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Antidiabetic potentials of common herbal plants and plant products: A glance

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Abstract
Right from time immemorial, herbal medicine has been in practice. This is so, as many plants have been discovered to have pharmacological properties and have been applied in the management of many patients with various ailments and diseases with successes. This has prompted great interest among researchers in this regard to study various plants with medicinal properties. This study looks at the various plants like *Anisopus mannii, Daniella olivieri, Detarium macrocarpum, Leptadenia hastate* and *Mimosa invisa*, *Vermonia amygdalia, Bidens pilosa, Carica papaya, Citrus aurantiifolia, Cimum gratissimum, Momordica charantia,* and *Morinda lucida* which have been adopted for anti-diabetic therapy and their pharmacological properties have been widely explored. They may also provide clue for the development of new and better oral drugs for diabetes mellitus.

Keywords: momordica charantia, morinda lucida, citrus aurantiifolia, anti-diabetic

1. Introduction
According to the World Health Organization (WHO), herbal medicines should be regarded as finished, labelled medicinal products that contain active ingredients in the aerial or underground parts of plants or other plant materials or combinations thereof, whether in the crude state or as plant preparations. The plant materials include juices, gums fatty oils, essential oils and any other substances of this nature.

Herbal medicine is sometimes referred to as herbalism or botanical medicine. It involves the use of herbs for their therapeutic or medicinal value. Herbs are plants or plant parts valued for their medicinal, aromatic or savoury qualities. They contain and produce a variety of chemical substances that act in the body (Holistic-online, 2007) [127]. Herbal medicines include herbs, herbal materials, herbal preparations and finished herbal products that contain an active ingredients parts of plants, or other plant materials, or combinations (WHO, 2012) [124].

Herbal medicines may contain excipients in addition to the active constituents. In some countries, herbal medicines may also contain, by tradition, natural organic or inorganic active constituents which are not of plant origin. Herbal medicine is the most primitive traditional approach to the treatment of diseases and ailments and it involves the use of plants and plant parts. There is no doubt that herbal medicines provided the first basis for therapeutics before the development or advent of orthodox medicine.

Despite the fact that, over the years, chemists have synthesized a large number of chemical substances, many of which have proved useful in modern therapeutics, plants still remain potential sources of useful products. Many drugs listed as conventional medications were originally derived from plants. Salicylic acid, precursor of aspirin was originally derived from *Salix alba* and the meadow sweet plant *Cinchona officinalis* is the source of malaria fighting quinine. Vincristine, used to treat certain types of cancer, comes from *Vinca major*. The *Papaver somniferum* yields morphine, codeine and paregoric (a medicine consisting of opium flavoured with camphor and benzoic acid), a treatment for diarrhoea. Since time immemorial man has used various parts of plants in the treatment and prevention of many ailments (Chah *et al.*, 2006) [19].

Historically all medicinal preparations were derived from plants, whether in the simple form of plant parts or in the more complex form of crude extracts, mixtures, etc. Today a substantial number of drugs are developed from plants which are active against a number of diseases. Although the medicine prescribed may contain only one single active item, it is often a mixture of many components. Medicines containing plant materials combined with chemically defined active substances including chemically defined isolated constituents of plants are not considered to be herbal medicines (Fabricant and Farnsworth, 2001) [37].

In the past two decades, there has been a global resurgence of interest in traditional medicine for the treatment of ailments that defy orthodox medicine principally because many diseases have defied or developed resistance to conventional drugs as well as a health system closer to the rural poor. As a result of this renaissance in unorthodox medicine, a lot of interest and attention have been drawn to the curative claims and norms (ethics) of herbal plants in different parts of the globe especially Africa and Asia (Awoyemi *et al.,* 2012) [15].

Primitive men observed and appreciated the great diversity of plants available to them. How medicinal plants came to be used in many cases is lost in prehistoric times, but ethnic knowledge of beneficial herbal drugs in various societies has been handed down from generation to generation by both oral means and on writing on papyri, baked clay tablets, parchments, and in manuscript herbals, printed herbals, pharmacopoeias. (Evans, 2002) [34].

Thousands of herbal medicines are used by people from every culture and various indigenous medicines are gradually being introduced into modern therapeutics. In developing countries about 80% of the people, especially the rural population, rely on the traditional medical remedies for their health care needs (Moody, 2007) [79]. In developed countries, there has been a resurgence of interest in herbal medicines due to a large extent on the preference of many consumers for products of natural origin. It is important however; to distinguish between herbal medicine supplied by a "qualified" medical practitioner as a result of a consultation and those herbal remedies (in the form of "teas") freely available to the public for self-medication (Bauer, 1998) [16].

The current WHO reports, indicates that over 85% of the population in sub-Saharan Africa, which includes Nigeria depends on herbal traditional medicine for their health care delivery needs (WHO, 1999) [121]. Even within a relatively small geographical area, the use of plants and herbs for food, maintenance of people's health and alleviation of numerous health problems such as mental disorders, diabetes, sickle cell anaemia, malaria and tuberculosis vary widely.

The use of plant-based systems has continued to play a key role in health care. Many reports estimated that approximately 80% of the population in developing countries still relies on traditional medicine (TM) for their primarily health care (WHO, 2003) [124]; Hostettmann and Marston, 2002) [55]. In some African countries such as Ghana, Mali, Nigeria and Zambia, the first line of treatment for 60% of the children with high fevers, resulting from malaria, is the use of herbal medicines at home (WHO, 2003) [124]. In these societies, the tradition of collecting, processing and applying plants and plant-based medications have been handed down from generation to generation. Traditional medicine, with medicinal plants as their most important component are sold in market places or prescribed by traditional healers in their homes (WHO 2003) [124].

The development of resistance to most of the available antimicrobial agents and the high costs of treatment consequent upon this resistance has necessitated a search for new, safe, efficient and effective agents for the management of infections (Okwu, 2009) [85]. This research for new effective agents against infectious diseases and other diseases such as, cancers, diabetes, cardio-vascular, neurological, respiratory disorders, etc has led to increased interest in existing information about the remedies of these diseases from natural sources, principally the plants (Karou *et al*., 2007; Ouattara *et al*, 2007) [88]. Because of this strong dependence on plants as medicines, ethno-pharmacological studies are being conducted to determine their safety and their efficacy and on the other hand to find out new active principles from plants (WHO 2007) [125].

Justification of the Study

This is research is an done with the aim of identifying and searching for new medicinal plants with anti-diabetic activity that can be effectively used in the treatment of diabetes and its complications.

Plants and Plant Products in Folk Medicine for Treatment of Diabetes Mellitus

Several plants possess high hypoglycaemic properties and as such are potential sources of new drugs to complement existing oral hypoglycaemic agents in the management of diabetes mellitus. Several species of herbal drugs have been described in the scientific and popular literature as having anti-diabetic activity (Valiathan, 1998) [188].

Biological actions of the plant products used as alternative medicines to treat diabetes are related to their chemical composition. Herbal products or plant products which are rich in phenolic compounds, flavonoids, terpenoids, coumarins, glycopeptide, alkaloids, steroids, and other constituents tend to show reduction in blood glucose levels (Crozier *et al.,* 2009) [25].

In Nigeria, several plants have been identified to have anti-diabetic effects among people in a selected district of Lagos state Nigeria (see tables 1a and 1b). They include *Vermonia amygdalia, Bidens pilosa, Carica papaya, Citrus aurantiifolia, Cimum gratissimum, Momordica charantia, Morinda lucida* (Gbolade, 2008). More recently in Nigeria, five plants have been added to the list of anti-diabetic drugs used traditionally for the treatment of diabetes. These plants include: *Anisopus mannii, Daniella olivieri, Detarium macrocarpum, Leptadenia hastate and Mimosa invisa* (Manosroi *et al.*, 2011) [76]. Marles and Farnsworth estimated that more than 1200 plant species representing 725 genera in 183 families are being used as folk medicine for diabetes (Marles *et al.*, 1995) [77].

Table 1: Some medicinal plants used in traditional medicine for treatment of diabetes.

Plant	Family	Part Used	Reference
Abroma augusta L.	Sterculiaceae	Root	Kar *et al*, 1999
Acourtia thurberi (Gray) Rev. et. King	Asteraceae	Root	Aguilar *et al.,* 1994
Ajuga iva L.	Lamiaceae	Aerial parts	Ziyyat *et al.,* 1997
Anthocleista djalonensis A. *Chev*	Loganiaceae	Leaves	Olubomehin *et al.,* (2013)
Artemisia herba-alba Asso	Asteraceae	Root	Subramoniam *et al*, 1996
Asianthus viminalis	Bignonaceae	Whole plant	Alarcon-aguilara *et al.,* 1998.
Beta vulgaris L.	Chenopodiaceae		Yoshikawa M, *et al*. (1996)
Bidens pilosa L.	Asteraceae	Whole palnt	Alarcon-Aguilara *et al.,* 1998
Bombax ceiba L.	Bombaceae	Leaves	Saleem *et al.* (1999),
Brassica oleracea L.	Cruciferae	Leaves	Roma-romos *et al.,* 1995

Bridelia micrantha (Hochst) Bail	Euphobiaceae	Leaves	Eton *et.,* 2008
Bauhinia monandra K	Caesalpiniceae	Stem bark	Abo *et al.,* 2004.
Caesakoubua bonducella L.	Leguminosae	Seeds	Rao *et al.,* 1994
Carica papaya L.	Cariceceae	Fruits	Olagunju *et al*., 1995
Capparis spinosa L.	Capparaceae	Fruit	Ziyyat *et al*., 1997
Ocimum gratissimum L. Var	Lamiaceae	Leaves	Aguiyi 2000
Cinnamomum tamal	Lauraceae	leaves	Kar *et al*., 1999
Ciccinia olitorius Wright and Am.	Cucurbitaceae	Aerial	Kar *et al*., 1999
Citrus aurantium L	Rutaceae	Fresh mull	Alarcon-Aguilara *et al*., 1998
Citrus colocynthis L	Cucurbitaceae	Fruit	Alarcon-Aguilara *et al*., 1998
Cnidosculus multilobum (L.ex.)	Euphorbiaceae	Leaves	Alarcon-Aguilara *et al*., 1998
Corchorus olitorius L.	Titiaceae	Leaves	Oliver-Bever, 1986
Eucalypyus globules labill	Myrtaceae	Flower	Hideo *et al.,* 1994
Exostema caribeaum (Jacq)	Rubiaceae	Bark	Alarcon-Aguilara *et al*., 1998
Euphorbia Preslli I.	Euphorbiaceae	Whole plant	Alarcon-Aguilara *et al*., 1998
Eysenhardita polystachia (Ort.) S.	Rubiaceae	Bark	Alarcon-Aguilara *et al*., 1998
Ficus bengalensis L.	Moraceae	stem-bark	Kar *et al*, 1999
Ficus carica L.	Moraceae	Flower, leaf	Ziyyat *et al*., 1997

Table 1b: Some medicinal plants used in the treatment of diabetes in traditional medicine.

Plant	Family	Part Used	Authors
Gongronema latifolium	Asclepidaceae	Leaves	Akah *et al* 2011
Gymnema sylvestre R. Br	Asclepidiaceae	Leaves	Kar *et al,* 1999
Magnifera indica L.	Anarcadiaceae	Leaves	Alarcon-Aguilara *et al.,* 1998
Marrubium vulgare L.	Lamiaceae	Aerial parts	Ziyyat *et al*., 1997
Momordica charantia L.	Cucurbitaceae	Leaves, fruits	Rivera, 1941
Menthe piperita L	Labiatae	Whole plant	Alarcon-Aguilara *et al*., 1998
Moriga oleifera Lam	Moringaceae	Stem bark	Kar *et al,* 1999
Neloumbo nucifera Gaertn	Nymphaceae	Rhizome	Mukherjee *et al*., 1995
Nerium oleander L.	Apocyanaceae	Leaves	Ziyyat *et al.,* 1997
Ocimum gratissimum L. Var.	Lamiaceae	Leaves	Aguiyi (2000)
Orthosiphon astamineus Benth	Lamiaceae	Whole plant	Mariam *et al.,* 1996
Parkia biglobosa (Jacq) Benth	Mimosoideae	Seed	Fred *et al.,* 2009
Physalis angulate	Solanaceae	Whole plant	Abo *et al.,* 2013
Piper sarmentosum Roxb	Piperaceae	Whole plant	Peungvicha *et al,* 1998
Psidum guajava L.	Myrtaceae	Fruits	Roman *et al,* 1995
Prenus amygdalus var amara CD	Rhamnaceae	Leaf	Ziyyat *et al*., 1997
Ravolfia tetraphylla L	Apocyanaceae	Leaves	Ibanez-Camacho 1983
Salpianthus macrodonthus Stand	Nyctaginaceae	Root	Perfumi and tacconi, 1996
Sesbania aegytiaca pers	Papillionaceae	Leaves	Kar *et al*, 1999
Spondias mombin Linn	Anacacardiaceae	Leaves	Fred *et al* 2009
Telfairia occidentalis Hook. F.	Cucurbitaceae	Leaves	Aderibigbe *et al,* 1999
Trigonalla foenum graceum L	Papillionaceae	Seed	Abdul-Barry *et al,* 1997
Zingiber officinale Rosc	Zingeberaceae	Rhizome	Kar *et al*., 1999

Source: (Abo K.A *et al.,* 2008) [5] ©2011 PharmaInter Science Publishers.

Review of Ant-Idiabetic Studies on Medicinal Plants

Chika *et al*., (2010) [22] reported the hypoglycaemic activity of aqueous leaf extract of *Combretum micranthum*. They tested three different doses (100, 200 and 400mg/kg body weight) of the extract. Their result revealed that the least dose (100mg/kg) had the highest hypoglycaemic activity producing a significant percentage blood glucose reduction of 24.6. This study, therefore demonstrated the potential antidiabetic property of *C. micranthum.* However, further studies, maybe necessary to isolate and chemically elucidate the hypoglycaemic principle which may serve as chemical lead for the development of novel antidiabetic drugs.

Aloe vera is the most well-known species of *Aloe*, a desert plant resembling the cactus in the liliaceae family. It is popularly used to treat burns and promote wound healing. The dried sap of the Aloe vera is a traditional remedy for diabetes in the Arabian Peninsula (Pandey *et al.*, 1995) [89]. Aloe gel, obtained from the inner portion of the leaves, contains glucomannan, a hydro-soluble fiber which may in part account for its hypoglycaemic effects (Pandey *et al*., 1995) [89]

Gymnema Sylvestre is another commonly used herb in Ayurveda. The plant is a woody climber that grows in tropical forests of central and southern India. According to common folklore, chewing the leaves causes a loss of sweet taste, hence the popular Hindi name of the plant "gurmar", meaning "destroyer of sugar". Studies of an ethanol leaf extract, in diabetic rat and rabbit model have reported regeneration of Islets of Langerhans, decreases in blood glucose and increases of serum insulin (Shanmugasundaram *et al.*, 1990) [100].

Polina *et al.,* 2010 [95] documented the enhancement of glucose uptake by aqueous root extract of *Sarcopoterium spinosum*. The extract was prepared by hot water decoction of the root from 30min. various concentration of the extract ranging from 0.001-10 mg/ml was administered to genetically diabetic mice. At concentration of 0.01, 0.1 and 1 mg/ml, the extract exhibited an insulin-like effect on glucose uptake in hepatocytes by inducing a 148±10, 133±23 and 119±14% increase in glucose uptake, respectively. These compared favourably with 160±12% increase obtained with insulin. Maximum glucose uptake activity was recorded at 0.01 mg/ml. Hence, this study revealed that aqueous root extract of *S. spinosum* exhibits an insulin-like action in target tissues, increases insulin secretion *in vitro* and improved glucose tolerance *in vivo*. These findings validate the traditional use of

S. spinosum for the treatment of diabetes mellitus.

Coccinia indica (Ivy gourd) is a creeping plant that grows wildly in many parts of the Indian subcontinent, and is used to treat "sugar-urine" (madhumeha) in Ayurveda, a traditional East Indian healing system. The mechanism of action is not well understood, but the herb appears to have insulin mimetic properties (Kamble *et al*., 1996) [63]

Several different plant species are often referred to as ginseng. The panax species (from the root panacea) are often noted for their "cure-all" adaptogenic properties, immune stimulant effects and their ability to increase stamina, concentration, longevity and overall well-being.

Mechanism of action includes decreased rate of carbohydrate absorption into the portal hepatic circulation, increased glucose transport and uptake mediated by nitric oxide, increased glycogen storage and modulation of insulin secretion.

Momordica charantia is a vegetable indigenous to tropical areas, including India, Asia, South America and Africa. The plant is commonly known as balsam pear, karela (karolla) and bitter melon. Active constituents are thought to be charantin, vicine and polypeptide – p (unidentified insulin like protein similar to bovine insulin). Theoretical mechanism includes increased insulin secretion, tissue glucose uptake, liver muscle glycogen synthesis, glucose oxidation and decreased hepatic gluconeogenesis. Studies in alloxan induced diabetic rabbits have suggested hypoglycaemic effects (Welhinda *et al*., 1986) [120].

Mechanisms of Action of Plants with Hypoglycaemic and Anti-Diabetic Activity

The anti-diabetic mechanisms involved in hypoglycaemic activity are numerous, examples are stimulation of insulin secretion, stimulating glycogenesis and hepatic glycolysis, pancreatic beta cell potassium channel blockers CAMP (cyclic adenosine monophosphate) stimulation, modulation of glucose absorption from the gut among others (Marles, 1995) [77]. Diasulin is a polyherbal drug, which controls blood glucose level by increasing glycolysis and decreasing gluconeogenesis with a lower demand of pancreatic insulin. It regulates the activities of hepatic glucose metabolic enzymes.

Medicinal plants have various mechanisms of action through which their antidiabetic activity are exhibited. These include promoting regeneration of cells of islets of Langerhans in the pancreas as exhibited by *Pterocarpus marsupium*, enhancement of insulin release and activity on the cells as exhibited by *O. europea* L. olive leaf, decrease peripheral glucose uptake at the duodenal cellular level and other aspects of small intestine exhibited by *M. indica* and *O. europea* L. olive leaf extracts and by restricting the rise of blood glucose levels caused by pituitary hormones responsible for inhibiting peripheral utilization of glucose as well as glycogenolysis exhibited by *Gymnema sylvestre*, and the presence of high level of fiber in plants which interferes with carbohydrate absorption (Yusuf *et al.,* 1994; Ahmad *et al.*, 2000; Hongxiang *et al*., 2009) [127, 9, 54].

The Challenge

Despite the medicinal usefulness of herbs, there are some criticisms levelled against it; such as lack of standardization, they are dispensed to patients with no specific amount of doses, dose not strictly regulated, since the production process is not standardized, they may contain varying amounts of the active ingredient and undeterminable quantity full of impurities. Now the question is "how do we formulate these herbal medicines to clear the above criticisms to compete with pharmaceutical drugs. This would involve critical research involving isolation and characterization of bioactive constituents of useful medicinal plants.

Also, and most importantly, the herbal medicines and even the orthodox medicine presently in use have actually not resulted to cure of the disease. There is therefore high need to explore alternative curative therapy through continuous exploration of the plant kingdom and validation of their potentials through comparative studies.

The Future Prospects

Thousands of herbal medicines are used by people from every culture and various indigenous medicines are gradually being introduced into modern therapeutics. In developing countries about 80% of the people, especially the rural population, rely on the traditional medical remedies for their health care needs (Moody, 2007) [79]. In developed countries, there has been a resurgence of interest in herbal medicines due to a large extent on the preference of many consumers for products of natural origin. It is important however; to distinguish between herbal medicine supplied by a "qualified" medical practitioner as a result of a consultation and those herbal remedies (in the form of "teas") freely available to the public for self-medication (Bauer, 1998) [16].

The rapidly increasing incidence of diabetes mellitus is a serious threat to human health in all parts of the world. Recently, new bioactive drugs have been isolated from plants and have shown anti-diabetic activity with more efficacy than oral hypoglycaemic agents used in clinical therapy. Therefore in recent years, Attention has been drawn towards identification of plants with anti-diabetic ability that may be useful to man (Malviya, 2010) [74]. They may also provide clue for the development of a new and better oral drugs for diabetes mellitus (Shukia, 2000) [101].

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