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*Review paper*

# The Role of Medicinal Plants in Management of Diabetes Mellitus

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**Diabetes Mellitus is a group of metabolic disorder that results in hyperglycemia due to decrease insulin production or inefficient insulin utilization. Based on World Health Organization (WHO) recommendation, diabetes mellitus is classified into three major subtypes: type 1 (insulin dependent diabetes mellitus), type 2 (non-insulin dependent diabetes mellitus NIDDM) and gestational diabetes (diabetes that develop when a woman is pregnant). Diabetes as a metabolic disorder have several marketed medications to alleviate its symptoms. However, this over the counter drugs/antidiabetics are expensive with its associated side effects. Medicinal plants are gaining importance in the management of Diabetes Mellitus as they are cost effective and also displays improved therapeutic effects with lesser side effects. The use of *Irvingia grandifolia* has been found to be efficacious in the management of the disease but the effect of this herb on plasma urea, creatinine concentrations and white blood cell count has not been characterized so far. The effect was investigated and found out that there is no pronounced effect of the herb on plasma creatinine concentration based on student distribution (t-test). Also, there is no significant effect on plasma urea concentration, white blood cell count (total and differential) also found from student distribution (t-test) after comparing treated animals with control animals.**

**Key words:** Diabetes Mellitus, Antidiabetics, Medicinal Plants, Hyperglycemia, Hypoglycemia, Plasma urea, Plasma Creatinine, White cell count.

## INTRODUCTION

Diabetes Mellitus is a chronic disorder of carbohydrate, fat and protein metabolism characterized by fasting elevations of blood glucose levels and a greatly increased risk of heart disease, stroke, kidney disease and loss of nerve function. Also, Diabetes Mellitus occurs when the pancreas does not secret enough insulin or if the cells of the body become resistant to insulin, hence the blood glucose cannot get into the cells for utilization which then leads to serious complications. The symptoms of diabetes are frequent urination, excessive thirst, appetite, etc. Depending on the type (Leslie and Elliott, 1994).

Diabetes Mellitus is classified into two major categories: type 1 and type 2. Diabetes Mellitus is the most common chronic and metabolic disease characterized by an increase in blood glucose levels due to absolute or relative insulin deficiency. Early symptoms of Diabetes include Polyuria, Fatique, Weight loss, and increase in urine glucose levels. In the absence of proper treatment, Cardiac, Vascular, Neurologic, Renal damage and Neuropathy may occur. Treatment includes diet, exercise and finally Medications (Islam, et al, 2018).

Type 1 or insulin dependent diabetes mellitus occurs most often in children and adolescents. It is associated with complete destruction of the beta-cells of the pancreas which produce the hormone insulin. Type 1 patients required life-long insulin for the control of blood sugar levels. Although the exact cause of type 1 diabetes is unknown, current theories suggests, it is due to injury to the insulin producing beta-cells of the pancreas coupled with some defect in tissue regeneration capacity. Type 1 patients appears to have an autoimmune component at its origin as antibodies for beta-cells of the pancreas (Amiel, 1993). It is probable that the antibodies to the beta-cells

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develop in response to cell destruction due to chemical, viral, or food allergy.

Type 2 or non-insulin dependent diabetes mellitus patients have elevated levels of insulin but the utilization by the cells are poor indicating a loss of sensitivity to insulin by the cells of the body. Obesity is a major contributing factor to this loss of insulin sensitivity with approximately 90% of individual with type 2 diabetes being obese. Diet is of primary importance in the management of this disease and should be implemented diligently before a drug is used (Marshall et al, 1991).

Currently, the main and effective treatment for diabetes is the use of insulin and other hypoglycemic drugs but these compounds also have many adverse side effects. Medicinal plants have a long history of usage and today, they are being extensively used for various diseases including diabetes treatment (Jamshidi-kia, et al, 2018).
Generally, the use of medicinal plants in the management of diabetes mellitus proves to be useful and *Irvingia grandifolia* is one that has been found to be efficacious (Onoagbe et al, 1999); but the effect of this herb on plasma urea, creatinine concentrations, and white blood cell count has not been evaluated.

The plasma urea is the end product of protein metabolism in the liver and cleared by the renal glomerular of the kidney in urine while creatinine is a by-product of the breakdown of creatine an energy storage compound in muscle and eliminated by the kidney. Disease process like diabetes mellitus can create secondary renal injury and elevate serum creatinine concentration (Braun et al, 2003). White blood cells fight infections through a process known as phagocytosis. In response to an acute infection, trauma or inflammation, white blood cell release a substance called colony-stimulating factor (C.S.F.). Colony stimulating factor stimulates the bone marrow to increase white blood cell production.

Blood glucose concentrations at any time is determined by the balance between the amounts leaving the blood into tissues. Under normal conditions, the blood glucose concentration is strictly regulated and the blood glucose concentration is maintained between 80-120 mg/ dl (4.4-6.7) mMol/L in between meals.

Impaired insulin action result in chronic metabolic disorder of carbohydrate, protein and fat metabolism of which death may result. Long standing metabolic derangement has been associated with permanent irreversible functional and structural changes in the cells of the body. The structural and functional changes lead to the development of well-designed clinical presentation referred to as complications of diabetes mellitus; which includes: hypertension, neuropathy, retinopathy, nephropathy, cardiomyopathy, etc. (Barkis, 1993).

Hyperglycemia results when insulin level is low and there is lower transport of glucose into cells and reduced extracellular utilization of glucose. Increased glucose in the blood increases the osmotic pressure of the extracellular fluid causing withdrawal of water from cells. There is no curative treatment for diabetes mellitus but can be managed.

## LITERATURE REVIEW AND DISCUSSION

Diabetes mellitus is a chronic condition associated with abnormally high levels of glucose in the blood. This is a major endocrine disorder affecting nearly 10% of the population all over the world. This is a disorder of carbohydrate metabolism caused by inadequate production or utilization of insulin, the hormone secreted by beta-cells of the pancreas needed to convert sugar, starches and other foods into energy needed for daily life. As a result, glucose builds up in the bloodstream. Despite the introduction of hypoglycemic agents, diabetes and related complications, continue to be a major medical problem (Hers, 1999).

Based on World Health Organization (WHO) recommendation, diabetes mellitus is classified into three types: Type 1 diabetes (insulin dependent diabetes mellitus IDDM) is also called juvenile onset diabetes. Type 1 diabetes is an autoimmune disease (a condition arising from and directed against a person's own tissues) in which the pancreas produces little or no insulin. Individuals with type 1 diabetes must take insulin throughout their lives to manage their condition. This type of diabetes accounts for 5%-10% of all diabetic cases. Type 2 diabetes (non-insulin dependent diabetes mellitus NIDDM) is also called adult-onset diabetes. Type 2 diabetes is a metabolic disorder resulting from the body's inability to properly use insulin. It occurs most frequently in people who are overweight, inactive and older than 40 years of age. Most people with type 2 diabetes do not need to take insulin to manage their condition and this accounts for 90% of all diabetic cases. Gestational diabetes is a type of diabetes that can develop when a woman is pregnant. Towards the end of a pregnancy (usually the third trimester) a woman may have higher than normal levels of glucose in her blood stream. One percent of all pregnant women develop gestational diabetes although it usually disappears after delivery, but the mother is at the risk of developing type 2 diabetes later in life (Takeshi et al, 2002).

## SIGNS AND SYMPTOMS

### Type 1 diabetes

While production of insulin diminishes gradually over a matter of years, the signs and symptoms of type 1 diabetes tend to appear abruptly, once 80% - 90% of the pancreatic cells can no longer make insulin. The signs and symptoms include excessive urination, excessive intake of water, unintended weight loss over several days, high levels of Glucose in the blood and urine, nausea and vomiting,

abdominal pain or discomfort, weakness and excessive fatigue, dehydration, blurred vision, irritability, increased susceptibility to infection, ketoacidosis-a potentially fatal condition marked by an accumulation of ketones (chemicals that build up in the blood stream when the body is forced to burn fat instead of glucose) and increased acidity of the blood.

**Type 2 diabetes**

Type 2 diabetes usually develops in older, overweight individuals who become resistant to the effects of insulin over time. The pancreas is usually producing enough insulin but for unknown reasons the body cannot use the insulin effectively. Insulin resistance is a major concern for type 2 diabetes. Blood sugar control worsens as abnormal fat stores increase and obesity increases insulin resistance. People with type 2 diabetes often have no symptoms and their condition is detected only when a routine examination reveals high glucose level.

Occasionally however, a person with type 2 diabetes may experience few symptoms which tend to appear slowly over time. These symptoms are numbness or burning sensation of the feet, ankles and legs, poor vision, fatigue, poor wound healing.

In some cases, symptoms may mimic type 1 diabetes and appear more abruptly, these are excessive urination and thirst, whole body itching, coma -in severe cases, high blood glucose may affect water distribution in brain cells causing a state of deep unconsciousness (Aikinson and Maclaren, 1994).

**RISK FACTORS**

**Type 1 diabetes**

Family history of type 1 diabetes, mother who had pre-eclampsia (a condition characterized by a sharp increase in blood pressure during the third trimester of pregnancy), family history of autoimmune diseases including myasthenia gravis, pernicious anemia, viral infections during infancy and mumps, child of an older mother.

**Type 2 diabetes**

Family history of type 2 diabetes, age older than 40years, excess body fat particularly around the waist. Sedentary lifestyle and high calorie diet, abnormal levels of triglycerides in the blood, high blood pressure (Aikinson and Maclaren, 1994).

**CAUSES OF DIABETES**

**Genetic considerations**.

Although genetics appear important in susceptibility to diabetes, environmental factors are important in its induction. A diet high in refined sugar, fiber-depleted carbohydrate is believed to be diabetogenic in susceptible phenotypes while a high intake of high fiber, complex carbohydrate-rich foods is protective. Obesity is another significant environmental factor as 90% of non- insulin dependent diabetes mellitus types are obese. Even in normal individuals, significant weight gain results in carbohydrate intolerance, higher insulin levels and insulin insensitivity in fat and muscle tissues. The progressive development of insulin insensitivity is believed to be the underlying factor in the genesis of non-insulin dependent diabetes mellitus (NIDDM). Weight loss alone can correct all of these abnormalities and either significantly improves the metabolic disturbances of diabetes mellitus or converts overt diabetes into sub- clinical diabetes (Campbell and Carlson, 1993).

**ETIOLOGICAL FACTORS IN INSULIN DEPENDENT DIABETES MELLITUS (IDDM)**

Insulin dependent diabetes mellitus is generally recognized to be due to an insulin deficiency. Although the exact cause is unknown, current theories suggests a hereditary beta-cell predisposition to injury coupled with some defect in tissue regeneration capacity. Causes of injury are most likely hydroxyl and other free radicals, viral infections and autoimmune reactions.

Alloxan, the uric acid derivative used to induce experimental diabetes in animals is a potent beta-cell toxin, causing destruction via hydroxyl radical formation.

Streptozotocin, the N-nitroso derivative of glucosamine has now replaced alloxan as the preferred agent for the destruction of beta-cell in the induction of experimental diabetes.

Circumstantial epidemiologic evidence suggests that dietary intake of the N-nitroso compounds found in smoked/cured meats is diabetogenic in susceptible individuals producing beta-cell damage by the same mechanism as streptozotocin (Campbell and Carlson, 1993).

**ETIOLOGICAL FACTORS IN NON-INSULIN DEPENDENCE DIABETES MELLITUS (NIDDM)**

Central to the pathogenesis of NIDDM is insulin insensitivity as evidenced by typically high level of circulating insulin, and the reversibility of hyperglycemia by dietary changes and/or weight loss is sufficient to restore insulin sensitivity.

**Obesity**

Obesity plays a major role in the etiology of NIDDM for many patients. Obesity is associated with insulin insensitivity

and adipose size distribution also seem to be important. The heterogeneity of human obesity has resulted in an attempt to identify subgroup using cellular criteria, two types have been identified: hyperplastic obesity (increase number of fat cells) and hypertrophic obesity (enlarged fat cells). The hypertrophic form is more closely associated with obesity that is diabetes, hyperinsulinemia, glucose intolerance, hypertension, and hyperlipidemia. Weight loss in particular, a significant decrease in body fat percentage is a prime objective in treating the majority of NIDDM patients since it improves all aspects of diabetes and may result in cure (Campbell and Carlson, 1993).

## DIAGNOSIS OF DIABETES MELLITUS

### Fasting Blood Glucose Level

The standard method of diagnosing diabetes involves the measurement of blood glucose concentrations. The normal fasting blood glucose level is between 80-120 mg/ dl. A fasting blood glucose measurement greater than 140 mg/ dl on two separate occasions is diagnostic of diabetes. Levels below 50 mg/dl indicate fasting hypoglycemia (Wyngaarden et al, 1992).

### Glucose Tolerance Test (GTT)

A more functional test of blood sugar control is the oral glucose tolerance test (GTT). The glucose tolerance test is a very sensitive test for diabetes mellitus. However, it is also very stressful to the patient and has a relatively low specificity. The National Diabetes Data Group recommends giving a 75 gram glucose dose, dissolved in 300 ml of water for adults, and(1.75 g/ kg) for an ideal body weight after an overnight fast in subjects who have been consuming at least 150 grams of carbohydrate daily for three days prior to the test. The patient is considered normal if the two hour plasma glucose is less than 140 mg/ dl and no value exceeds 200mg/ dl. A confirmatory diagnosis of diabetes mellitus requires that plasma levels be above 200 mg/ dl at both two hours and at least once between zero time and two hours.

Medications that impair glucose tolerance (diuretics, glucocorticoids, nicotinic acid) may invalidate the results.

### Glucose-Insulin Tolerance Test (GITT)

Relying on blood sugar levels alone is often not adequate in diagnosing blood sugar disorders. Several studies have shown that the glucose-insulin tolerance test (GITI) is more sensitive in the diagnosis of both hypoglycemic and diabetes than the standard glucose tolerance test. The glucose-insulin tolerance test uses a standard 6 hour glucose tolerance test coupled with measurements of insulin levels. The G-ITT appears to be one of the best diagnostic indicators for faulty sugar metabolism. As many as two-third of subjects with suspected diabetes or hypoglycemia that have normal glucose tolerance tests will demonstrate abnormal insulin tolerance tests (Rubin et al, 1992).

## COMPLICATIONS OF DIABETES MELLITUS

### Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is a life threatening complication that develops when insulin stores are depleted. It is always caused by non-compliance with insulin treatments. Diabetic ketoacidosis often develop through:

1. The process is usually triggered in insulin deficient patients by a stressful events most often pneumonia or urinary tract infections.
2. Severely low insulin levels cause excessive amounts of glucose in the bloodstream (hyperglycemia).
3. Fat breakdown then accelerates and increases the production of fatty acids. These fatty acids are converted into chemicals called ketone-bodies which are toxic at high levels. Symptoms include nausea and vomiting. Breathing may be abnormally deep and rapid with frequent sighing. The heartbeat may be rapid. Cerebral edema is a rare but very dangerous complication that occurs in l% of ketoacidosis cases and results in coma, brain damage or death in many cases. Others include adult respiratory distress syndrome.

Ketoacidosis is a serious condition of glucose build-up in the blood and urine. A simple urine test can determine if high ketone levels are present (Nordlie, et al, 1999).

### Hypoglycemia

Intensive insulin control increases the risk of hypoglycemia (insulin shock) which occurs if blood glucose levels fall below normal. Hypoglycemia may also be caused by insufficient intake of food or excess alcohol intake. Usually the condition is manageable but occasionally it can be severe or even life threatening particularly if the patient fails to recognize the symptoms.

Risk factors of severe hypoglycemia: young children are at higher risk for hypoglycemia. Specific risk factors for severe hypoglycemia are: Intensively controlling blood glucose level. Having long term diabetes. Being less educated on the condition.

### Symptoms

Mild symptoms usually occur at moderately low and easily correctable levels of blood glucose. These include: Sweating, trembling, hunger, rapid heartbeat. Severely low glucose levels can precipitate neurologic symptoms such as confusion, weakness, disorientation, in rare cases coma,

seizure and death. (Nordlie, et al, 1999).

## MEDICINAL PLANTS USED IN THE MANAGEMENT OF DIABETES MELLITUS

Several plant species have been studied as potential therapeutic agents in the management of diabetes and its related complications, its efficacy as a hypoglycemic agents.

### *Irvingia Grandifolia* (Epo Oro)

This medicinal plant have anti-diabetic effect by lowering the level of blood glucose in experimental animals. The efficacy of this plant as an anti-diabetic agent has been established for long by the past scientist who had research on it. It was found that *Irvingia grandifolia* decrease basal blood glucose by approximately 50% in normal rabbits and rats (Onoagbe, et al, 1999). Studies also shows that *Irvingia gradifolia* might enhance the rate of synthesis or secretion of insulin from the beta cells of the pancreas of diabetic animals since only mild diabetics was established in the animals.

The anti-diabetic activity of this plant can also be extended to treatment of human diabetes since they can effectively lower blood glucose in the treated animals.

### *Momordica Charantia* (Bitter Melon)

*Momordica charantia* also known as bitter melon is a member of the curcurbitaceae family and commonly used as a traditional remedy for diabetes. The fruit of this plant and juice of the fruit have been used in treatment of diabetes. Compounds isolated from the fruit of the plant that are believed to contribute to its hypoglycemic activity include charantin (a steroid glycoside) and polypeptide 'p' or plant insulin (a 166 residue insulin mimetic peptide). *Momordica charantia* has been hypothesized to act via both pancreatic and extra pancreatic mechanisms with decreased hepatic glucose output, increased glucose uptake and utilization by peripheral tissues, decreased intestinal glucose absorption and increased muscle glycogen synthesis (Marles, et al, 1995). Bitter Melon increases the anti-hyperglycemic effects by inhibiting protein tyrosine phosphatase 1B (PTB 1B), activating AMPK, increasing the expression of type 4 glucose (GLU T4), enhancing beta cellularity and insulin effects (Asadi-Samani, et al, 2017).

### *Trigonella Foenum Graecum* (fenugreek)

It is commonly used as a spice in cooking and in small quantities is categorized as "generally recognized as safe" by the United States Food and Drug Administration. Fenugreek is a member of the leguminosae (fabaceae) family. Bioactive compounds isolated from fenugreek seeds include saponin (diosgenin), alkaloids (carpaine), amino acid (Arginine), coumarins, mucilaginous fibers, these compounds plays a role on increased glucose absorption (Marles, et al, 1995). Typical doses of fenugreek used in research studies have varied a great deal; 5-100g/ day. Few significant side effects with use up to 6 months have been implicated. Side effects associated with high doses of fenugreek are cramping, diarrhea, flatulence (Sharma, et al, 1996). The therapeutic effect of fenugreek seed on diabetes is partly due to the direct stimuli of amino acid called hydroxyisoleucine-4 on insulin secretion from beta-cells.Fenugreek anti-hyperglycemic mechanisms were associated with increased insulin secretion, increased insulin sensitivity by cells for glucose uptake and energy production and inhibition of endogenous glucose synthesis (Jamshidi-kia, et al, 2018). Trigonella foenum graecum has been used for numerous indications including the hypoglycemic and anti-hyperlipidemic properties of the seed powder taken orally. Fenugreek is also the most recommended plant for treating diabetes in the Fars region of Iran and in West Algeria. It has efficacy in reducing blood glucose, produce a significantly reduced insulin resistance and improve fasting and post prandial blood glucose levels in diabetic patients and can be used in management of both type 1 and type 2 diabetes (Kassaian, et al, 2009).

### *Gymnema Sylvestre* (gurmar)

*Gymnema sylvestre* also called gurmar has been used as a traditional treatment for diabetes in India. It is a member of the Aclepiadaceae (milk weed) family. The leaf when chewed is reported to decrease the ability of the taste buds to detect sweet tastes. *Gymnema sylvestre* is reported to increase glucose uptake and utilization and improve the function of pancreatic beta-cells which produce insulin. The active constituents of *gymnema sylvestre* are believed to be gymnemic acids (a mixture of acid insoluble triterpenoid saponins) and amino acid derivatives (choline). Gymnema sylvestre gymnemic acid molecules have a receptor on the surface of the outer layers of the intestine that prevents the absorption of sugar molecules by the intestine which leads to a decrease in blood sugar levels. Typical doses of *gymnema sylvestre* range between 400-600mg/L of a standardized extract usually provided in divided doses. *Gymnema sylvestre* has no known toxic effects and has been used for up to 30 months in research studies (Shimuzu, et al, 1997).

### *Panax quinquefolius* (ginseng)

The term ginseng is used to refer to several distinct plant species with differing effects. American and Asian (Panax ginseng) belong to the Panax family (Aralicaea) of ginseng. Ginseng supplements significantly improves fasting blood

glucose level and post-prandial blood glucose levels. It has been hypothesized that ginseng may alter gastrointestinal absorption of glucose, increase glucose transporter number, glucose uptake and increase insulin release. The active constituents of ginseng root are Panax glycan, vitamins and flavonoids. The dose of ginseng used in clinical trials in subjects with diabetes varied widely with one using 3grams/ day and another 100-200mg/ day. Side effects of high dose of ginseng include excitation,nervousness, diarrhea, chest pain and headache. These side effects were dependent on dose and duration of use (Vogler, et al, 1999). Ginseng has a blood glucose lowering effect that stimulates insulin secretion, protects pancreatic islets, stimulates glucose uptake and increase insulin sensitivity (Jamshidi-kia, et al, 2018).

***Aloe Barbadenesis* (aloe)**

*Aloe barbadenesis* more commonly known as aloe vera is one of several hundred plants of the Lilliacae family. Two forms of aloe extracts are available, aloe gel and aloe juice. Aloe gel is a mucilaginous extract which contains the polysaccharides gluco-mannan and has been used orally as a treatment for type 2 diabetes and hyperlipidemia. The active components of aloe gel are not known but may include vitamins, minerals (chromium), saponins.
Oral use of aloe gel decreased fasting blood glucose (by more than 100 mg/ dl). Typical doses of oral aloe gel used for treatment of type 2 diabetes ranged between ½ teaspoon twice daily and 1 tablespoon daily. There were no adverse effects reported with the use of aloe, although theoretical concerns include additive hypoglycemia in subjects using hypoglycemic medications (Vogler, et al, 1999). The polyphenols of this plant in the islands-β works by increasing the stimulation of Langerhans cells, stimulating more insulin to be released due to the presence of compounds such as flavonoids and glycosides in this plant (Kavishankar, et al, 2011).

***Allium Sativum and Allium Cepa* (garlic and onions)**

Garlic and onions best known for their cardiovascular and lipid lowering effects has also been studied for their hypoglycemic effects. Research in humans and animals is minimal with some but not all, initial research suggesting that members of the allium family have mild hypoglycemic activity. The active constituents are believed to be volatile sulfur containing compounds (diallyl disulfide oxide), (allylpropyl disulfide), s-allyl cystein and s-allyl mercaptocysteine. It is hypothesized that sulfur-containing compounds decrease the rate at which insulin is degraded effectively increasing circulating insulin levels (Agarwal, 1996). Garlic stimulates insulin secretion. Effect is by restoration of insulin secretion and sensitivity, inhibition of intestinal absorption of glucose and gluconeogenesis. Red Onions exerts its effect by repair of insulin responses by cells and inhibition of glucose intestinal absorption. It also stimulates the β-cells of the pancreasfor insulin secretion (Rahimi-mediseh, et al, 2017).

**Catharanthus roseus (L)**

Is an ornamental shrub that belongs to the family Apocyaneae. It was previously known as Vinca rosea (L). It is widely distributed around the world due to its high survivability in a variety of habitats and use as an ornamental plant. Catharanthus roseus is used traditionally as a medicinal plant for treatment of diabetes in several countries including Nigeria. Roots and leaves of this plant contain more than 100 alkaloids. The two leaf alkaloids which are important in medicine are Vinblastine and Vincristine. Fresh leaf juice of C. roseus has been reported to reduce blood glucose in diabetic rabbits. Leaf and other parts of C. roseus also widely used as an infusion for treatment of diabetes and it has gained acceptance from the Pharmaceutical Industries (Al-shaqha, et al, 2015).

## CONCLUSION

The study shows that *Irvingia grandifolia* can be employed in the management of diabetes mellitus by poor Africans who cannot afford the cost of using insulin injection and the techniques involved. Also, due to side effects encountered on drugs such as pioglitazone, sulfonylureas, meglitimides and Alpha-glucoside inhibitors used in the management of diabetes mellitus, it is better to resort to medicinal plants such as *Irvingia grandifolia* if the safety is assured as found out in this experimental research. Though, research is also still in progress on the effects of *Irvingia grandifolia* on tissue enzymes activity, and if totally found out that no significant effect exist, and the safety guaranteed, it will serve as a new relief for diabetic patients especially the Africans who cannot afford the cost of using other managements options. For now, no curative treatment for diabetes exist but be managed.

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