*Materials and methods:* Ethnobotanical information was obtained from a literature search of electronic databases such as Google Scholar, Pubmed and Scopus up to 2013 for publications on medicinal plants used in diabetes management, in which the place of use and/or sample collection was identified as Nigeria. 'Diabetes' and 'Nigeria' were used as keywords for the primary searches; and then 'Plant name – accepted or synonyms', 'Constituents', 'Drug interaction' and/or 'Toxicity' for the secondary searches.

*Results:* The hypoglycemic effect of over a hundred out of the 115 plants reviewed in this paper is backed by preclinical experimental evidence, either *in vivo* or *in vitro*. One-third of the plants have been studied for their mechanism of action, while isolation of the bioactive constituent(s) has been accomplished for twenty three plants.

Some plants showed specific organ toxicity, mostly nephrotoxic or hepatotoxic, with direct effects on the levels of some liver function enzymes. Twenty eight plants have been identified as *in vitro* modulators of P-glycoprotein and/or one or more of the cytochrome P450 enzymes, while eleven plants altered the levels of phase 2 metabolic enzymes, chiefly glutathione, with the potential to alter the pharmacokinetics of co-administered drugs.

*Conclusion:* This review, therefore, provides a useful resource to enable a thorough assessment of the profile of plants used in diabetes management so as to ensure a more rational use. By anticipating potential toxicities or possible herb–drug interactions, significant risks which would otherwise represent a burden on the country's healthcare system can be avoided.



**Contents**



*Abbreviations:* AAN, aristolochic acid nephropathy; ADME, absorption, distribution, metabolism and excretion; CYT P450, cytochrome P450; DPP-IV, dipeptidyl peptidase IV; GLP1, glucagon like peptide 1; GLUT4, glucose transporter 4; GSH, glutathione; GST, glutathione-S-transferase; IDDM, insulin dependent diabetes mellitus; NIDDM, non-insulin dependent diabetes mellitus; P-GP, P-glycoprotein; PPARγ, peroxisome proliferator activated receptor gamma; STZ, streptozotocin; WHO, World Health Organization

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## 1. Introduction

### 1.1. Diabetes

Diabetes is a chronic metabolic disorder characterized by high blood glucose levels. This is either as a result of insufficient endogenous insulin production by the pancreatic beta cells (otherwise known as type-1 diabetes); or impaired insulin secretion and/or action (type-2 diabetes). type-1 diabetes is an autoimmune disease characterized by T-cell mediated destruction of the pancreatic beta cells. In type-2 diabetes, there is a gradual development of insulin resistance and beta cell dysfunction, strongly associated with obesity and a sedentary lifestyle (Zimmet et al., 2001). Due to a higher incidence of the risk factors, the prevalence of diabetes is increasing worldwide, but more evidently in developing countries. Current estimates indicate a 69% increase in the number of adults that would be affected by the disease between 2010 and 2030, compared to 20% for developed countries (Shaw et al., 2010).

Administration of exogenous insulin is the treatment for all type-1 diabetic patients and for some type-2 patients who do not achieve adequate blood glucose control with oral hypoglycemic drugs. Current drugs used in diabetes management can be categorized into three groups. Drugs in the first group increase endogenous insulin availability. These include the sulphonylureas such as glibenclamide, the glinides, insulin analogs, glucagon-like peptide 1 (GLP-1) agonists and dipeptidyl peptidase-IV (DPP-IV) inhibitors. The first two members of this group act on the sulfonylurea receptor in the pancreas to promote insulin secretion. GLP-1 agonists and DPP-IV inhibitors on the other hand act on the ileal cells of the small intestine. The second group of drugs enhance the sensitivity of insulin. This includes the thiazolidinediones, which are agonists of the peroxisome proliferator-activated receptor gamma (PPARγ) and the biguanide metformin. The third group comprises the α-glucosidase inhibitors such as acarbose, which reduce the digestion of polysaccharides and their bioavailability (Chehade and Mooradian, 2000; Sheehan, 2003). All the existing therapies however have limited efficacy, limited tolerability and/or significant mechanism based side effects (Moller 2001; Rotenstein et al., 2012).

Despite the existing pharmacotherapy, it is still difficult to attain adequate glycemic control amongst many diabetic patients due to the progressive decline in β-cell function (Wallace and Matthews, 2000). In Nigeria, polytherapy with two or more hypoglycemic agents to achieve better glucose control is common practice (Yusuff et al., 2008). There is also a high incidence of diabetic complications and hyperglycemic emergencies (Gill et al., 2009; Ogbera et al., 2007, 2009). In the presence of these, the number of prescribed drugs increases to an average of four per day for each patient (Enwere et al., 2006). This need for the chronic intake of a large number of drugs with their attendant side effects in addition to their high costs which is often borne by the patients themselves is the identified reason for non-adherence to therapy amongst diabetic patients. As a result, patients often have recourse to alternative forms of therapy such as herbal medicines (Yusuff et al., 2008).

### 1.2. Traditional herbal medicines in diabetes management

A number of reviews on medicinal plants used in the management of diabetes in different parts of the world (Bailey and Day, 1989; Marles and Farnsworth, 1995), as well as those used specifically in certain regions, such as in West Africa (Bever, 1980), Central America (Andrade-Cetto and Heinrich, 2005) and Asia (Grover et al., 2002) exist. These reviews have highlighted the dependence of a large percentage of the world population on traditional medicine for diabetes management. This is also corroborated by the WHO fact sheet (No. 134), which estimates that about 80% of the population in African and Asian countries rely on traditional medicine for their primary healthcare (WHO, 2008). It also recognizes traditional medicine as 'an accessible, affordable and culturally acceptable form of healthcare trusted by large numbers of people, which stands out as a way of coping with the relentless rise of chronic non-communicable diseases in the midst of soaring health-care costs and nearly universal austerity' (WHO, 2013).

Ethnobotanical surveys of plants traditionally used in diabetes management in different parts of Nigeria have been carried out (Abo et al., 2008; Etuk and Mohammed, 2009; Gbolade, 2009; Soladoye et al., 2012). These medicinal plants are used either alone as a primary therapeutic choice, or in conjunction with conventional medicines. On an average, approximately 50% of diabetic patients visiting hospitals in urban cities like Lagos and Benin have used some forms of traditional medicine during the course of their disease management (unpublished results of field work conducted by first author). Unfortunately, clinicians are either unaware of their patients' herb use or the identity of the herbal product being taken. To complicate matters further, herbal practitioners are usually unwilling to divulge the identity of the constituents of their preparations to patients. Most patients are also not interested in finding this out as they consider herbal preparations to be 'safe'; thereby making it difficult to ascertain if the herb may have a significant contributory role to the efficacy or failure of the treatment.