

**BIOLOGICAL EFFECT OF THE BIHERBAL FORMULATION OF  
*Irvingia gabonensis* and *Ocimum gratissimum* ON INDUCED DIABETIC IN  
ALBINO RATS**



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BENIN CITY**

**NOVEMBER, 2025**

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**BENIN CITY**

**A PROJECT SUBMITTED IN THE DEPARTMENT OF SCIENCE LABORATORY  
TECHNOLOGY AND SUBMITTED IN PARTIAL FULFILMENT OF THE  
REQUIREMENTS FOR THE AWARD OF A BACHELORS (B. Sc.) DEGREE IN THE  
UNIVERSITY OF BENIN, BENIN CITY, EDO STATE, NIGERIA.**

**NOVEMBER, 2025**

## CERTIFICATION

This is to certify that the project was carried out by **Esther Owen OYEMWINMINA (MISS)** Matriculation number **LSC2003196**, a 500 Level student of the Department of Science Laboratory Technology, Faculty of Life Sciences, University of Benin, in partial fulfillment of the requirement for the award of a Bachelor of Science degree, B.Sc. (Hons.) in Science Laboratory Technology.

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## **DEDICATION**

I dedicate this seminar work to God almighty, who has been my source of inspiration and strength.

## ACKNOWLEDGMENTS

I would like to specifically thank my supervisor “Dr. P. O. Obaro” and his wife “Dr. (Mrs.) O. E. Obaro for support and encouragement. And also, my profound appreciation to the Dean of Science Laboratory Technology, Prof. J.O. Osarumwense and the entire staff of the Faculty of Science Laboratory Technology.

My esteemed regards to my lovely family Dr. and Mrs. Christopher Oyemwinmina for their unending love and support towards my educational pursuit. My siblings Divine, Praise, Efosa and Nosa. And also, to my lovely colleagues, Joy, Queen, Annabel, Uyi and other friends thanks for your support and care, you all are the best.

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## ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia and associated complications such as dyslipidemia and organ dysfunction. The limitations of synthetic anti-diabetic agents and their side effects have heightened interest in medicinal plants. This study investigated the hypoglycemic and anti-diabetic potentials of the leaves of *Irvingia gabonensis* (Bush mango) and *Ocimum gratissimum* in normoglycemic and Streptozotocin-induced diabetic Wistar rats. Ethanol extract of the combined leaves of *Irvingia gabonensis* and *Ocimum gratissimum* was obtained through cold maceration and subjected to acute toxicity and efficacy studies. No signs of toxicity were observed at doses up to 5000 mg/kg, suggesting a wide safety margin. The extracts significantly reduced blood glucose levels, improved lipid profiles by lowering triglycerides, LDL, and total cholesterol while increasing HDL, and restored liver function markers (AST, ALT, ALP, and total protein) towards normal values. These effects were comparable to glibenclamide, a standard Antidiabetic drug. These findings provide scientific evidence supporting the ethno medicinal use of *Irvingia gabonensis* and *Ocimum gratissimum* in diabetes management. This study concludes that these plants exhibit potent anti-diabetic properties, and may serve as safe, natural alternatives or complementary therapies for diabetes and related complications.



## CHAPTER ONE

### 1.0

### INTRODUCTION

#### 1.1 BACKGROUND OF STUDY

*Irvingia gabonensis* (Bush Mango) is a species of African trees in the genus *Irvingia*, sometimes known by the common names wild mango, African mango, or bush mango (Burkill, 2021). They bear edible mango-like fruits, and are especially valued for their fat- and protein-rich nuts.

*Irvingia* species collectively known as Bush mango or dika nut, are economically important fruit species, native to moist lowland tropical forest in central and west Africa (Amit *et al.*, 2022). Natural geographical distribution of both species span through the humid forest zones of West and Central Africa, including Angola, Cameroon, Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of Congo, Equatorial Guinea, Gabon, Ghana, Guinea-Bissau, Liberia, Nigeria, Senegal and Sierra Leone, Sudan, Uganda, Sao Tome and Principe (Kengni *et al.*, 2021). In Africa, *I. gabonensis* is the commonest one. In Nigeria, two varieties of this species were identified in 1974, *I. gabonensis* var. *gabonensis* (with sweet edible fruit) and *I. gabonensis* var. *excelsa* (with bitter fruit). *Irvingia gabonensis* (wild bush mango) is a bush plant that produces seeds called dika, locally known as ogbono in Ibo, oroapon in Yoruba and magoron kurmi in Hausa. It is abundant on the Eastern region of Nigeria such as in Imo State and Enugu State. It is also abundantly found on some parts of Cross River State such as in Ikom, Betim and Biase. This genus of plant is found in AkwaIbom State in less abundant and mainly within interior villages (Etukudo *et al.*, 2023). The bush mango tree grows naturally in the humid low land forests of tropical Africa but is widely planted in central and western Africa (Ladipo *et al.*, 2021). It is cultivated mainly for these seeds while the leaves and

stem bark are used in traditional African medicine against fever and stomach ache. This traditional tree is common in dense evergreen rain forests but is also found near riverbanks (Atangana *et al.*, 2021) it has been reported to be used as a source of timber and to make utensils, and also as food and medicine (Okoronkwo *et al.*, 2024).

*Irvingia gabonensis* Kernel oil and also the findings support with the study (Okoduwa, *et al.*, 2023) also reported the increase in HDL and decreased in LDL, TG, TC in anti-diabetic potential of *Ocimum gratissimum* leaf fractions in fortified-Diet fed streptozotocin treated rat model of Type -2 diabetes. that effectively lowers blood sugar levels for an extended period. It is used alongside dietary measures to manage blood glucose in individuals with non-insulin-dependent diabetes mellitus (Type II diabetes) and is frequently prescribed for gestational diabetes mellitus. Like other drugs in the sulfonylurea class, glibenclamide works by binding to ATP-sensitive potassium-channel receptors, which stimulates insulin release from the pancreas (Nathan *et al.*, 2024).



**Plate 1.1: Bush mango Tree with fruits**      **Photo Credit: Oyemwinmina Esther (2025)**

## **1.2. BIOLOGY OF *Ocimum gratissimum***

Scent leaf (*Ocimum Gratissimum*), also referred to as African basil, clove basil, or efin in Yoruba, is a multifaceted herb indigenous to Africa, Madagascar, and certain parts of Asia. Renowned for its aromatic qualities, it enhances various dishes and has a long-standing history in traditional medicine. In the last decade, many researchers have focused on medicinal plants and their bioactive compounds due to their promise in treating and preventing serious conditions, including arthritis, diabetes, cancer, and stroke. This perennial herb is not only known for its strong scent but also for its market potential. Scent leaf belongs to the Lamiaceae family. Besides being a flavor enhancer for fish, meat, soups, and stews, it is employed in treating numerous ailments such as pain, fever, inflammation, anemia, diarrhea, and infections caused by fungi and bacteria. It contains a significant amount of macronutrients beneficial for the body, and when consumed in appropriate quantities, the leaves provide substantial nutritional benefits (Chaachouay *et al.*, 2022).



**Plate 1.2:** Aerial Part of an *O. gratissimum*

**Photo Credit:** Esther Oyemwimina (2025)

### **1.3. TAXONOMY OF *Ocimum gratissimum***

Scent leaf is classified within the Plantae kingdom, belonging to the Lamiaceae family (commonly known as the mint family) and is identified as the species *Ocimum gratissimum*. This perennial shrub can reach heights of 2 to 5 meters. It is known by various names including Efinrin (in Yoruba), Nchanwu (in Igbo), and Afeu (in Efik).

Scientific Name: *Ocimum gratissimum*

Kingdom: Plantae

Phylum: Anthophyta

Class: Dicotyledoneae

Order: Lamiales

Family: Lamiaceae

Genus: *Ocimum*

Species: *gratissimum*.

### **1.4 Statement of the Problem**

Over the years, the problems of diabetic in both men and women and general diseases have increased worldwide (Yeap *et al.*, 2020). The research is therefore designed to study the possible outcome of the use of *Irvingia gabonensis* (bush mango) and *Ocimum gratissimum* (scent leaf) as anti-diabetic agent.

### **1.5 Justification of the Study**

The recent interest in herbal drugs is growing with the advent of new culture “return to nature” a good rational for the evaluation of the potentials of some reputable medicinal plants as a remedy for diabetic disorders.

The use of *Irvingia gabonensis* and *Ocimum gratissimum* has not been scientifically documentation in spite of the traditional usefulness.

## **1.6 AIM OF STUDY**

The study was aimed to determine biological effect of the biherbal formulation of *Irvingia gabonensis* and *Ocimum gratissimum* on induced diabetic in albino rats

## **1.7. OBJECTIVES OF STUDY**

1. Extraction of the bi herbal formulation of *Ocimum gratissimum* and *Irvingia gabonensis* using ethanol solvent.
2. Determination of the hypoglycemic effect of bi-formulation of *Ocimum gratissimum* and *Irvingia gabonensis* extract on normoglycemic Wistar rats.
3. Determination the anti-diabetic effect of bi- herbal formulation of *Ocimum gratissimum* and *Irvingia gabonensis* extract on Streptozotocin induced diabetic wistar rats.

## CHAPTER TWO

### 2.0

### LITERATURE REVIEW

#### 2.1 HYPOGLYCEMIA

Hypoglycemia is a sudden complication of diabetes where blood glucose levels drop below normal, with the term literally meaning “under-sweet blood.” This dangerous condition, which can be life-threatening to patients and others around them, is typically caused by factors such as excessive insulin or oral hypoglycemic drugs, inadequate food intake, or intense physical activity. Commonly used diabetes medications like insulin and sulfonylureas are frequent culprits of hypoglycemia among diabetic individuals. Symptoms of hypoglycemia include sweating, tremors, rapid heartbeat, palpitations, anxiety, hunger, confusion, slurred speech, mood swings, double vision, fatigue, insomnia, and are often self-diagnosed (Alagiakrishnan and Mereu, 2020). Hypoglycemia is a frequent metabolic emergency that happens due to an imbalance between the brain’s energy needs and the available glucose levels, even with normal oxygen levels in the blood. About 7% of patients who come to the emergency department with altered mental states have hypoglycemia, and around 20% of diabetic patients on insulin or other antidiabetic drugs will experience symptoms requiring emergency attention. Severe hypoglycemia, if not treated, can lead to serious consequences like neural damage, cognitive issues, coma, seizures, or even death. Both single and recurring episodes of hypoglycemia can lead to physical and mental problems and increase the risk of death while also hindering normal glucose levels (Guettier and Gorden, 2020).

Diabetic individuals, particularly males, adolescents, and those over 55, are at high risk of severe hypoglycemia, especially if they are physically active, have a low-carb diet, drink alcohol, or

have kidney or liver issues, along with tightly controlled glucose levels, changes in insulin or medication, infections, other health problems, or multiple medications. A recent study showed that severe hypoglycemia can cause brain damage in specific regions like the cortex and hippocampus, with the level of damage linked to seizure-like activity. The cortex becomes more sensitive to damage after a severe hypoglycemic episode, which is common in elderly individuals with diabetes, altering their cognitive and hormonal responses to low blood sugars (Pai and George, 2025).

The American Diabetes Association defines hypoglycemia as abnormally low blood sugar levels that can lead to various symptoms and serious complications. Factors such as lifestyle, medication choice, and comorbid conditions can increase the risk of hypoglycemia in diabetic patients. It is crucial for patients to be aware of hypoglycemia symptoms and how to manage them promptly to avoid hospitalization. Education on self-management and monitoring of blood sugar levels can help reduce the risk of hypoglycemia. Healthcare professionals play a vital role in educating patients on hypoglycemia to prevent severe episodes and complications (Dejagar and Schweizer, 2021).

## **2.2. DIABETES MELLITUS**

Diabetes Mellitus (DM) is a complex chronic condition characterized by the body's improper handling of glucose over a long period. Continuous care is essential to prevent or delay serious complications and early death. One proposal suggests referring to diabetes as "premature atherosclerosis with associated hyperglycemia" to emphasize the common clinical challenges faced by patients. Global estimates indicate that diabetes affects over 400 million people currently, with a projected 50% increase in the next 25 years. The International Diabetes Federation predicts a rise from 451 million to 693 million diabetics by 2045, with roughly half

going undiagnosed. Serious complications such as heart attack, stroke, kidney failure, nerve damage, vision problems, and limb amputations can arise from uncontrolled diabetes, impacting both quality of life and financial aspects for individuals, families, and society as a whole (Cole and Florez, 2020).

The global healthcare cost of diabetes exceeded USD 700 billion in 2017 and is expected to rise significantly in the next quarter century, posing challenges to resources and healthcare systems worldwide. Managing diabetes requires self-care, lifestyle changes, and education, with ongoing monitoring, team collaboration, regular patient-provider communication, and community support (Fatehi *et al.*, 2018). While medication and lifestyle adjustments can aid in controlling blood sugar levels, individualized approaches are necessary due to differences in disease progression, risk factors, and patient responses. Innovative strategies, including digital interventions, are vital to enhancing diabetes care, particularly in regions with limited healthcare resources. Research shows that only a small proportion of diabetic patients receive adequate services, indicating a need for novel approaches to improve healthcare effectiveness in the face of the increasing prevalence of diabetes (Lambrinou *et al.*, 2019).

### **2.3 CLASSIFICATION OF DIABETES MELLITUS**

According to the American Diabetes Association (2008), diabetes can be classified into the four following general categories:

#### **2:3:1 TYPE 1 DIABETES**

Type 1 diabetes is also known as insulin-dependent diabetes (IDDM) and typically affects children and young adults. The onset of type 1 diabetes is usually sudden and can be life-threatening. This type of diabetes is often characterized by the presence of antibodies against glutamic acid decarboxylase, islet cells, or hormones, which play a role in the destruction of beta

cells. Type 1 diabetes results from the destruction of beta cells, leading to an absolute deficiency of insulin. The rate of beta cell destruction can vary, occurring rapidly in some individuals and more slowly in others (Roshan *et al.*, 2020)

### **2:3:2 TYPE 2DIABETES**

Ketosis-resistant diabetes mellitus is another term for Type 2 diabetes, which is characterized by a progressive defect in insulin secretion on a background of insulin resistance. Individuals with this type of diabetes often do not respond effectively to insulin. Long-term complications affecting blood vessels, kidneys, eyes, and nerves are common in both types of diabetes and are major causes of morbidity and mortality. Obesity, sedentary lifestyle, aging, and genetic factors are predisposing factors that increase the risk of developing complications in individuals with this type of diabetes (Ross and Wilson 2020).

### **2:3:3 GESTATIONAL DIABETES MELLITUS**

Gestational diabetes mellitus (GDM) refers to diabetes diagnosed during the second or third trimester of pregnancy that is not clearly overt diabetes. (Baynes,2025) states that GDM includes women who develop Type 1 diabetes mellitus or have undiagnosed asymptomatic Type 2 diabetes mellitus discovered during pregnancy. Most women with GDM are reported to experience the onset of the disorder in the third trimester of pregnancy.

### **2.3.4 A DIFFERENT TYPE OF DIABETES MELLITUS (Monogenic Types)**

Certain types of diabetes are caused by factors other than the usual reasons. This includes individuals with beta-cell function genetic defects like neonatal diabetes and maturity-onset diabetes of the young, those with exocrine pancreas disorders like cystic fibrosis, and drug-

induced diabetes as a side effect of treating conditions such as HIV/AIDS or post-organ transplantation. These cases make up less than 10% of all diabetes cases (Baynes, 2025).

### **2.3.5 MODY**

Genetics play a significant role in identifying various types of diabetes, with type 2 diabetes having a genetic basis that is not completely understood. The most prevalent type is maturity-onset diabetes of the young (MODY), an inherited form linked to mutations in certain genes like glucokinase and HNF-1a found in liver or pancreatic cells. MODY is inherited as a dominant trait through autosomes (Egan and Dinneen, 2019).

## **2.4 PRE-DIABETES**

“Impaired glucose tolerance” (IGT) and “impaired fasting glucose” (IFG) refer to conditions that fall between normal glucose levels and full-blown diabetes. These conditions are often labeled as “pre-diabetes,” even though they are not classified as actual diseases. They are important because they are strong indicators of the potential development of diabetes later on (Egan and Dinneen, 2019).

### **2.4.1 EPIDEMIOLOGY OF DIABETES MELLITUS**

The term “DM” is becoming more familiar to people around the world, gaining prevalence in every nation. The combination of various risk factors has contributed to the global diabetes epidemic, affecting both type 1 and type 2 diabetes. Type 2 diabetes is now one of the most common diseases worldwide, with every country seeing an increase in patients. Currently, an estimated 382 million people have diabetes globally, with 175 million of them undiagnosed, and the highest incidence is seen in those aged 40 to 59 (Guariguata *et al.*, 2024). By 2035, it is predicted that this number will soar to over 592 million. In 2014, it was estimated that 422

million people (8.5% of the population) worldwide had diabetes. These figures are significantly higher than previous projections, posing a major challenge for healthcare systems. The prevalence of diabetes is on the rise worldwide, especially among young people. According to the World Health Organization, by 2030 the global prevalence of diabetes is expected to reach 4.4%, affecting around 366 million people, a 114% increase since 2000 (Shaw *et al.*, 2020).

## **2.5 SIGNS AND SYMPTOMS OF DIABETES MELLITUS**

In diabetes mellitus, cells fail to metabolize aldohexose in a normal way and are effectively starved. The long-term effects of diabetes mellitus include the progressive development of special complications such as retinopathy with possible visual defects, kidney disorders that can lead to kidney failure and pathologies with a risk of foot ulceration, neurological joints and involuntary characteristics. Pathology and sexual dysfunction. People with polygenic diseases are at greater risk of the disease. Several other symptoms are determined for.

- I. Gluconeogenesis from amino acids and macromolecules of the body, causing muscle atrophy, tissue breakdown, and increased blood sugar levels.
- II. The destructive metabolism of body fat, cathartizes a number of their energy bodies and the excessive production of organic compounds (Ross And Wilson, 2020; American Diabetes Association, 2020).

## **2.6 PATHOGENESIS AND PHYSIOPATHOLOGY OF DIABETES MELLITUS**

There is a clear connection between hyperglycemia and both physiological and behavioral responses. Type 1 diabetes results from an autoimmune attack on insulin-producing B cells, and hyperglycemia becomes evident when only 10 to 20% of these functional cells remain. This autoimmune process, which leads to pancreatic “insulinitis,” can develop over many years (typically 5 to 10 years or more before diabetes manifests). It occurs within a genetically

susceptible context, driven by certain triggers, and can be identified through blood tests for autoantibodies prior to the onset of hyperglycemia (Baynes, 2025).

The destruction of B cells is primarily caused by infiltration from CD4 helper T cells and CD8 cytotoxic T cells, occurring without clinical symptoms for several years. During this time, autoantibodies against specific pancreatic antigens are formed. While these autoantibodies do not directly cause damage, they serve as reliable indicators of the ongoing autoimmune process. The four key autoantibodies include:

1. Anti-islet antibodies (islet cell antibody: ICA).
2. Anti-GAD antibodies (glutamate acid decarboxylase), which target a common enzyme that is prominent in the pancreas, indicating an autoimmune response against B cells.
3. Anti-insulin autoantibodies, predominantly found in children.
4. Anti-IA2 antibodies, which target a membrane phosphatase in B cells.

Although insulin deficiency is the primary defect in Type 1 diabetes, there is also an issue with insulin administration. Insulin deficiency causes unchecked lipolysis and elevated plasma free fatty acid levels, which hinder glucose metabolism in peripheral tissues. This situation diminishes glucose utilization, and insulin deficiency further decreases the expression of essential genes for insulin response in target tissue. As a result, the significant metabolic disturbances from insulin deficiency in Type 1 diabetes encompass metabolic issues involving glucose, lipids, and proteins (Fagninou *et al.*, 2019).

In summary, Type 1 diabetes is characterized by the autoimmune destruction of insulin-producing pancreatic cells by infiltrating CD4<sup>+</sup> and CD8<sup>+</sup> T cells and macrophages (Baynes, 2025).

For Type 2 diabetes, the primary pathophysiological defects involve reduced insulin secretion due to pancreatic  $\beta$ -cell dysfunction and impaired insulin action resulting from insulin resistance. The  $\beta$ -cells may increase insulin production to meet the excessive demand when insulin resistance is prominent.

In terms of gestational diabetes, its pathophysiology resembles that of Type 2 diabetes, suggesting that gestational diabetes may represent an early stage of Type 2 diabetes occurring during pregnancy (Baynes, 2025).

## **2.7 FACTORS CAUSING DIABETES MELLITUS**

The main contributor to Type 1 Diabetes Mellitus (T1DM) is environmental influences. One significant factor that contributes to insulin resistance and the development of Type 2 Diabetes Mellitus (T2DM) is obesity. The prevalence of diabetes mellitus is increasing due to lifestyle changes associated with urbanization and westernization, which include poor dietary choices, lack of physical activity, obesity, and low socioeconomic status (Taloyan *et al.*, 2021). Various risk factors are associated with the onset of type 2 diabetes. Unchangeable risk factors consist of aging, family history, and genetic predispositions in specific ethnic groups. However, the most prevalent risk factors driving the rise in diabetes cases are related to unhealthy diets, inactivity, and smoking, often leading to overweight conditions, abnormal lipid levels, high blood pressure, and impaired glucose tolerance. Environmental elements such as low socioeconomic status, living conditions, stress, and exposure to toxins like mercury and arsenic also play a role in diabetes development (Joshi and Shrestha, 2020).

## **2.8 DIAGNOSIS OF DIABETES MELLITUS**

Diabetes mellitus is diagnosed using either HbA1c levels or plasma glucose measurements, including fasting plasma concentration (FPG) or the Oral Glucose Tolerance Test

(OGTT)(McDonald And Warren, 2014). Cutoff values for glucose and HbA1c are determined based on their relationship with retinopathy Diagnosing diabetes requires plasma glucose levels of at least 126 mg/dl (7.0 mmol/L) after fasting, 200 mg (11.1 mmol/L) after a 2-hour OGTT, an HbA1c of 6.5% or higher, or a random plasma glucose level of at least 200 mg/dl (approx. 6.76 oz) accompanied by symptoms of hyperglycemia. These standards have the endorsement of the American Diabetes Association, the World Health Organization, and the Endocrine Society, as well as numerous researchers and affiliated organizations. have evaluated the pros and cons of different diagnostic tests for diabetes. For asymptomatic patients, it is recommended to repeat the HbA1c test after two weeks to verify any single potentially diagnostic result (Sacks *et al.*, 2021).

## **2.9. MANAGEMENT OF DIABETES MELLITUS**

The National Health Service (NHS) allocates over 10% of its annual budget to manage diabetes among its patients, with more than half of that expenditure directed towards treating those with severe consequences of the condition. If treatment expenses are not significantly reduced, the rising number of diabetes patients in the UK will considerably affect NHS finances and may jeopardize patient care. The increasing prevalence of diabetes will escalate the burden of its treatment and prevention, leading to significant financial implications for healthcare. Integrating national guidelines into routine clinical practice has been associated with heightened prescription of medications and the adoption of technology. This includes greater use of anti-hyperglycemic drugs and improved management of glycemic levels to meet the recommended HbA1c targets. Empowering and educating patients is essential for the effective execution of these strategies, alongside the support of a varied specialized care team (Rama and Tejomurtula, 2024).

## **2.10. TREATMENT OF DIABETES MELLITUS**

The primary objective in managing type 1 and 2 diabetes is to gradually enhance glycemic control through both medication, exercise, dietary modifications, as highlighted by the (American Diabetes Association, 2020).

### **2.10.1 DIET THERAPY**

Diet therapy encompasses maintaining nutritious eating habits and achieving a healthy weight. A healthy diet involves consuming foods from all food groups, selecting low-calorie options, and maintaining consistent carbohydrate intake at each meal. Individuals with type 2 diabetes should focus on carbohydrates sourced from fruits, vegetables, low-fat dairy, and whole grains. They are also encouraged to keep track of their carbohydrate intake by calculating the carbohydrate content of their meals (American Diabetes Association 2021).

### **2.10.2. PHYSICAL THERAPY**

Consistent physical activity, such as exercising, is vital for controlling diabetes. Individuals with diabetes who engage in regular exercise tend to achieve improved glucose control, reduced cardiovascular risks, and overall better health (Kanaley *et al.*, 2022).

### **2.10.3 INSULIN THERAPY**

Insulin therapy serves as a substitute for the insulin that the body typically produces. Individuals with type 1 diabetes must administer insulin daily.

For those with type 2 diabetes, insulin becomes necessary when other treatments and medications are ineffective in managing blood sugar levels (Elsayed *et al.*, 2023).

Insulin can be administered in two primary methods:

- I. Basal dose – this offers a consistent level of insulin continuously throughout the day and night, aiding in the regulation of blood glucose by controlling the liver’s glucose release, especially during longer intervals without meals (Elsayed *et al.*, 2023).
- II. Bolus dose – this involves administering insulin during meals to assist in transferring the absorbed sugar from the bloodstream into muscle and fat, and it can also help in reducing elevated blood sugar levels (Elsayed *et al.*, 2023).

There are different types of insulin, including premixed or mixed insulin, long-acting insulin, regular or short-acting insulin, intermediate-acting insulin, and rapid-acting or fast-acting insulin.

#### **2.10.4. ANTI-DIABETES DRUG**

Antidiabetic medications are aimed at regulating blood sugar levels in people with diabetes mellitus. They assist in managing glucose metabolism and can operate through different methods, including enhancing insulin production, increasing insulin sensitivity, or slowing down carbohydrate absorption. Notable examples are metformin and sulfonylureas, such as Gilbenclamide (Elsayed *et al.*, 2023).

#### **2.10.5. HERBAL TREATMENT FOR DIABETES**

In recent decades, there has been a significant increase in research focused on traditional medicine, leading to the emergence of plant-based therapies that are environmentally friendly, cost-effective, and typically safe, moving these treatments into the mainstream. Examples such as *Ocimum gratissimum* (Scent leaf) and *Irvingia gabonensis* (Bush mango) contain phytochemicals that can be utilized in the treatment and management of diabetes (Elsayed *et al.*, 2023).

## 2.12. GILBENCLAMIDE

Glibenclamide, also referred to as glyburide, is a second-generation. Thus, the reduced biosynthesis of fatty acids in turn will reduce the production of VLDL particles, thus limiting the formation of LDL particles and resulting in low serum triglycerides and cholesterol concentrations (Ali, 2004). This result is consistent with those of (Ngondi *et al.*, 2025; Dzeufeit, *et al.*, 2020) who reported an increase in HDL-cholesterol and a decrease in LDL-cholesterol in normal rats treated with

### **Mechanism of Action**

The drug works by blocking ATP-sensitive K<sup>+</sup> channels, resulting in cell depolarization and the release of insulin. This same mechanism also underlies the drug's extra pancreatic effects in the liver, skeletal muscle, heart muscle, and smooth muscle (Frederico *et al.*, 2017).

## CHAPTER THREE

### 3.0 MATERIALS AND METHODS

#### 3.1. COLLECTION OF PLANT SAMPLES

Plant samples of *Irvingia gabonensis* and *Ocimum gratissimum* were collected from the Capitol area behind the University of Benin and were verified by Professor H.A. Akinnibosun from the Department of Plant Biology and Biotechnology, Faculty of Life Sciences at the University of Benin, Benin City. The leaves were detached from the stems and allowed to dry at room temperature for seven days. Subsequently, they were air-dried in an electric oven (COV-8320-C) for 48 hours at 45°C.

The dried samples were then ground into a fine powder using an electric blender (SC-1589). Each sample's powder was placed in airtight containers and labeled for the subsequent extraction process.

#### 3.2. EXTRACTION PROCESS USING COLD MACERATION

Five hundred grams (500 g) each of the powdered plant samples (1:1) were weighed using an electronic Weighing balance (A-123) and transferred into a glass container and 500 ml of ethanol (110-54-3) was added to the container. The mixture was macerated with a spatula for even maceration the mixtures are then covered, air-tightened and vigorously shaken as many times as possible and left upright in a dark cupboard for 72 hours.

After the estimated time, the mixtures were taken out, shook and transferred into a cheese cloth placed on a container. The mixture was macerated and shaft out leaving behind the concentrate of each plant samples, The concentrate was transferred into a crucible and placed in a water bath (WB-4MS) and concentrated at 45°C for 24hrs.

The concentrated samples underwent complete air-drying in an electric oven at 45°C for 24 hours. Subsequently, the dried extract was transferred to airtight containers, appropriately labeled, and stored under refrigeration using an electronic refrigerator (TR-131L).

### **3.4 Acute Effect of Ethanol extract of the Bi-herbal formulation**

Acute Effect of Ethanol extract of Bi-herbal formulation of *Irvingia gabonensis* and *Ocimum gratissimum* on the blood sugar level normoglycemic and STZ Induced Diabetic Rats was carried out on twenty (20) rats which were randomly assigned to one of four groups, each consisting of five animals:

Group 1: Normoglycemic rats + 2 ml/kg Distilled water

Group 2: STZ induced diabetic rats + 2 ml/kg Distilled water

Group 3: Normoglycemic rats + 1000 mg/kg IGAOGE)

Group 4: STZ induced diabetic rats + 1000 mg/kg IGAOGE

The blood sugar level of normoglycemic rats and those of the Streptozotocin (STZ) induced diabetic rats after administered a single dose of 1000 mg/kg of the extract (IGAUGE) were recorded from 0- 72 hours.

### **3.5 Anti-diabetic Study**

*Irvingia gabonensis* and *Ocimum gratissimum* was administered to normoglycemic and diabetic induced Wistar rats using streptozotocin.

Twenty (20) rats were randomly assigned to one of four groups, each consisting of five animals:

Group 1: Control group (Distilled water was administered)

Group 2: Standard treatment group (Glibenclamide was administered)

Group 3: Extract treated groups (received 50 mg/kg IGAUGE)

Group 4: Extract treated group (received 100 mg/kg IGAOGE) After 30 days administrations, the animals' blood was collected and analyzed for various biochemical parameters, including liver enzymes, lipid profiles, and total protein

Thirty (30) days oral administration of *Irvingia gabonensis* and *Ocimum gratissimum* at the doses of 50 and 100 mg/kg to streptozotocin induced diabetic rats after which the animals were anesthetized and blood was collected from the abdominal aorta. Collected blood samples were screened for the following parameters: Alkaline phosphates (ALP), Aspartate amino transferase (AST), Alanine amino transferase (ALT) and total protein (TP).

### **Experimental animals**

Albino rats weighing 200 to 250 g were purchased from the Department of Pharmacology Animal House Facility of Pharmacy University of Benin.

### **3.6. Blood glucometer check**

Accu-check active glucometer and visual blood glucose test stripes, products of Roche diagnostic GmbH, D-68298 Mannheim, Germany were used for the fasting blood glucose level estimation

### **Drugs/chemical**

Glibenclamide, Ethanol (110-54-3), Streptozotocin.

### **Apparatus**

Beakers (50 ml,100 ml,200 ml,1000 ml), cages, cotton wool, crucible, cheese cloth, cover slip, distilled water, feed plates, glass slides, hand gloves, masking tape, methylated spirit, measuring cylinder (1000 ml), oral gastric tube, pelletized feed, pocket pH meter, rat restrainer.

## **Equipment**

Centrifuge (HV-8M), Electric blender (Sc-1589), Electric oven (COV-8320-C), Microscope (labron-307), Refrigerator (TR-131L), Water bath (WB-4MS).

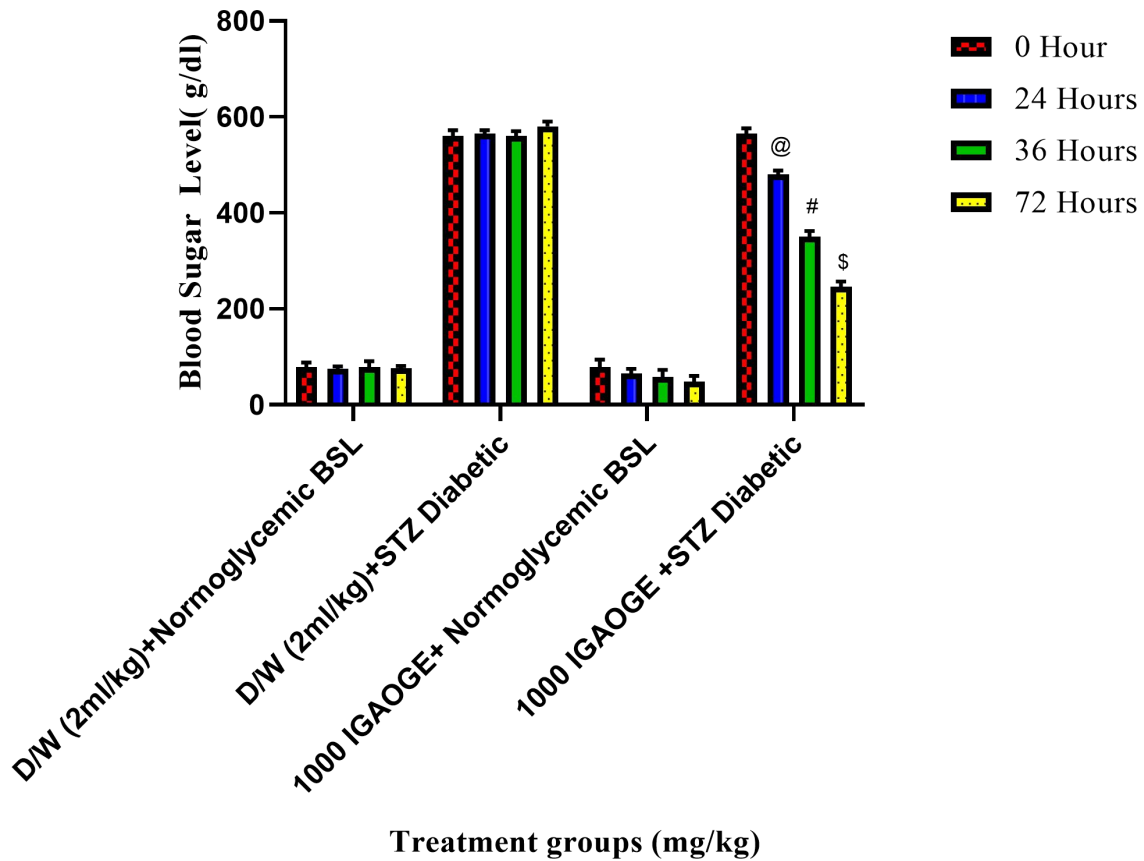
### **3.7. Statistical Analysis**

The results from the studies were expressed as mean  $\pm$  SEM. Statistical analysis were carried out using graph pad prism 6 version software (UK). Comparisms between the control and treated groups were analysed using one-way ANOVA and, Dunnett's multiple comparisms test. \* =  $P < 0.05$ , was regarded as indicating significant difference.

## CHAPTER FOUR

### 4.0

### RESULTS



**Figure 4.1:** Acute Effect of Ethanol extract of Bi-herbal formulation of *Irvingia gabonensis* and *Ocimum gratissimum* on the blood sugar level normoglycemic and STZ Induced Diabetic Rats Results are expressed as mean  $\pm$  SEM (n = 5), @, #, and \$ indicate significant p-values at P< 0.01, 0.001 and 0.0001 respectively.

**Key:** IGAOGE = *Irvingia gabonensis* and *Ocimum gratissimum* Extract

**Table 4.1:** Effect of Ethanol extract of *Irvingia gabonensis* and *Ocimum gratissimum* Extract on blood sugar level of diabetic rats

Groups mg/kg	Day 0	Day 5	Day 15	Day 30
Control	76.2±0.6	85.1±1.9	91.1±0.7	87.2±0.9
D. Control	506.1±30	610.7±24	630±12	626.3±17
Gliben 50	540±3.6	150±0.3 <sup>a</sup>	134±9.0 <sup>c</sup>	50±2.2 <sup>d</sup>
IGAUGE 200	528.3±1.9	168.4±2.7 <sup>a</sup>	62.1±1.1 <sup>d</sup>	97.2±6.3 <sup>d</sup>
IGAUGE 400	528±36	179±1.8 <sup>b</sup>	28±0.8 <sup>d</sup>	75.01±6.0 <sup>d</sup>

Results are expressed as mean ± SEM (n= 5), with significant P-values <sup>a,b,c,d</sup>= p <0.05, 0.1,0.01 and 0.001

**Key:** IGAUGE= *Irvingia gabonensis* and *Ocimum gratissimum* extract, D. Control =Diabetic control, Gilben. = Gilbenclamide, and blood sugar level (BSL) = blood sugar level.

**Table 4.2:** Effect of Ethanol *Irvingia gabonensis* and *Ocimum gratissimum* extract on liver function indices

Parameter	Control	Gilben.	D. Control	IGAUGE	IGAUGE
		mg/kg	Strep induced	50 mg/kg	100 mg/kg
ALP	65.2±0.2	60.2±1.3*	100.0±2.3	50.05±1.2 <sup>a</sup>	48±0.5 <sup>a</sup>
ALT	50.1±0.7	47±0.5	109±1.0	40.5±1.0 <sup>a</sup>	39±0.9 <sup>a</sup>
AST	55.0±0.9	43.6±0.1	104.6±0.4	48.0±1.6 <sup>a</sup>	40±1.7 <sup>a</sup>
T P	6.9±0.4	6.1±0.7	14.2±1.0	6.5±1.09 <sup>a</sup>	6.7±0.3 <sup>a</sup>

Results are expressed as mean ± SEM (n= 5) <sup>a</sup>= p <0.05 represent significant decrease

Note: *Irvingia gabonensis* and *Ocimum gratissimum* extract, D. Control =Diabetic Control, Gilben. = Gilbenclamide.

**Table 4.3:** Effect of Ethanol extract of *Irvingia gabonensis* and *Ocimum gratissimum* on Lipid profile indices

Parameter	Control	D. Control	IGAUGE	IGAUGE
			50 mg/kg	100 mg/Kg
TG	63.0±0.9	108.0±2.0 <sup>d</sup>	50.0±1.0	48.7 ±0.8 <sup>d</sup>
HDL	64.0±0.1	17.05±.4 <sup>d</sup>	49±0.5 <sup>d</sup>	44.5 ±1.7 <sup>d</sup>
LD	51±1.0	180.1±0.3 <sup>d</sup>	24.0±1.2 <sup>d</sup>	26.0 ±1.4 <sup>d</sup>
TC	84.0±3.0	160.6± 0.9 <sup>d</sup>	79.0± 0.2 <sup>d</sup>	78.3± 1.1 <sup>d</sup>

Results are expressed as mean ± SEM (n= 5), significant p-value <0.0001(<sup>d</sup>).

**Key** IGAUGE = *Irvingia gabonensis* and *Ocimum gratissimum* extract, D. Control =Diabetic Control, Gliben. = Gilbenclamide.

## CHAPTER FIVE

### 5.0

### DISCUSSION

Oral acute toxicity refers to the negative effects that arise from ingesting a substance in one or more doses over a 24-hour period (Ofeimum *et al.*, 2021). The acute toxicity study results indicated that the ethanol extract of *Irvingia gabonensis* and *Ocimum gratissimum* showed a significant safety margin, as the animals could tolerate an oral dosage of up to 1000 mg/kg of the extract. According to the toxicity evaluation by the joint FAO/WHO Expert Committee on Food Additives (WHO, 2010), if no fatalities occur at an oral dose of 2000 mg/kg, the substance can be regarded as non-toxic. The considerable safety margin via oral administration supports its therapeutic application by traditional healers.

Blood sugar level tests are conducted to diagnose and monitor diabetes Mellitus, assess metabolism, evaluate insulin function, screen for pre-diabetes and insulin resistance, and investigate symptoms such as hypoglycemia (American Diabetes Association, 2020; WHO, 2019). IGAOGE is a bi-herbal formulation known to contain bioactive compounds that help lower blood sugar levels. The results show ethanol extract of *Irvingia gabonensis* and *Ocimum gratissimum* at a single dose of 1000 mg/kg significantly reduces blood sugar levels for 72 hours. These findings align with two previous studies by (Egesie *et al.*,2022; Mohammed *et al.*, 2024), which reported a notable decrease in blood glucose levels after administering an aqueous extract of *Ocimum gratissimum* at 500 mg/kg in diabetic rats induced by streptozotocin. Additionally, the results corroborate the work of (Dzeufreit *et al.*,2020), which also found a significant reduction in blood glucose levels after administering n-Hexane extract of *Irvingia gabonensis* and *Ocimum gratissimum* in STZ-induced diabetic rats.

Transaminases (AST and ALT) are crucial enzymes that facilitate the conversion of amino acids into  $\alpha$ -keto acids, which are then processed through the Krebs cycle and electron transport chain for complete metabolism. These enzymes serve as specific indicators of liver damage. When liver cells (hepatocytes) are injured, the integrity of the liver cell membrane is compromised, allowing cytoplasmic enzymes like AST and ALT to leak into the bloodstream, leading to elevated serum levels. Additionally, alterations in membrane-bound alkaline phosphatase (ALP) can disrupt membrane permeability and affect metabolite transport. The heightened gluconeogenesis and ketogenesis observed in diabetes may contribute to the increased activity of these transaminases, in diabetic rats, raised levels of AST and ALT in serum indicate compromised liver function (Egesie *et al.*, 2022). And reduction in liver indices (AST, ALP, ALT and TP) indicates improved liver function, reduced liver damage or inflammation, increased protein synthesis and resolution of viral hepatitis (Kumar *et al.*, 2022; Li *et al.*, 2020). Administration of IGAOGE to streptozotocin-induced diabetic rats resulted in decreased serum activity of AST, ALT, and ALP at doses of 50 mg/kg and 100 mg/kg compared to the diabetic control group ( $p \geq 0.05$ ), this shows the hepatoprotective abilities of IGAOGE at various doses. These findings align with previous research by (Denis *et al.*, 2023), which demonstrated a significant decrease in ALT and AST levels, indicating the hepatoprotective effects of the hydroethanolic extract of *Irvingia gabonensis* and *Tetrapleura tetraptera*. Additionally, this is consistent with Agbai *et al.* (2012), who also reported notable reductions in AST and ALT levels after administering methanolic extracts of *irvingia gabonensis* and *Ocimum gratissimum* in STZ-induced diabetes. The Total protein decrease slightly in the standard group and the treatment group when compared to the control group but significantly reduce when compared to the

diabetic control group. This shows that IGAOGE has the ability to reduce excessive total protein in any diabetic individuals without any adverse reactions.

Hyperlipidaemia is a common complication of diabetes, primarily resulting from the excessive release of fat from adipose tissue due to inucose utilization, or the suppression of hormone-sensitive lipase by insulin (Sharma *et al.*, 2010). This study observed elevated levels of total cholesterol (TC), triglycerides (TG) , low-density lipoprotein cholesterol (LDLc) and decrease in (HDLc) high- density lipoprotein cholesterol in diabetic rats, consistent with previous findings of increased TG, LDL and TC in diabetic individuals (Nwogor, 2016). Notably, the significant decrease in TG, LDL and TC and increase in HDL observed in the 50 mg/kg and 100 mg/kg treatment groups suggests that IGAOGE may have the potential to improve lipid metabolism disturbances in diabetes. This effect is attributed to the phytochemicals found in *Irvingia gabonensis* and *Ocimum gratissimum*. The increase in HDL helps to prevent and reduce the risk of coronary diseases, certain cancers and stroke. Consequently, the decreased biosynthesis of fatty acids leads to a reduction in the production of VLDL particles, which in turn limits LDL particle formation, resulting in lower serum triglyceride and cholesterol levels (Ali, 2004). This finding aligns with the results of (Ngondi *et al.*, 2025; Dzeufeit *et al.*, 2020), who observed an increase in HDL cholesterol and a decrease in LDL cholesterol in normal rats treated with *Irvingia gabonensis* Kermel oil. Additionally, it supports the study by (Okoduwa *et al.*, 2023), which reported an increase in HDL and reductions in LDL, triglycerides, and total cholesterol in a rat model of Type 2 diabetes that was treated with anti-diabetic fractions from *Ocimum gratissimum* leaves incorporated into a fortified diet.

STZ, a potent diabetes-inducing compound, works by compromising pancreatic function or triggering high blood sugar levels in research animals (Srinivasan and Manikandan, 2022;

Matthews and Favaloro, 2020). The increase in diabetic levels of the diabetic control indicate the diabetogenic effects of STZ, after prolonged exposure. This might be the reason for abnormalities in blood sugar level, lipid profiles (HDL, LDL, TG, TC) and the liver functions (ALT, AST, ALP) of the diabetic control group.

Glibenclamide is a sulfonylureas, which is a known Antidiabetic and hypoglycemic drugs that acts by stimulating the pancreatic B cells to secrete or release more insulin (Akpan *et al.*, 2022). This work shows significant reduction of diabetes and hyperglycemia in the Glibenclamide group from day 5 to day 30. This ascertains that prolonged administration of Glibenclamide has the ability to reduce hyperglycemia and diabetes in diabetic patients.

The animals administered IGAOGE at 50 mg/kg and 100 mg/kg for 30 days administrations through oral route shows similar effects with the standard group (Glibenclamide) and shows significant reduction at  $P \leq 0.0001$  of diabetes compared to the diabetic control group after the 30 days treatment, the IGAOGE might be working with a similar mechanism like glibenclamide as the results gotten from the combinations and glibenclamide were comparable. This shows that IGAOGE has anti diabetic properties and also has a hypoglycemic effect on the streptozotocin induced diabetic rats in the treatment group. The increase in significant reduction of the 100 mg/kg at  $P \leq 0.0001$  might be due to the higher dose administered. The results align with the research conducted by (Denis *et al.*, 2023), which examined samples and effectively demonstrated the antidiabetic properties of the hydroethanolic extract of *I. gabonensis* and *Tetrapleura tetraptera* in STZ induced diabetic also agrees with the study reported by (Akinnsaya and Ajayi, 2024) on Antidiabetic potentials of aqueous leaf extract of *Ocimum gratissimum* and *Veroninia amygdalina* in diabetic induced rabbit.

## CONCLUSION

This study indicates that *Irvingia gabonensis* and *Ocimum gratissimum* have notable anti-diabetic benefits, positioning them as useful complementary treatments for diabetes management. These plants help manage blood sugar levels, enhance insulin effectiveness, reduce bad cholesterols and increase good ones, to decrease the risk of cardiovascular disease risk, decrease oxidative stress, and the acute toxicity shows that it is safe for consumption and providing a natural approach to alleviating diabetes symptoms and associated complications.

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