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## PHYTOCHEMICAL SCREENING AND REVIEW OF MEDICINAL PLANTS USED IN THE MANAGEMENT OF DIABETES IN EBONYI STATE, NIGERIA

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### ABSTRACT

**Introduction:** Diabetes is acknowledged and referred to as Nigerian silent epidemics with increased projection of its infection raising from 9.41 million in 2021 to 11.98 million in 2030 and subsequent increase to 18.79 million in 2045 respectively. The total relative expenditure which accrued due to diabetics outweighs ₦745 billion per annum with financial morbidity average of ₦300,000 per person. This has influenced relatively the choice for alternative medicine in most villages and local setting.

**Aim:** This study assessed possible plants used locally for the treatment of diabetics in Ebonyi state and their phytochemical constituent.

**Methods:** Six local communities in Ebonyi State, Nigeria were visited and 5 traditional healers, 5 elderly (men and women) and 5 vendors of medicinal plants each were selected to be the respondent from each of the communities, giving a total of 90 respondents. A total of 5 plants were generally accepted as commonly used in the management of diabetes. The plants were collected, identified, reviewed, and phytochemicals screened.

**Results:** The review of the plants constituent justifies their use as antidiabetes plants. Twelve plants were identified as commonly used for the management of diabetics in the locality evaluated and they include: *Andrographis paniculata*, *Azadirachta indica*, *Persea americana* Mill, *Vernonia amygdalina* Delile, *Blighia unijugata* L., *Catharanthus roseus* (L.) G. Don, *Loranthus micranthus*, *Momordica charantia*, *Bridellia feruginea*, *Trigonella foenum-graecum*, *Gongronema latifolium* (Benth) and *Carthamus tinctorius*. The plants were observed to originate from divers families. The phytochemical screening showed in abundance the presence of alkaloid, tannin, phenol, saponin, anthraquinone and other phytoconstituents at varying concentration. The plants identified were also used for other ailments

**Conclusion:** Ebonyi state is endowed with various plants known to have therapeutic activities against diabetics and these plants have been exploited locally in the management of this disease. The known activities exhibited by this plants could be associated to their phytochemical constituent and their abundance in this area.

**Keywords:** Diabetics, medicinal plants, Ebonyi state, phytochemical constituents

## INTRODUCTION

Diabetes Mellitus (DM) is a chronic disease characterized by post prandial hyperglycaemia, polyphagia, polyuria and polydipsia; resulting from insulin resistance, and deficiency of insulin production from pancreatic cells<sup>(1)</sup>. An estimated 422 million people currently live with Diabetes in the world. DM can also result in complications like diabetic ketoacidosis, strokes, heart disease, fatigue and diabetic retinopathy<sup>(2)</sup>. Sustained hyperglycemia occasioned by diabetes that isn't treated early enough can lead to severe damage to major organs like the kidney, leading to multiple organ dysfunctions<sup>(3)</sup>.

Nigeria currently has the highest number of diabetes cases in Africa with about 3.9 million persons living with the disease as far back as 2013<sup>(4)</sup>. Diabetes remains a global health challenge that has a lot of impact on the economy. It is projected that the number of persons with diabetes worldwide may further increase especially in developing countries where low standards of living condition people to make poor lifestyle choices that may predispose them to DM as well as the absence of efficient and affordable interventions for the management of the disease.

Since ancient times, naturopathic disease therapy has been thoroughly researched, and it is gaining traction in the current environment<sup>(5)</sup>. Diabetes mellitus is a serious endocrine illness that affects about 10% of the world's population and is a major source of concern<sup>(6)</sup>. In its most severe form, the disease affects major body systems, resulting in multi-organ problems. Oral hypoglycemic medicines such as sulphonylureas and biguanides are the most commonly used treatments, although their negative side effects are a significant drawback. Herbal medicines are becoming more popular as a

result of better outcomes and safer usage in comparison to commercially accessible pharmaceuticals, as well as more effective treatment of health problems<sup>(7)</sup>. Anti-diabetic plants are of special interest to ethnobotanists since they are known to have medical effects in diverse regions of the world, and a number of them have exhibited varying degrees of hypoglycemic and antihyperglycemic efficacy<sup>(8)</sup>. Bioactive substances found in many plant species can be isolated and employed as medications, lead compounds, or pharmacological agents. All of these tried-and-true techniques might be the key to treating diabetic complications. The chemical structures of phytomolecules are important for their anti-diabetic properties. Several plant species that are rich in compounds such as flavonoids, phenolics, terpenoids, coumarins, and other bioactive have been found to lower blood sugar levels<sup>(9)</sup>. Various antidiabetic plant extracts, such as fenugreek (*Trigonella foenum-graecum*) and gymnema (*Gymnema sylvestre*), have been utilized and evaluated in the treatment of diabetes for their activity as well as possible negative effects<sup>(10)</sup>.

## MATERIALS AND METHOD

### Sample Collection and Identification

Six local communities in Ebonyi State, Nigeria were visited and 5 traditional healers, 5 elderly (men and women) and 5 vendors of medicinal plants each were selected to be the respondent from each of the communities, giving a total of 90 respondents. These communities were Okposi, Uburu, Oshiri, Onisha-igboeze, Ikow and Afikpo. A total of 12 plants were commonly identified. The plants were characterized by a taxonomist from the Department of Biology, Federal University Ndufu-Alike, Ikwo, Ebonyi State, Nigeria.



### Extraction of Plant Materials

The leaves of the plants were collected and washed, then air-dried at room temperature for two weeks, after which they were pulverized into powder. The ethanol extracts were prepared by soaking 100 g each of the dry powdered plant materials in 1 litre of ethanol at room temperature for 24 hours with intermittent shaking. The extract was filtered using a Whatman (No.42) filter paper (125 mm).

### Qualitative Analysis of Phytochemical Substance

The extracts were subjected to phytochemical analysis to detect the presence of following biomolecules using the standard qualitative procedures<sup>(11)</sup>.

- a) Test for Alkaloids: 1ml of 1% HCl was added to 3ml of extract in a test tube and was treated with few drop of Meyer's reagent. A creamy white precipitate indicted the presence of alkaloids
- b) Test for Terpenoids: 5 ml of extract was mixed with 2 ml of  $\text{CHCl}_3$  in a test tube. 3 ml of concentrated  $\text{H}_2\text{SO}_4$  was carefully added to the mixture to form a layer. An interface with a reddish brown coloration was formed for the presence of terpenoids
- c) Test for Saponins: 5 ml of extract was shaken vigorously to obtain a stable persistent froth. The frothing was then mixed with 3 drops of olive oil and observed for the formation of emulsion, which indicated the presence of saponins.
- d) Test for Flavonoids: A few drops of 1%  $\text{NH}_3$  solution was added to the extract in a test tube. A yellow coloration was observed for the presence of flavonoids.
- e) Test for Tannins: To 0.5 ml of extract solution, 1 ml of distilled water and 1-2 drops of ferric chloride solution were added and observed for brownish green or a blue black coloration.

f) Test for Glycosides: 10 ml of 50%  $\text{H}_2\text{SO}_4$  was added to 1ml of extract in a boiling tube. The mixture was heated in boiling water for 5min. 10ml of Fehling's solution (5 ml of each solution A and B) was added and boiled. A brick red precipitate indicated presence of glycosides

g) Test for Phenols: Ferric Chloride Test: Extracts were treated with 3-4 drops of ferric chloride solution. Formation of bluish black colour indicates the presence of phenol.

h) Test for Steroids: 2 ml of acetic anhydride was added to extract and then 2 ml of  $\text{H}_2\text{SO}_4$  was added, the colour changes from violet to blue or green in samples extract indicates the presence of steroids.

i) Test for Anthraquinone: Powdered leaves of the plants was boiled with dilute sulphuric acid. Filtered and allowed to cool. Diluted ammonia is added to the filtrate which is extracted with chloroform or benzene. The ammonical layer turns from pink to red in the presence of anthraquinones derivative.

j) Test for Carbohydrate: A few drops of Molischs solution was added to 2 mL of aqueous solution of the extract, thereafter a small volume of concentrated sulphuric acid was allowed to run down the side of the test tube to form a layer without shaking. The interface was observed for a purple colour as indicative of positive for carbohydrates.

## RESULTS

### Plant Identification and Review

Twelve plants were identified as commonly used for the treatment of diabetes. The plants include: *Andrographis paniculata*, *Azadirachta indica*, *Persea americana* Mill, *Vernonia amygdalina* Delile, *Blighia unijugata* L., *Catharanthus roseus* (L.) G. Don, *Loranthus micranthus*, *Momordica charantia*, *Bridellia feruginea*, *Trigonella foenum-graecum*, *Gongronema*

*latifolium* (Benth), *Carthamus tinctorius* (Table 1). The qualitative phytochemical

screening of the plants are presented in Table 2 below.

**Table 1: Plants used in Folk Medicine for Treatment of Diabetes in Ebonyi State, Phytochemicals and other Uses**

Picture	Phytochemicals and Uses
	<p>Phytochemical Constituent: glycosides, saponins, tannins and alkaloids            Common Name: Bitter weed, King of Bitters, create            Local Name: ewe korobi-jogbo in Yoruba, meje-meje in Igbo            Part Used: Whole Plant            Location found: Okposi            Other uses: antihepatitic, antihepatotoxic, antibiotic, antimalarial, anti-HIV, antithrombogenic, antiinflammatory and antipyretic</p>
<p><i>Andrographis paniculata</i> Family: Acanthaceae</p>	
	<p>Phytochemical Constituent: Alkaloids, Flavonoids, Saponins, reducing sugar            Common Name: Neem            Local Name: Dongoyaro in Yoruba, Ogwonnuoria in Igbo            Part Used: Leave, Bark            Location found: Uburu, Okposi            Other uses: leprosy, eye disorders, bloody nose, intestinal worms, stomach upset, loss of appetite, skin ulcers, diseases of the heart</p>
<p><i>Azadirachta indica</i> Family: Meliaceae</p>	



***Persea americana* Mill**  
Family: Lauraceae

Phytochemical Constituent: saponins, phenols, tannins, flavonoids, alkaloids, steroids, and glycosides

Common Name: Avocado

Local Name: Ube bekee in Igbo, Igba in Yoruba

Part Used: Seed, Leave

Location found: Okposi, Oshiri

Other uses: diarrhea, dysentery caused by helminths and amoebas, toothache, intestinal worms, diabetes, skin rashes, infectious processes caused by fungi and bacteria, asthma, high blood pressure and rheumatism, malaria and typhoid fever; to lower high blood cholesterol, to stimulate uterine contractions and to ease painful menstruations.



***Vernonia amygdalina* Delile**  
Family: Asteraceae

Phytochemical Constituent: alkaloids, tannins, flavonoids, saponins, triterpenoids, steroids, cardiac glycosides, and reducing sugar

Common Name: Bitter Leave

Local Name: Ewuro (Yoruba), Shuwaka (Hausa), Onugbo (Igbo)

Part Used: Leave

Location found: Okposi, Uburu

Other uses: treat fever, malaria, diarrhoea, dysentery, hepatitis and cough, as a laxative, fertility inducer. They are also used as a medicine for scabies, headache and stomach-ache



***Blighia unijugata* L.**  
Family: Sapindaceae

Phytochemical Constituent: tannins, saponins, flavonoids, cardiac glycosides and anthraquinones

Common Name: Triangle-tops

Local Name: Ako-isin in Yoruba, Okpu ulla in Igbo, Gwanja-kusa in Hausa

Part Used: Root, bark, leaf

Location found: Item- Ikwo

Other Uses: rheumatism, kidney pain and stiffness.





***Catharanthus roseus* (L.) G. Don**  
Family: Apocynaceae

Phytochemical Constituent: alkaloids, phenols, saponins, tannins, terpenoids, steroids, flavonoids

Common Name: Madagascar-Periwinkle (C)

Local Name: Iyere in Yoruba, Oziza in Igbo

Part Used: Whole plants

Location found: Oshiri, Ugwulangwu

Other Uses: sedative, analgesic, rheumatism, kidney pain and stiffness



***Loranthus micranthus***  
Family: Loranthaceae

Phytochemical Constituent: tannins, alkaloids, steroids and terpenoids

Common Name: Mistletoe

Local Name: Ogbuotele/ egbu nkita in Igbo

Part Used: Leaf

Location found: Agubia Ikwo

Other Uses: high blood pressure (BP) and gastrointestinal, neuroprotective, tranquilizing, anticancer, immunomodulatory, antiviral, diuretic and hypotensive agent, wound healing, gerontological effects



***Momordica charantia***

Phytochemical Constituent: terpenoids and saponins, reducing sugar, proteins, flavonoids and phenolic

Common Name: Balsam pear, bitter gourd, bitter melon, karela, wild cucumber and bitter cucumber.

Local Name: Kakayi /Okwunuolo in Igbo, Daddasu (Hausa) and Ejirin (Yoruba)

Part Used: Fruits and Leaves

Location found: Uburu, Oshiri, Ugwulangwu

Other Uses: womb infections, malaria, dysentery, and worm infections, treatment of gonorrhoea, Jaundice and other liver diseases,



Family: Cucurbitaceae



***Bridellia feruginea***

Family: Euphorbiaceae

cure ulcers and burns, measles, chicken pox, scabies and malaria, colds, fevers, rhinitis, pneumonia, toothaches and mouth infections, measles, hepatitis.

Phytochemical Constituent: alkaloids, flavonoids, tannin, glycosides, anthraquinone, and saponins

Local Name: Kirni, Kimi (Hausa), Maren (Fulani), Iralodan (Yoruba), and Oha, Ede, Ola in Igbo.

Part Used: leaf, stem bark, and root

Location found: Item-Ikwo

Other uses: Arthritis and boils, to prevent pregnancy, to cause labor, for malaria, AIDS/HIV, anemia, asthma, cancer, colic, cough, diabetes, diarrhea, enlarged spleen, gonorrhea, hernia, joint pain, menstruation that is abnormal or painful, stomachaches and other stomach problems, syphilis, thrush, to kill parasites, urinary tract infections, yellow fever, yellow skin discoloration (jaundice), as an insecticide, and as a strong laxative.



***Trigonella foenum-graecum***

Family: Fabaceae

Phytochemical Constituent: Alkaloids, flavonoids, steroids, tannins, free amino acid, saponins.

Common Name: Fenugreek seed, sicklefruit fenugreek, Goat's Horn, Greek Clover, Greek Hayseed.

Local Name: Mkpur oka oyibo in Igbo, Kimba in Hausa, Eru in Yoruba

Part Used: Seed, Leaf

Location found: Uburu

Other uses: respiratory infections (bronchitis and pneumonia), reduce fever, ease childbirth and to increase milk flow, stomach problems, Abscesses, Anemia, Asthma, Boils, Body Odour, Bronchitis, cancer, Eyes/swollen, Fevers, Gallbladder Problems, Heartburn, Inflammation, Sinus Problems, Ulcers.



***Gongronema latifolium* (Benth)**

Family: Asclepeadaceae

Phytochemical Constituent: Flavonoids, saponins, alkaloids, sterol  
Common Name: Bush buck (C)  
Local Name: Utazi in Igbo, Arokeke in Yoruba  
Part Used: Leaves and stem  
Location found: Okposi, Uburu, Oshiri  
Other Uses: Digestive problems, such as loss of appetite, dyspepsia, colic and stomachache, constipation, dysentery and intestinal worms.



***Carthamus tinctorius***

Family: Asteraceae

Phytochemical Constituent: Tannin, phenolics, flavonoids, alkaloids  
Common Name: Safflower  
Local Name: Nsi igwurube in Igbo  
Part Used: Leaf, flower and seed  
Location found: Oshiri, Onicha, Isu  
Other uses: dysmenorrhea, amenorrhea, postpartum abdominal pain and mass, trauma and pain of joints, preventing heart disease, including “hardening of the arteries” (atherosclerosis) and stroke.

**Table 2: Qualitative Evaluation of the Phytochemical Composition of Antidiabetics Plants Used in Ebonyi State**

S/N	Plants	Phytochemical constituents									
		Tannins	Phenols	Flavonoids	Saponins	Steroids	Alkaloid	Terpenoids	Glycoside	Antraquinone	Carbohydrate
1	<i>Andrographis paniculata</i>	+	+	++	+	+	++	-	-	-	-
2	<i>Azadirachta indica</i>	++	+++	+	++	+	++	+	+	-	+
3	<i>Persea americana Mill</i>	++	++	+++	+	+	-	+	+	-	-
4	<i>Vernonia amygdalina Delile</i>	++	-	++	++	+	+	-	+	+	-
5	<i>Blighia unijugata L</i>	+	+	++	+	+	++	-	-	-	-
6	<i>Catharanthus roseus (L.) G. Don</i>	++	-	++	++	+	+	-	+	+	-
7	<i>Loranthus micranthus</i>	+	-	+	+	-	++	-	+	-	+
8	<i>Momordica charantia</i>	+	+	++	+	+	++	-	-	-	-
9	<i>Bridellia feruginea</i>	++	+++	+	++	+	++	+	+	-	+
10	<i>Trigonella foenum-graecum</i>	++	+++	+	++	+	++	+	+	-	+
11	<i>Gongronema latifolium (Benth)</i>	+	+	++	+	+	++	-	-	-	-
12	<i>Carthamus tinctoriu</i>	++	-	++	++	+	+	-	+	+	-

+++ : Highly present, +: Moderately present +: Slightly present

## DISCUSSION

The use of herbs by locals in Ebonyi state for the treatment of diabetes is predated to centuries. Significant therapeutic outcome have been recoded but little information have been documented scientifically to justify their use/ folk claims. This discussion tried to compare the phytochemicals constituent of the plants to the bioactivity exhibited by the plants in the management of diabetics.

### *Andrographis paniculata*

The study conducted by Forbes *et al.*,<sup>(12)</sup> acknowledged *Andrographis paniculata*, as 'King of Bitters' due to its very bitter chemical constituent of kalmeghin and andrographolide; and its native to Asia (India and China). Phytochemical analysis of the plants leave, which is commonly used in ethnomedicine contain flavonoid glycosides, diterpene, lactones, glycosides, flavonoids

and diterpenoids (Andrographolide)<sup>(13)</sup>. Chao and Lin,<sup>(14)</sup> reported that Andrographolide constitute 1.2%, 4% and 6% content of dried stem, whole plant and the plant leaf extracts. Other types of diterpenoids that have been isolated from the plant are 14-deoxy-11, 12-didehydroandrographide, deoxyandrographolide, isoandrographolide, rebaudioside and neoandrographolide<sup>(15)</sup>. Saravanan *et al.*,<sup>(16)</sup> reported that rebaudioside has antihyperglycemic effect on diabetic rats. The mechanism of this bioactive diterpenoids act by up-regulating the activities of hepatic enzymes responsible for the metabolism of carbohydrates. This result in antihyperglycemic activity with strong insulin-secreting effect in specific pancreatic cell lines expressing insulin and glucokinase<sup>(17)</sup>. With these bioactive



constituents, the plant has been reported to have potency against chancre, syphilis, diabetes, tonsillitis, gonorrhoea, eczema, typhoid fever, diphtheria, common cold, epilepsy, depurative and dandruff<sup>(18)</sup>. Other medicinal properties associated with *Andropogon paniculatus* include: antimicrobial, hepatoprotective and antiparasitic effects, maintaining systolic blood pressure and treatment of liver ailments<sup>(19)</sup>. Further study of this plant showed that it's safe and effective clinically under controlled study in reducing symptoms of uncomplicated upper respiratory tract infections<sup>(20)</sup>. These findings give justification for its use in ethnomedicine.

#### ***Azadirachta indica* (Neem)**

*Azadirachta indica* popularly called Neem, is of the family of Meliaceae. Various studies have established its medicinal and biopesticide efficacy<sup>(21)</sup>. The plant is predominant in Asia, Africa and Europe continents<sup>(22)</sup>. For better medicinal value, new leaves and flowers emerged in March and April<sup>(23)</sup>. The leaves majorly contain Azadirachtin as bioactive constituent, which has antifungal, antiviral, insecticidal and antibacterial properties<sup>(24)</sup>. Other bioactives isolated from Neem oil as reported by various studies include: nimbolides meliacin, nimbidin, gedunin, nimbin, salannin, and valassin while the seed was said to contain tignic acid<sup>(25)</sup>. Further assessment of Neem showed that the kernels contain 30-50 percent oil, which is used in insecticide and soap production while triterpenes also called limnoids is used in pharmaceuticals industries<sup>(26)</sup>. However, 4 types of limnoids are commonly used in insecticidal and pesticidal production, they include meliantriol, azadirachtin, nimbin and salannin<sup>(27)</sup>. Oil extracts are the most often utilized form of Neem, and phytochemical study has verified the presence of substantial

levels of triterpenes, flavonoids, and saponins, while other components like catechins and nimbins appear to be present in smaller concentrations<sup>(28, 29)</sup>. Limonoids, tannins, alkaloids, terpenoids, reducing sugar, catechins, sterols, and gallic acid are among the other metabolites discovered in Neem extracts<sup>(28, 29, 30, and 31)</sup>. Several studies on the hypoglycemic effect of neem in animals have been conducted around the world, most commonly using rats and mice, and all of the findings have shown a substantial antidiabetic activity<sup>(32, 33, 34, and 35)</sup>. A study conducted by Akinola *et al.*<sup>(32)</sup> showed that lesions in pancreatic islet cells improved when treated with Neem while that of Shraavan *et al.*,<sup>(36)</sup> showed that on administering of 250mg/kg (single dosage trial) consistently for 15 days in diabetic rats, there were significant reduction in urea (13%), cholesterol (15%), glucose (18%), creatinine (23%), and triglycerides (32%), while lipids reduced by 15% after 24-hour treatment period than the control group.

#### ***Persea americana* MILL**

*Persea americana* commonly called Avocado is a dicotyledonous plant in the family of Lauraceae found globally. Its fruits makes it one of the few economically important *Persea* species<sup>(37)</sup>. Its fruits are pyriform to spherical in shape and can weigh up to 2.3 kg<sup>(38)</sup>. The oil extracted from Avocado using cold-press method are mainly monounsaturated fat and its quantity varies depending on the variety and the length of time<sup>(39)</sup>. The plant possesses a lot of vital and active phytochemical constituents such as terpenoid, glycosides, alkanols, flavonoids, coumarin (aliphatic acetogenins)<sup>(40, 41)</sup>. The study conducted by Oberlies *et al.*<sup>(42)</sup> identified moderately cytotoxic compounds against cancer cell lines from its unripe fruits such as 1,2,4-trihydroxyheptadec-16-ene, 1,2,4 trihydroxynonadecane and 1,2,4-

trihydroxyheptadec-16-yne. The study conducted by Anita *et al.*,<sup>(43)</sup> showed that single dosage administration of the aqueous leaf extract of the plant had  $60.02 \pm 6.83\%$  drop in blood glucose level after 6hrs observation resulted into hypoglycemic effects in normal rats. This finding was further supported by the studies conducted by Zdychova and Komers,<sup>(44)</sup> Lima *et al.*,<sup>(45)</sup> and Marrero-Faz,<sup>(46)</sup>.

### ***Vernonia amygdalina* DELILE**

*Vernonia amygdalina* (VA) commonly called bitter leave is found in the wild in most tropical African countries while some cultivates it as vegetable including Nigeria<sup>(47)</sup>. Proximate analysis of the plant showed that it is rich in protein (62.2%), crude carbohydrate (22%), ash (9.95%), crude fiber (16%), and crude fat (3.45%)<sup>(48)</sup>. Yeap *et al.*<sup>(47)</sup> reported significant concentration of chlorine, copper, ferum, potassium, manganese, nickel, sodium, sulphur<sup>(47)</sup>, phosphorus, calcium, potassium, magnesium, zinc, iron, and several vitamins such as Vitamin A, C, and E have also been reported<sup>(48)</sup>. Phytochemical analysis of bitter leave revealed the presence of saponins, phenolics, tannins, alkaloids, terpenes, steroidal, sesquiterpene lactones, flavonoids, triterpenoids, steroids, and cardiac glycosides<sup>(49, 50, and 51)</sup>. For the management of diabetes, the fresh leaves of *Vernonia amygdalina* are mainly crushed and squeezed to extract the exudates, then it's consumed as drink. This has been shown to have effective and safe medication for diabetes control<sup>(52)</sup>. The study conducted by Atangwho *et al.*<sup>(53)</sup> for the period of 14 days showed that on administration of 200 mg/kg, 400 mg/kg, and metformin to streptozotocin-induced diabetic rat models, hypoglycemia of significant low glucose level was observed. He explained that this could only be possible by inhibiting gluconeogenesis while also potentiating

glucose oxidation via the pentose phosphate route. However, Edet *et al.*,<sup>(54)</sup> study showed that on administration of *Vernonia amygdalina* there exist an increased pancreas cell mass production and increased proliferation of the cells of the pancreatic islets of Langerhans, as evidenced by the RNA content of the post mitochondrial supernatant and entire homogenate produced by pancreas fractionation. The anti-diabetic impact of a combination of metformin (50 mg/kg) and aqueous extracts of VA leaf (100 mg/kg) suggested that the aqueous leaf extract and metformin were effective, additive, and safe in the treatment of diabetes mellitus. Several published investigations have verified the blood sugar reducing effect of VA leaf<sup>(55)</sup>.

### ***Blighia unijugata***

*Blighia unijugata* (Baker) is a forest trees widely spread in Tropical Africa. Locally, it's used in the treatment of rheumatism, diabetics, cardiovascular diseases, dysentery, yellow fever and epilepsy. Also, the pods, roots and leaves are used for their anthelmintic, hemostatic and tonic properties. Mineral analysis of the fresh leaves of *Blighia unijugata* according to Offor *et al.*,<sup>(56)</sup> contain higher concentrations (mg/100g) of calcium ( $66.20 \pm 0.01$ ), potassium ( $62.12 \pm 0.02$ ), magnesium ( $60.20 \pm 0.09$ ), phosphorus ( $33.72 \pm 0.02$ ), iron ( $22.44 \pm 0.01$ ), sodium ( $14.33 \pm 0.02$ ), zinc ( $12.47 \pm 0.03$ ) and manganese ( $2.15 \pm 0.01$ )<sup>(56)</sup>. These minerals according to Speich,<sup>(57)</sup> assists the diabetics patients in better oxygen transport, muscle contraction, normal heart rhythm, bone health, pains relieve, enzyme activation, nerve impulse conduction, immune functions, and acid- base balance of the blood. Phytochemical analysis study by Oloyede *et al.*,<sup>(58)</sup> revealed that the plant has pentadecanoic acid (14-methyl-, methyl ester) (38.34%) in abundant, followed by

carbonic acid, propyl-en-2-yl undecylpropyl ester (36.79%), and 9-octadecanoic acid (Z)-methyl ester (24.86%). Other chemical compound found in abundant in stem bark was 1, 3-dimethoxybenzene (79.01%) while the root contained limonene (20.51%), *trans*-13-octadecanoic acid (16.74 %), and *cis*-vaccenic acid (9.50%). Their study further revealed that *B. unijugata* root had 83.96% inhibition at 100 mg/ml, better than  $\alpha$ -tocopherol when tested for antioxidant activity. Other phytochemicals were glycosides, saponins, pentacyclic triterpenoids friedelin, tannins, and epifriedelinol<sup>(59)</sup>. The plant antimicrobial activity testing revealed activity against *S. aureus*, *C. albicans* and *M. gypseum*<sup>(59)</sup>. The study conducted by Ojo *et al.*,<sup>(60)</sup> revealed that *B. unijugata* has glucose-reducing power, radical scavenging and iron chelation ability. This was possible by high production of  $\alpha$ -amylase and  $\alpha$ -glucosidase inhibitory activities<sup>(60)</sup>. These bioactive constitute probably justify its use in folk medicine as antidiabetic plant.

#### ***Catharantus roseus* (L.) G. DON**

*Catharantus roseus* (Madagascar periwinkle) is native to Madagascar and it's commonly used as ornamental perennial herb<sup>(61)</sup>. Phytochemical analysis of the plant showed that it contain wide spectrum of alkaloids including heterocyclic (pyrrolizidine, pyrrole, pyridine, quinolone, piperidine, norlupinane, isoquinoline or indole) and non-heterocyclic once (cathinone, ephedrine and colchicine)<sup>(62)</sup>. These vast composition of bioactive chemicals might be the scientific bases for its leaves and flowers been used as antidiabetics, as experimental evaluation showed their ability to reduce blood glucose levels by 20%, 49% and 58% in diabetic rats using water, dichloromethane and methanol extracts respectively<sup>(63)</sup>. The study conducted by Singh *et al.*,<sup>(64)</sup> observed also a

sudden increase in hypoglycemic enzymes due to increased glucose consumption in the liver. Another study conducted by Jayanthi,<sup>(65)</sup> further showed that on administration of 500 mg/kg body weight of the plant using dichloromethane and methanol extracts in the ratio 1:1 for 20 days, there were significant decrease in blood glucose, urea and cholesterol levels. Also, hexokinase activity increased, but glucose-6 phosphatase and fructose 1,6-biphosphatase activity fell considerably.

#### ***Loranthus micranthus***

Assessment of the antidiabetic activity of the methanolic extracts of *L. micranthus* leaves parasiting on *P. americana*, *B. nitida*, *K. acuminata*, *P. macrophylla*, and *A. indica* by Osadebe *et al.*,<sup>(66)</sup> showed that 400 mg/kg *L. micranthus* possesses significant dose-dependent antihyperglycemic effects in alloxan-induced diabetic albino and normoglycemic rats respectively. This dose was observed to produces highest activity of 82.59% reduction of blood sugar level after 24 h administration and evaluated by o-toluidine spectrophotometric method which is statistically comparable with glibenclamide used as positive control that had 83.34% reduction of blood sugar level after 24 h administration. Further reports by Osadebe *et al.*,<sup>(66)</sup> showed that the plant from different host trees had no acute toxicity at LD50 values of 11650, 11650, 5900, 5900, and 5900 mg/kg. The leaves of *L. micranthus* parasitic on *K. acuminata*, *A. indica*, and *B. nitida* showed more significant antihyperglycemic activity among the other host trees investigated. Their results demonstrated that the antidiabetic effect of the extract was found to be dependent on the host plant species and the best season of harvest for effective antidiabetic activity is at the peak of the rainy season. Their findings revealed 39.2% and 47.5% fasting blood



sugar reduction after 6 hours consumption of 400 mg/kg for April and July samples, respectively, with 8.3% difference due to effect of seasonal variation on chemical content of leaves. Higher concentration for flavonoids in peak of the rainy season compared to the onset of rainy season could be responsible for the observed higher anti-diabetic activity in July. Another study conducted by Uzochukwu *et al.*,<sup>(67)</sup> further revealed that even 200 mg/kg of the plant harvested from *K. acuminata* had significant antidiabetic activity within three hours of administration against alloxan-induced diabetic rats.

#### ***Momordica charantia***

*Momordica charantia* (also called bitter melon (BM) or bitter guard) is a plant that is used as food and natural medicine. *Momordica* extract contains phenolic components such as epicatechin, catechin, gentisic acid, chlorogenic acid, and gallic acid<sup>(68)</sup>. *Momordica charantia* are commonly found in the tropics. Phytochemical studies showed the presence of steroids, proteins, flavonoids, alkaloids, triterpenes, saponins and acids<sup>(69)</sup>. Due to these wide spectrum of phytochemicals, the plant has anti-fertility, anti-tumor, anti-fungal, anti-cancer, anti-bacterial, anti-parasitic, antiviral and hypoglycaemic characteristics<sup>(70)</sup>. According to Liu *et al.*,<sup>(71)</sup> minerals such as potassium, sodium, calcium, phosphorus, and magnesium are abundant in BM, especially in the fruit and leaves. The seeds are the finest natural suppliers of chromium, with 5.65 mg/100g, and zinc, with 45.45 mg/100g. Fruits and leaves are used to treat a variety of ailments in traditional medicine, including gout, diabetes, rheumatism, worms, colic, liver and spleen disorders. According to Chekka & Mantipelly.,<sup>(72)</sup> the plant contains among its phytochemicals *Momordica*, which is made

up of alkaloids and peptides that are similar to insulin and also charantin, a group of steroidal saponins, which gives it hypoglycaemic properties<sup>(73)</sup>. All parts of the plant, including the fruits, contain the bitter chemical called *Momordica*, made up of two saponin families (oleanane and cucurbitane-type triterpenoids), plant insulin (a polypeptide found in nature), vicine, karavilosides, and glycosides, which has a highly bitter flavor<sup>(74, 75)</sup>. These substances stimulate glucose absorption and glycogen synthesis in the liver, muscles, and fat cells, hence regulating blood sugar and acting as hypoglycaemic agents<sup>(76)</sup>. TP-Insulin, a polypeptide found in fruits and seeds, reduces and normalizes blood sugar levels in rats. Bitter melon contains a bioactive molecule called lectin, which has insulin-like action. It connects the two insulin receptors and mimics the action of insulin. Lectin decreases blood glucose levels by acting on peripheral tissues having insulin-like action. The alcoholic extract of charantin, which is made up of mixed steroids, is a powerful hypoglycaemic drug that is used to treat diabetes and reduce blood sugar levels. The bitter melon fruit enhances the insulin action by increasing glucose absorption in cells via stimulating insulin release. Fresh and dried fruit extracts reduced blood sugar levels in diabetic mice. Bitter gourd extracts show hypoglycaemic, anti-diabetic, hypolipidemic, and hepato-renal protective actions in alloxan-induced diabetic rats. Bitter melon reduces capillary permeability at the arteriolar and capillary level, which helps to prevent microvascular dysfunction, a frequent diabetes consequence. Charantin, one of the hypoglycaemic chemicals, is a steroidal saponin made up of a 1:1 combination of sitosteroyl glucoside and stigmasteryl glucoside. When delivered orally or intravenously to rabbits, charantin

causes hypoglycemia <sup>(77)</sup>. Another hypoglycaemic agent of bitter guard is P-insulin, a polypeptide of 166 amino acids and a molecular weight of roughly 11,000 Da. Polypeptide-pZnCl<sub>2</sub> has been shown in clinical tests to have a blood sugar reducing effect. When given intraperitoneally, vicine, a pyrimidine nucleoside found in seeds and fruits, can cause hypoglycemia in rats. Momordica extracts high in charantin improve insulin sensitivity in type 2 diabetics <sup>(78)</sup>.

### ***Bridelia ferruginea***

*Bridelia ferruginea* (Euphorbiaceae) is a shrub commonly growing up to a height of 45 feet in the Savannah or in open spaces of coastal districts. Bark, roots, fruits and leaves are used mainly as decoctions in tradomedicine. It's used in the treatment of thrush and type 2 diabetics. The study conducted by Batomayena *et al.*,<sup>(79)</sup> showed that 50mg/kg of leaf extract of *Bridelia ferruginea* exhibited significant hypoglycaemic, hepatoprotective and kidney function restoration ability when tested on fructose drinking mice. This might be attributed to the presence of good phytochemicals such as terpenoids, saponins, tannin, flavonoids, alkaloids and catechol present in the plant.

### ***Trigonella foenum-graecum* L. (Fenugreek)**

*Trigonella foenum-graecum* L. popularly known as Fenugreek is a medicinal herb in the Leguminosae (Fabaceae) family <sup>(80)</sup>. The fresh and dried leaves, and seeds are used as vegetable, spice, and medicinal legume plant in many parts of the world. The eating of leaves is increasingly becoming popular due to its reported ability to stabilize insulin, diabetes symptoms, hemoglobin levels and blood sugar <sup>(81)</sup>.

Proximate analysis of the plant leaves showed the presence of moisture (86.1%),

carbohydrate (6.4%), protein (4.4%), mineral (1.5%), fiber (1.1%), fat (0.9%) while the seeds had 44.1, 26.2, 5.8, 7.2, and 13.7 percent for carbohydrate, protein, fat, fiber, and moisture, respectively. Minerals (Ca, P, Fe, Zn, and Mn) and vitamins (A, B1, C, and nicotinic acid) are abundant in fenugreek <sup>(82)</sup>. Fresh 100g fenugreek leaves contain 220.97mg ascorbic acid and 19mg -carotene, according to Meghwal and Goswami <sup>(83)</sup>, whereas Srinivasan <sup>(84)</sup> reported vitamin C, -carotene, thiamine, riboflavin, nicotinic acid, and folic acid amounts of 52mg, 2.3mg, 40g, 310g, 800g, 0 (zero).

Phytochemical screen showed the presence of flavonoids, polysaccharides, saponins, amino acids, fatty acids, vitamins, saponins, fixed oils, and many identified alkaloids <sup>(84)</sup>. Homorientin saponaretin, disogenin, neogigogenin, neogitogenin, gitogenin and trigogenin are among the chemicals found in *Trigonella foenum-graecum* L. <sup>(85, 86)</sup>.

Dietary fiber has long been recognized as having considerable health benefits for diabetics. Although the action mechanism of Fenugreek in humans is uncertain, animal studies have indicated that dietary fiber can delay stomach emptying, diminish gastric inhibitory peptide synthesis, and insulinotropic hormone production <sup>(87)</sup>. Various studies have substantiated the hypoglycemic and hypocholesterolemic effect of Fenugreek seeds in rats <sup>(88)</sup>, mice <sup>(89)</sup>, rabbits <sup>(90)</sup>, and dogs <sup>(91)</sup>. The study conducted by Srinivasan *et al.*, <sup>(87)</sup>, showed that herbal formulation from Fenugreek seed had high effect on people with moderate and severe diabetes conditions by improving diabetes and suppressed glycosuria. Trigonelline was suggested to be the bioactive substance in Fenugreek, however, the study conducted by the National Institute of Nutrition of India further justified the findings of Srinivasan *et al.*, <sup>(87)</sup>, as fenugreek had therapeutic efficacy

on animals with both type-1 and type-2 diabetes. Fractionate from Fenugreek seed (4-hydroxyisoleucine) has been reported to show anti-diabetic effects through improving insulin absorption. This was evident in the study by Das *et al.*,<sup>(92)</sup> who reported that soluble fenugreek fibre of 25g in daily meal of diabetes patients had a significant impact on the reduction of glycemic index.

### ***Gongronema latifolium***

*Gongronema latifolium*, generally called “utazi” in Igbo and “arokeke” in Yoruba communities in Nigeria, is native to south eastern, Nigeria<sup>(93)</sup>. *G. latifolium* has been widely used in folk medicine as a spice and vegetable and for maintaining healthy blood glucose levels<sup>(93)</sup>. Ugochukwu *et al.*<sup>(94)</sup> documented the ethno-medical usage of this plant in managing diabetes mellitus. From various studies, the plant has been discovered to exhibit hypolipidemic, normoglycemic and antioxidative activities, however, dosage in herbal formulation has remained a problem<sup>(95)</sup>. Experimental studies by Ogundipe *et al.*,<sup>(96)</sup> and Ajiboye *et al.*,<sup>(97)</sup> both documented the hypoglycemic, hypolipidemic, antioxidative and related gene expressions of aqueous extract of *Gongronema latifolium* leaf in alloxan-induced diabetic rats. While Morebise *et al.*<sup>(93)</sup> demonstrated its anti-inflammatory properties. All the studies acknowledged that the presence of significant phytochemicals such as saponins (asterglycosides), flavonoids, glycosides, essential oil, alkaloids<sup>(98)</sup> as well as vitamins, proteins, fatty acid and minerals like calcium, phosphorus, magnesium, copper and potassium<sup>(99)</sup> contributed to the active observed in the plant.

### ***Carthamus tinctorius* (Safflower)**

The safflower (*Carthamus tinctorius* L.) is a member of the Compositae or Asteraceae family of plants<sup>(100)</sup>. It is mostly produced for the seed, which is used as an edible oil or

birdseed, or for the flowers, which are used as sources of dye or medicinal purposes<sup>(101, 102, 103, and 104)</sup>. The plant contain significant concentration of poly unsaturated fatty acid (PUFA), vitamin A, phosphate, calcium and iron<sup>(105)</sup>. Aqueous extract of Safflower has proven to restore abnormalities associated with alloxan-induced diabetic metabolic, as it exhibited hypolipidemic activity effect at 200 mg/kg and 300 mg/kg dosages when compared to the diabetes control group and resolved complications associated with atherosclerosis or hyperlipidemia in diabetes rats<sup>(106)</sup>. Its flowers have also been shown to regenerate and replenish Langerhan islets, causing insulin levels to rise. When safflower is ingested, the beta cells of the Langerhans islets release more insulin. In diabetic rats' livers, it also has the capacity to repair protein breakdown and enhance glycogenesis<sup>(106)</sup>. Qazi *et al.*,<sup>(107)</sup> observed that insulin levels in *Carthamus tinctorius*-treated groups were significantly higher than in diabetes control groups. The study conducted by Takahashi and Miyazawa,<sup>(108)</sup> showed that safflower seed has active -glucosidase inhibitory activity and this property has been identified in its serotonin derivatives (N-p-coumaroyl serotonin and N-feruloyl serotonin). The 50% inhibitory concentration values for these substances were determined to be 47.2 mol/L and 99.8 mol/L, respectively, while the 50% inhibitory concentration values for the reference medications (acarbose and 1-deoxynojirimycin) were assessed to be 907.5 mol/L and 278.0 mol/L, respectively. The presence of a hydroxyl group at the 5-position in the serotonin moiety, as well as the coupling of cinnamic acid and serotonin, were essential in the structure of the serotonin derivative for -glucosidase inhibitory effects.



## CONCLUSION AND RECOMMENDATION

This study identified possible candidate plants that could be compounded/formulated as drugs for the treatment of diabetes, as they are commonly used for the treatment of diabetes in Ebonyi state. The phytochemical assay observed in this study correlated with other studies and justifies reasons for its use in ethnomedicine. Therefore, further studies are required in formulation, dose, pharmacological evaluation, synergistic assessment and clinical trials. This will go a long way in controlling crude methods of herbal consumption and also proffer better and more effective novel drugs for the treatment of diabetes.

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