

A Review on Selected African Medicinal Plants with Effectiveness in the Management of Type II Diabetes Mellitus

Nkala BA^{1*}, Mbongwa HP¹ and Qwebani-Ogunleye T²

¹Department of Human Physiology, School of Laboratory Medicine and Medical Sciences, College of Health Sciences, University of KwaZulu-Natal, Durban, South Africa

²Institute of Traditional Knowledge and Traditional Medicine, Vaal University of Technology, Southern Gauteng Science and Technology Park, Sebokeng, South Africa.

***Corresponding Author:** Nkala BA, Department of Human Physiology, School of Laboratory Medicine and Medical Sciences, College of Health Sciences, University of KwaZulu-Natal, Durban, South Africa.

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Abstract

Type II diabetes mellitus is a metabolic disorder characterised by hyperglycaemia due to a defect in insulin production and/or resistance by the cells. Bioactive compounds with antidiabetic, antioxidant and anti-inflammatory properties are potential solutions towards the management of type II diabetes mellitus. Bioactive compounds, which naturally occur in medicinal plants, such as antioxidants, play a vital role in scavenging free radicals. Free radicals are naturally formed in the body and play a pivotal role in many normal cellular processes. However, at high concentrations, free radicals can be hazardous to the body and damage all major components of cells, including DNA, proteins, and cell membranes. The damage to cells caused by free radicals, especially the damage to DNA, may play a role in the development of cancer, neurodegenerative disorders, cardiovascular diseases, diabetes and other chronic health conditions. Therefore, it is anticipated that increased knowledge of plants with hypoglycaemic, antioxidant and anti-inflammatory activity will not only impact, but also revolutionize phytomedicine industrial and pharmaceutical processes. This review will look into the investigation of plants used for the treatment and management of diabetes type II.

Keywords: Antidiabetic; Antioxidant; Anti-Inflammatory; Hypoglycaemic and Natural Products

Introduction

Type II diabetes mellitus (T2DM) is a metabolic disorder characterised by hyperglycaemia due to a defect in insulin production and/or resistance by the cells. In the past decades (34 years from 1980 to 2014), has witness global prevalence of T2DM jumped a staggering 314 million cases from 108 million to 422 million according to a study done by the World Health Organisation [1]. Bears., *et al.* [2] estimated that T2DM would increase from 4.0% in 1995 up to 5.4% in the year 2025. In South Africa, the prevalence of T2DM in adults is on the rise too. In the short space of 9 years T2DM prevalence increased from 5.5% in 2000, to 9.0% in the year 2009 [3].

The effects of T2DM is further observed with the economic devastation experienced by the suffers of diabetes whom on average R9, 000 higher hospitalisation costs as compared to the non-diabetic in in 2009 as reported by Ncube-Zulu and Danckewert [4], in their study that reported R27, 000 (2,250 USD) per hospitalisation compared to R18, 000 (1,500 USD) for non-diabetic patients. This is the global context where the total health expenditure is projected to be between 1.1 to 2.0 billion USD in 2030 [5]. Moreover, the current conventional drug therapies are not completely effective in the T2DM management, exacerbating the problem is the various associated adverse effects of these therapies currently in usage [6].

The search for alternative therapies to address such challenges is therefore imperative [7]. Plants used for their medicinal properties in fight against T2DM have shown to be able to alleviate one or more symptoms. A total cure for the disease still eludes the medical fraternity [8]. Medicinal plants have also showed to be effective in delaying complications of the diseases and rectifying metabolic abnormalities. The use of plants for medicinal purposes has the advantage of having none or few side effects [9].

Natural products continue to play a significant role in drug discovery and development. Plants are recognised as a useful source of highly biological active drugs for the treatment of various ailments. Thus, promising plants should continue to be fractionated and evaluated for their efficacy and toxicity potential; especially in the local context. South Africa boasts a rich fauna and flora kingdom and much success has already been reported in human and animal practise involving the tapping into the potential of using plants for their medicinal properties [10,11]. These include the treatment of infections, anti-helminthic activity, anti-malarial activity, anti-diarrhoeal activity, anti-cancer activity and antidiabetic potential [12,13].

According to the World Wild Fund (WWF), South Africa's Western Cape is more botanically diverse than the richest tropical rainforest in South America, including the Amazon. It contains 3.0% of the world's plant species and 20% of Africa's. Of the more than 8,500 fynbos species, nearly 6,000 of them are endemic [14]. Very few of these plants have been explored for their phytochemicals and pharmacological potential so the chances of finding plants with medicinal purposes definitely exists [15]. Furthermore, bioactive compounds with anti-inflammatory, antioxidant and antidiabetic properties are potential solutions towards the management of T2DM.

Medicinal plants

Medicinal plants serve as important sources of pharmaceutical, cosmetic and traditional medicine [16]. However, their use in these industries has declined since the discovery of synthetic drugs and their production at a larger scale. Interestingly, despite this decline it is important to note that, half of these synthetic drugs are of natural origin are synthesized using chemical characteristics and structure derived from their natural counterparts, thereby, highlighting the importance of medicinal plant's role in drug

discovery [17]. Medicinal plants play an important role in providing promising solutions for the treatment and management of certain diseases [18]. The use of medicinal plants in drug discovery by the international community is expected to increase, as more literature, focusing on their safety and efficacy, becomes available [18].

While the global community tries to come to terms with the use of plants for medicinal use. The use of traditional medicine practices has been entrenched in cultural practice throughout developing countries [19]. WHO [20] estimated that 75% of South Africans rely on traditional medicine as the primary treatment for their healthcare needs. The use of medicinal plants in the South African traditional medicine context can be traced back thousands of years through cave drawings [21]. The harvesting of these plants has led to the establishment of shops and ultimately growth of commercial trades, which include healing, therapeutic and spiritual purposes. The informal trade of these plants are boosted as the adoption of the use of traditional medicines in urban settings continues [22]. Liu and Wang [23] have estimated that approximately 85,000 plant species are used globally. Essentially, in the United States represents 35% of this market, followed closely by Europe that encompasses Germany, France, UK, Italy and Scandinavia, with 33%. Africa contributes less than 1% to the market (USD 520 million) [24].

Herbal medicine in the global market from African

Only a few of these plants have been used for herbal medicine in Africa make their way onto the global market. These plant species include *Agathosma betulina* (Buchu), *Aloe ferox* (Cape aloe), *Aspalathus linearis* (herbal tea), *Herpagophytum procumbens* (devil's claw), *Hypoxis hemercolidea* (African potato), *Merwillia natalensis* (*Scilla natalensis* planch), *Pelargonium sidoides* (Umckaloabo), *Sclerocarya birrea* (marula), *Siphonochilus aethiopicus* (wild ginger) and *Sutherlandia frutescens* (cancer bush) [15]. Interestingly, these species contain among other things antioxidant, anti-inflammatory and antidiabetic properties; of which are essential constitute for the treatment and management of diabetics and other cardiovascular disease. In a review by Street and Prinsloo [15] detailed on phytochemicals and bioactivity of these commercially use medicinal plants. It is evident that certain plants possess antidiabetic, antioxidant and anti-inflammatory properties; of which is the key towards the treatment and management of certain diseases.

Inflammation has been defined as a major factor for the progression of various chronic diseases/disorders, including diabetes, cancer, cardiovascular diseases etc. [25]. The production of free radical from different biological and environmental sources are due to an imbalance of natural antioxidants which further leads to various inflammatory associated diseases [26]. It has been observed that natural compound based antioxidant and anti-inflammatory have gain momentum for the preventive role in protecting against the generation of free radicals and therefore natural based antioxidants and anti-inflammatory are one of the more valuable therapeutic agents to reduce the illnesses triggered by oxidative stress [27].

The use of plants is motivated by their affordability, availability and most importantly by the remedial beliefs that certain communities have. Essentially, the following factors need to be taken into considerations when dealing with plants such as the right time for harvesting, collection and use, does not address critical concerns such as safety, efficacy and the mode of action; which is not thoroughly understood.

Aetiology of type II diabetic mellitus

T2DM is one of the top six leading causes of diseases in the world and it accounts for death of approximately 1.6 million people in 2015 [1]. T2DM results from the inability of the pancreas to produce insulin or the inability of the body's metabolic system to use the insulin produced. Various pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the β -cells of the pancreas in insulin deficiency to abnormalities that result in resistance to insulin action [28]. The cause of diabetes is not thoroughly understood, however, it is believed that it is associated with various factors such as – genetics bad dietary habits, obesity and the adoption of a sedentary lifestyle. The disease is noticeable from the first stage, which is an increase in glucose or hyperglycaemia. This is due to the body being unable to metabolise sugar and other dietary substance like lipids and proteins and will lead to disorders affecting almost all of the body [29]. Diabetic patients are prone to develop chronic illness resulting in neurological, cardiovascular, retinal and renal complications, which may lead to premature death [30].

The management of type II diabetes mellitus

Daily management of T2DM

Daily management of T2DM involves, among other things, the control of blood glucose levels, which should be between 4.0 to 6.0 mmol/L [28]. Primarily lifestyle interventions are used for T2DM management, but if these lifestyle interventions fail to control blood glucose levels then it becomes crucial to consider pharmacological treatment. Essentially, the following therapies should be considered namely: - taking insulin injections, administering oral medication, following a healthy diet, being physically active, controlling blood pressure levels (i.e. should be kept below 130/80mmHg) and controlling cholesterol levels (i.e. 5 mmol/L or less) [31]. In addition to diabetic medication, one should consider interventions such as making healthy choices, being physical active, controlling blood pressure and controlling cholesterol levels [20].

Drug treatment

The initial and standard drug that is used for the treatment of type 2 diabetes in adults is metformin. In some instances, metformin is contraindicated or not tolerated. The following drugs are considered namely: - a dipeptidyl peptidase-4 (DPP-4) inhibitor or pioglitazone or a sulfonylurea [32]. It is imperative to exercise caution when prescribing pioglitazone, when a person is at high risk of the adverse effects of the drug. The reason being, pioglitazone is associated with an increased risk of heart failure, bladder cancer and bone fracture [33]. Metformin can also be used in conjunction with insulin injection or added, especially when glycaemic targets are not met. In order to control glycaemic bolus insulin can be used, since it is rapid-acting analogues [34].

The management of T2DM is a global concern and it has been observed that available therapy is not being tolerated by patients due to side effects mentioned here above. The side effects can of serious concern such as liver problems, lactic acidosis and diarrhoea [35]. Interestingly, the available therapy is mainly responsible for the improvement insulin sensitivity, increasing insulin production and decrease the amount of glucose in the blood.

However, side effects are not satisfactory and it is imperative to investigate on natural compounds for the treatment of T2DM, of which is believed to have lesser adverse effects [36].

Alternative treatment

The conventional drugs that are used for the management of diabetes have been observed to have some adverse effects. Therefore, it is vital to investigate alternative therapies that have less or no side effects and which are effective in the management of diabetes. Some medicinal plants have been demonstrated to have lesser side effects and have ability to treat various diseases [37]. Moreover, natural bioactive compounds isolated from medicinal plants that have anti-hyperglycaemic activities have been confirmed experimentally [38]. Bioactive compounds that are associated with antidiabetic effects are glycosides, alkaloids, citric acid, malic acid, polyterpenes, cyanhidric acid, essential oils, allicine, nerolidol, pectins, terpenoids, flavonoids, carotenoids, sterols, triperpenes and protein (bixine) [12]. Medicinal plants have been used in ancient times throughout the world for the management of T2DM [39].

It has been noted that, the use of medical plants in the developing countries has gained momentum, whereby many people do not have access to conventional antidiabetic therapy. Essentially, it is not only about the affordability of a conventional drug, but the cost of transport to the nearest health care facilities plays a role in making conventional drug unaffordable among other issues [40]. The developed countries have also shown interest in the investigation of antidiabetic herbal remedies as an alternative therapy. It is believed that they are motivated by factors such as adverse reactions, high secondary failure rates and cost of conventional drugs [41]. Furthermore, WHO has endorsed the use of medicinal plants for the management of T2DM and further recommended more research on the evaluation of hypoglycaemic/hyperglycaemic properties of diverse plant species [42].

The mechanism of action is not thoroughly understood, however, natural plants have been observed to restore pancreatic tissue by causing an increase in insulin output or decrease in the intestinal absorption of glucose. Essentially, treatment with plants has been observed to protect β -cells and smoothing out fluctuation in glucose levels. The other possible mechanism of action that has been reported is the inhibition of α -glucosidase and α -amylase, the effects on glucose uptake and glucose transports, the enhancement of insulin secretion and pancreatic β -cell proliferation, the inhibition of protein tyrosine phosphate 1B activity and antioxidant activity have been studied in depth [43].

For the purpose of the broader study, plants will be investigated for antidiabetic, antioxidant and anti-inflammatory properties. Essentially, the purpose of this review reflects on the selected African medicinal plants that has been reported by healers and herbalist to be used in the treatment of diabetes. It is imperative to note that not all of these plants are scientifically validated for their use in the traditional medicine practices. However, few of these plants have been reported for their phytochemistry, bioactivity; and most importantly for their use in the treatment and management of diabetes.

Lippia javanica (The lemon bush tea/or fever tea)

Xhosa people use it to disinfect meat that has been contaminated by anthrax. It has been reported to be used in various traditional medicine such as have further reported this plant to be used for the treatment of various ailments including diabetes, fever, cough, bronchitis and influenza. *L. javanica* consists of the following phytochemicals alkaloids, sterols, terpenoids, flavonoids, tannins and saponins. It is important to note that nothing has been reported on bioactivity of this plant in literature [44,45].

Euclea natalensis (Natal guarri)

It has variety of traditional remedies such as to treat worms, stomach disorders, toothache, headache, chest complaints pleurisy, urinary tract infections, venereal diseases, schistosomiasis, dysmenorrhoea and for scrofulous swellings, abnormal growths on skin and leprosy. Furthermore, Deuschländer, *et al.* [12] reported that this plant is used by Venda herbalist for the treatment of diabetes. The phytochemicals and bioactivity of this plant was reported on the review by Deuschländer, *et al.* [12].

Schkuhria pinnata (Dwarf marigold)

S. pinnata have been used as a bactericide in open wounds, to treat acne, malaria and inflammation, and as a blood purifier and diuretic. In addition to this, this plant is used by traditional healers and herbalist in Ga-Rankuwa, Gauteng to treat diabetes. The phytochemicals and activity of *S. pinnata* has not been reported on in literature [12,46].

Clerodendrum myricoides (Blue cat's whiskers)

It has numerous medicinal uses ranging from the treatment of snakebites, reduce bodily swellings, relief indigestion, to treat colds, chest pains and headaches, as well as being applied to bleeding gums. In addition to this, *C. myricoides* has been reported

to be used for the treatment of impotence. Impotence is defined as one the manifestations of autonomic neuropathy in diabetes. Nothing has been reported on phytochemicals in *C. myricodes*, except on its family (Verberaceae) reported to have various compounds such as anthraquinones, terpenes, steroidal saponins, alkaloids and flavonoids. Furthermore, nothing has been reported on *C. myricodes* bioactivity except for Clerododrum genus [47].

***Euclea crispa* (Blue guarri)**

It is used for stomach disorders, measles, coughs and constipation. It has been further reported to be taken orally as a remedy for diabetes and also prevents rheumatisms and epilepsy [47]. According to our knowledge nothing has been reported on *E. crispa* phytochemicals or bioactivity in literature.

***Ziziphus mucronata* (Buffalo thorn)**

It has various medicinal uses per each region and the most common one is to treat boils, swollen glands, wounds and sores. The decoction of *Z. mucronata* has been reported to be used in the treatment of diabetes. The *in vivo* studies conducted have confirmed antidiabetic activity of *Z. mucronata*. Furthermore, phytochemicals such as alkaloids was reported in this plant [12,48].

***Vernonia oligocephala* (Bicoloured-leaf vernonia)**

The medicinal use for this plant is used to relief of stomach ache reliever which is taken a tonic. The phytochemicals that has been identified from *V. oligocephala* are flavonoids, glycoside, polyphenols, saponins and steroids. In Eastern and West Cape Province this plant has been reported to be used for treatment of diabetes by traditional healers [49].

***Erythrina lysistemon* (Coral tree)**

The bark is used to treat sores, wounds, abscesses and arthritis. Furthermore, the leaves infusions are used as ear drops to relieve earache, and decoctions of the roots are applied to sprains. *E. lysistemon* poses the following phytochemicals flavones, isoflavones, isoflavanones, alkaloids, pterocarpans phenolic acids. Essentially, the bioactivity of these phytochemicals have been validated. Nothing has been reported for the treatment of diabetes for this plant, however, it is promising plant due to its phytochemicals identified [50].

Conclusion

Type II diabetes mellitus (T2DM) is a major endocrine disorder and its growth or prevalence is ascribed to a number of factors that include but are not limited to obesity, social structure, hormonal imbalance, and hereditary. The use of medicinal plants has been observed since the ancient time for the treatment of various diseases. Essentially, medicinal plants have been noted to have lesser side effects; hence, the need to explore rich and potential plants with antidiabetic activity became necessary. The poor management of the diabetes can lead to neurological, cardiovascular, retinal and renal complications. Medical plants with antidiabetic, antioxidant and anti-inflammatory activities is essential for the management of diabetics and other related cardiovascular diseases. However, from our review, it is apparent that plants possess essential compounds to fight diseases such antidiabetic, antioxidant and ant-inflammatory properties. Certain medical plants have shown to have hypoglycaemic effects and can be used for the treatment of type of secondary complications of type II diabetes mellitus. Researchers have reported on the ability of plant to treat and manage T2DM, however, it is imperative to understand the exact mechanism of action of medicinal plants with antidiabetic and insulin mimetic activity.

Antioxidants have been demonstrated for their ability to scavenge free radical and this have served a key element towards the prevention and treatment of disease associated with oxidants or free radicals. It is important to note that antioxidants are derived from food and medicinal plants; of which more research have been focusing on them for various nutritional function and health benefits. The availability of antioxidants varies from plants to plants that is why it is imperative to investigate plants broadly in search for potential plants species. The ability of medicinal plants to possess anti-inflammatory properties have been explored.

T2DM has been observed to be a global concern, of which affecting large population. It is associated with decreased insulin production or resistance towards its action. Medicinal plants ability to treat diabetes patients, both insulin dependent and non- insulin dependent diabetes has been widely reported. Recent developments have justified the role of medicinal plants for the management of diabetes, however, it would be unwarranted to assure that all plants can be blindly used in diabetic patients.

Medicinal plants with promising antidiabetic, antioxidant and anti-inflammatory effect will need to be further validated for toxic effects, herb-drug interaction etc. In our future studies, selected plants will be evaluated for their cytotoxic effect, antidiabetic, antioxidant and anti-inflammatory properties and moreover, the minimal inhibitory concentration and minimal bactericidal concentration will also be studied. Therefore, it is anticipated that increased knowledge of plants with hypoglycaemic, antioxidant and anti-inflammatory activity will not only impact, but also revolutionize phytomedicine industrial and pharmaceutical processes.

Conflict of Interests

The authors declare that they do not have any conflict with respect to the publication of this paper.

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