Diabetes mellitus in Nigeria and the on-going search for a cure from medicinal plants: a review

O A Oridupa and A B Saba

Introduction

Nigeria is endowed with a rich history of traditional medicine which pre-dates the slavery era, and has been transferred, although ineffectively, down through generations. The knowledge and use of whole plants, plant parts, products, and combinations have guided the historic traditional healers of Yoruba and Igbolands. Herbal medicines are usually provided by a traditional healer (herbalist), who uses natural products in attempting to cure many diseases including diabetes mellitus.[1] The prevalence of diabetes is between 2 and 7% of the population, increasing with age (≥40 years) to between 10 and 14%. Despite significant achievements in treatment modalities and preventive measures, the prevalence of diabetes has risen exponentially in the last decade.[2]

The management of diabetes is one of the major areas that is exploring the potential of plant-based drugs. Diabetes is a heterogeneous disease and the antidiabetic activities of different plant drugs may be a result of several mechanisms, including: inhibition of enzymatic pathways such as those of glycosidase, α-amylase, and hepatic glucose metabolising enzymes; inhibition of glycosylation of haemoglobin; modulation of glucose absorption from the gut; and plant antioxidant effects.[3]

Diabetes is a metabolic disorder characterised by hyperglycaemia, abnormal lipid and protein metabolism, along with specific long-term complications affecting the retina, kidney, and nervous system.[4,5] Hyperglycaemia is due to beta-cell dysfunction, relative insulin deficiency, and an abnormal post-prandial rise in blood glucose.[6] Pancreatic α-amylase breaks large polysaccharides (starch) into disaccharides and oligosaccharides, while α-glucosidases break disaccharides down into monosaccharides (glucose) which are readily absorbed into the bloodstream.[7] Inhibition of these two enzymes is the mechanism adopted by many commercially available drugs for the management of type 2 diabetes.[8]

Thus, inhibition of intestinal α-glucosidase will delay absorption of glucose after starch conversion, moderating the postprandial blood glucose elevation, thus mimicking the effects of dieting on hyperglycaemia.[9] Chronic amylase inhibition may also be useful for treating type 2 diabetes and obesity.[10] Hyperglycaemia is an important factor in the development and progression of the complications of diabetes mellitus.[11] Chronic hyperglycaemia causes many of the major complications of diabetes, including nephropathy, retinopathy, and macro- and micro-vascular damage, which may be traced back to oxidative stress from hyperglycaemia.[12]

There is increasing evidence in both experimental and clinical studies which indicates the involvement of oxidative stress in the development and progression of diabetes.[13,14] This is usually accompanied by increased production of free radicals or impaired antioxidant defences.[15] The formation of free radicals occurs disproportionately in diabetes due to glucose oxidation, non-enzymatic glycation of proteins, and subsequent oxidative degradation of glycated proteins. A decline in the antioxidant defence mechanisms coupled with abnormally high levels of free radicals may lead to damage of cellular organelles and enzymes, increased lipid peroxidation, and development of insulin resistance.[16] Thus, one therapeutic approach for treating diabetes is to decrease post-prandial hyperglycaemia.[6]

The growing number of individuals with diabetes, coupled with the side-effects of some current drugs has led to the increased interest in the search for alternatives.[17,18] No entirely satisfactory and effective therapy is yet available for diabetes,[19] and this fact has encouraged ethnomedicinal approaches to the management of diabetes.

Ethnomedicinal approaches to managing diabetes

Local healers do not usually rely on laboratory investigations to diagnose diabetes mellitus in their patients. The diagnosis is made during the consultation process by identifying symptoms such as frequent urination, sexual dysfunction, swollen legs, hands and stomach, obesity, fatigue, and profuse sweating. In some cases, healers will instruct patients to urinate on locally prepared formulations and to return in a couple of days for a diagnosis. At present, diabetes is among the diseases that are most extensively treated with traditional medicines. This is evident by the propensity of ethnobotanical surveys of medicinal plants used for the management

Olayinka A Oridupa and Adebowale B Saba, Department of Veterinary Physiology, Biochemistry & Pharmacology, University of Ibadan, Ibadan, Nigeria.
Correspondence to: Olayinka A Oridupa. Email: olayinkaolumide2000@yahoo.com

of diabetes from different African sub-regions including West Africa[1,20,21]

Interestingly, the African continent has large numbers of medicinal plants that have been explored for their folkloric treatment of diabetes. A review by Mohammed *et al*[1] of African plants with antidiabetic effects showed that plants of the *Asteraceae* and *Lamiaceae* families were the most investigated, and West Africa had the highest number of investigated plants. Although promising results were reported in many cases, unfortunately only a few studies reported the partial characterisation of bioactive principles and/or mechanisms of action.

An estimation conducted in 2004 by the Diabetes Association of Nigeria (DAN) put the diabetes population in Nigeria at about 10 million, with about half living in Lagos State.[22,23] The report of a study on the knowledge and usage of medicinal plants in five districts of Lagos State showed that the traditional healers in this region had developed effective and easily recognisable diagnostic tools, with 80% of the local healers who replied confirming that they rarely referred their patients but usually treated referred cases (96%) themselves. Principal antidiabetic plants prescribed by the traditional healers or self-prescribed included *Vernonia amygdalina*, *Bidens pilosa*, *Carica papaya*, *Citrus aurantiifolia*, *Ocimum gratissimum*, *Momordica charantia*, and *Morinda lucida*. Dietary recommendations also accompanied therapy.[23]

Another ethnobotanical survey from Irepodun Local Government Area of Osun State, Nigeria reported that a total of 45 plant species belonging to 29 families were used for the treatment of diabetes in the area. Prominent among them were *Rauvolfia vomitoria*, *Aframomum meleguata*, *Momordica charantia*, *Xylopia aethiopica*, *Senna* spp, and *Vernonia amygdalina*. Herbal remedies were prepared from either dried or freshly collected plants, and traditional solvents of choice included water, lime, and aqueous extracts from fermented maize. The survey revealed that leaves are the part of the plant most often used in herbal preparations. Residents in the study area found the traditional medicine cheaper than orthodox medicines.[24]

In an ethnobotanical survey by Soladoye *et al*,[25] about 132 different plants species belonging to 56 families were reported for the treatment of diabetes in the regions of south-western Nigeria captured in the study. The most prominent plants reported were *Senna alata*, *Curculigo pilosa*, *Cucurmeropsis mannii*, *Anthocleista* spp, *Vernonia amygdalina*, and *Allium* spp. Most of these plants were readily available in this region.

A study by Etuk *et al*.[26] in the north-western region of Nigeria reported that 34 plant species were cited by the local healers for management of diabetes. Two plants, *Mangifera indica* and *Vernonia amygdalina*, were most used. None of the herbalists interviewed had formal education; they inherited the knowledge of their practices from their parents, relatives, or friends.

Over 40 individual medicinal plants and five combinations of two or three plants from Nigeria have been documented by various researchers to demonstrate a potent anti-diabetic effect. The greatest amount of research has focused on three species: *Gongronema latifolium*, *Vernonia amygdalina*, and *Ocimum gratissimum*. These plants are discussed in detail below.

Gongronema latifolium

Gongronema latifolium (Asclepiadaceae) is a plant that has received much attention as a hypoglycaemic agent in Africa. Almost all of its parts are claimed to have antidiabetic effects. Aqueous leaf extract was found to decrease the fasting blood glucose in streptozocin-induced type 1 diabetic rats,[27] with an insulin-like activity as the probable mechanism of effect. Akah *et al*[28] reported the hypoglycaemic effect of methanol extracts of *G. latifolium* in alloxan-induced diabetic rats. Adebajo *et al*[29] also reported an insulinotropic and glucose-lowering effect of the combined root and stem bark methanol extracts. Ethanol extracts of the roots and twig showed a protective effect against alterations on the markers of kidney function in a type 1 diabetes model of rats.[30] Fasting blood glucose dropped by more than 60% for a single dose of the twig extract compared with 43% for the root extract.[1]

Vernonia amygdalina

Vernonia amygdalina (Asteraceae) commonly called 'bitter leaf', is used in folkloric medicine and many studies have investigated its use in both type 1 and type 2 animal models of diabetes and human subjects. Some of the investigations reported amelioration of hyperlipidaemia and hyperketonaemia associated with diabetes, as well as antioxidant properties.[31,32] *V. amygdalina* administered at 5%, 10%, and 15% inclusion in broiler finisher and normoglycaemic rat feed showed dose-dependent reductions in glucose levels without apparent toxicity to the liver and kidney.[33,34] Eteng *et al*[35] reported that *V. amygdalina* can prevent the macrovascular complications associated with diabetes, while Olorunfemi *et al*[36] reported that the hexane/ethyl acetate fraction obtained from the methanol leaf extract maintained full tissue architecture and protected the germinal epithelium and seminiferous tubules in streptozocin-induced type 1 diabetes.

Ocimum gratissimum

Ocimum gratissimum (Lamiaceae) is used widely as a condiment or spice (basil) in different cultural settings in Africa, and also for the traditional management of diabetes.[37] *O. gratissimum* methanol leaf extract significantly ($p<0.05$) decreased blood glucose levels in both normal rats and type 1 diabetes models by 56% and 69%, respectively.[38] Egesie *et al*[39] concluded that the extract appeared non-toxic as evidenced by normal serum levels of liver enzymes and bilirubin. Oguanobi *et al*[40] reported its ability to alleviate derangements in serum and biliary bilirubin, cholesterol, and electrolytes in neonatal streptozocin-induced diabetic rats.

Conclusion

Most of the medicinal plants described require further studies to progress potential drug candidates. Unfortunately, most of the documented research is self-funded which limits the scope of research. More attention should be paid to these plant sources of drugs for diabetes, which could be a promising resource for Nigeria.

Author declarations

The authors confirm that they have no competing interests to declare, that no animals were used in the research and that no informed consent was required from patients.

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