THE COMPARATIVE EFFECT OF TREATMENT WITH LISINOPRIL/GLIBENCLAMIDE OR AQUEOUS FRACTION OF *CLEOME RUTIDOSPERMA*/*HUNTERIA UMBELLATA* SEED ON BODY WEIGHT, BLOOD GLUCOSE CONCENTRATION, LIPID PROFILE, AND HEMODYNAMICS OF HYPERTENSIVE/DIABETIC WISTAR RATS.

BY

JONAH OTIBHOR FAVOUR

LSC2103764

A PROJECT REPORT SUBMITTED TO THE DEPARTMENT OF BIOCHEMISTRY, FACULTY OF LIFE SCIENCES,

UNIVERSITY OF BENIN,

BENIN CITY

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF A BACHELOR OF SCIENCE (B.Sc.) IN BIOCHEMISTRY

OCTOBER, 2025.

CERTIFICATION

This is to certify that this report was carried out by Otibhor Favour JONAH, with matriculation number LSC2103764 to the department of Biochemistry, Faculty of Life Sciences, University of Benin contributing to the partial fulfillment of the award of Bachelor of science (B.sc) degree in Biochemistry and is approved for its contribution to knowledge and literary presentation.

DR. OLUSANYA OLASHEINDE

(Project Supervisor) Signature and Date

DR. S.I. OJEABURU

(Project Coordinator) Signature and Date

PROF. E.C. ONYENEKE

Head of Department Signature and Date

External supervisor Signature and Date

DEDICATION

I dedicate this work to God Almighty, the source of all knowledge and wisdom.

I would also like to express my heartfelt gratitude to my parents (Mr and Mrs Abhulimen), my Pastors (Pastor John and Pastor Nancy Jibril),my sister and friends. Their unwavering moral support, encouragement, and belief in my abilities have been instrumental in my academic journey.

This dedication I tribute to their love, sacrifices and continuous encouragement.

ACKNOWLEDGEMENTS

I sincerely thank Almighty God for His unwavering strength, guidance, and provision throughout this journey. My heartfelt appreciation goes to my project supervisor, **Dr. Olusanya Olaseinde**, for his invaluable support and guidance during the course of the experiment and the preparation of this report.

I also wish to extend my gratitude to our laboratory technician, **Dr. Akpe**, and **Mr. Ibeh**, for their technical assistance and dedication. Special thanks to the Head of Department, **Prof. E. C. Onyeneke**, for granting me the opportunity to enhance my academic and research skills through this project.

My deepest appreciation goes to my parents, **Mr. and Mrs. Abhulimen**, and my siblings for their constant encouragement, love, and support throughout my studies in the Department of Biochemistry, University of Benin.

Finally, I express sincere thanks to my project colleagues and the entire research team for their teamwork, cooperation, and commitment, which greatly contributed to the successful completion of this work.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABSTRACT

This study evaluated the comparative effects of standard pharmacotherapy (Lisinopril/Glibenclamide) and an aqueous extract combination of *Cleome rutidosperma* and *Hunteria umbellata* on metabolic and cardiovascular parameters in hypertensive/diabetic rats. The hypertensive/diabetic rats showed reduced body weight, elevated fasting blood glucose, and increased blood pressure indices confirming disease induction. Treatment with Lisinopril/Glibenclamide significantly restored body weight and normalized blood glucose and blood pressure. The plant extract also improved these parameters, with a more pronounced effect on weight gain, moderate glucose lowering, and significant reductions in systolic, diastolic, and mean arterial pressures. Cardiovascular autonomic function was improved as indicated by heart rate stabilization. Lipid profile analysis revealed that, while standard therapy unexpectedly increased total cholesterol and LDL cholesterol, the combined Cleome/Hunteria extract markedly improved lipid profiles by reducing total cholesterol, LDL cholesterol, triglycerides, and eliminating detectable VLDL levels, while significantly increasing HDL cholesterol. These results suggest that the plant extract may modulate lipid metabolism more effectively than standard drugs. Overall, the findings demonstrate that *Cleome rutidosperma* and *Hunteria umbellata* aqueous extract exert beneficial effects on anthropometric, glycemic, hemodynamic, and lipid parameters in hypertensive/diabetic rats. This suggests potential cardiometabolic protective properties via biochemical pathways involving glucose homeostasis, vascular tone regulation, and lipid metabolism. Further mechanistic and clinical investigations are warranted to confirm its therapeutic viability. This summary aligns with literature reporting reduced body weight gain in hypertensive and diabetic rat models due to metabolic derangement and catabolism. The plant extract's enhancement of body weight may reflect improved anabolic state and nutrient utilization, while its lipid-lowering effect suggests modulation of lipoprotein metabolism enzymes.

CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW

INTRODUCTION TO HYPERTENSION AND DIABETES UNDER COMORBIDITY DISORDER

Hypertension is a long- term health disorder is characterized by persistent elevation in the systolic BP ≥140 and/or diastolic BP ≥90 mmHg, which is equivalent to a 24-hr ambulatory blood pressure monitoring (ABPM) average of ≥130/80 mmHg or an home blood pressure monitoring (HBPM) average of ≥135/85 mmHg (Ramzy, 2019). It is a major global health challenge and one of the leading risk factors for serious complications such as cardiovascular disease, stroke, kidney damage, premature death, and metabolic disorders including diabetes mellitus.

Diabetes mellitus (DM), like hypertension, is a wide-spread health problem associated with end organ damage, dysfunction, and failure in organs and tissues including the retina, kidney, nerves, heart, and blood vessels. It is defined as a state of hyperglycemia in either fasting or postprandial states (Alam *et al.,*2014)

The coexistence of hypertension and diabetes greatly increases the risk of target organ damage, including heart failure, kidney disease, and cerebrovascular accidents, making their comorbidity a serious public health concern (Naha *et al.,*2021). When both hypertension and diabetes are present in an individual, their overlapping effects create a stronger combined influence, thereby escalating the risk of cardiovascular, renal, and cerebrovascular complications (American Diabetes Association, 2022).

Because of the severe health risks linked to the coexistence of hypertension and diabetes, lifestyle modification remains a cornerstone of prevention. Practices such as maintaining a

balanced diet, engaging in regular exercise, achieving healthy body weight, and avoiding smoking or excessive alcohol intake are strongly recommended (World Health Organization, 2023). Alongside these measures, strict compliance with prescribed medications and continuous medical follow-up are critical in lowering complications and enhancing overall wellbeing (American Diabetes Association, 2022). In this context, examining the history and prevalence of both disorders provides a clearer understanding of their magnitude and the increasing burden they pose on public health.

1.1.2 HISTORY OF THE PREVALENCE OF HYPERTENSION AND DIABETES

Both hypertension and diabetes have been recognized for thousands of years, with early medical writings describing their symptoms long before their underlying causes were understood. Over time, advances in medical science provided clearer definitions and treatment strategies, turning these conditions from mysterious ailments into well-studied disorders (Carretero and Oparil, 2000).

1.1.2.1 HISTORY OF HYPERTENSION

Hypertension has been recognized since ancient times, with Chinese medical records as early as 2600 BCE describing it as the “hard pulse disease,” a term used to characterize the sustained force of the arterial pulse (Carretero and Oparil, 2000).

References to symptoms resembling high blood pressure were also noted by Egyptian and Greek physicians, although the condition was not scientifically explained.

A significant advancement occurred in 1896 when Scipione Riva-Rocci introduced the sphygmomanometer, an instrument that allowed physicians to measure blood pressure accurately and laid the groundwork for modern understanding and management of hypertension (Oparil and Schmieder, 2015).

1.1.2.2 HISTORY OF DIABETES MELLITUS (DB)

The history of diabetes can be traced back to ancient Egypt, where the Ebers Papyrus of about 1500 BCE described an illness characterized by frequent urination, now known as diabetes mellitus (Tattersall, 2009).

In the 2nd century CE, the Greek physician Aretaeus of Cappadocia gave a detailed description of the disease and introduced the term “diabetes,” meaning “to pass through.”

A major breakthrough came in 1921 when Frederick Banting and Charles Best discovered insulin, which changed diabetes from a fatal condition to one that could be controlled as a long-term disorder (Bliss, 1982)**.**

1.1.2.3 PREVALENCE OF HYPERTENSION AND DIABETES

The occurrence of hypertension and diabetes has changed dramatically over time, moving from uncommon disorders to major global health concerns. In the early 20th century, both conditions were rarely reported, partly because of poor diagnostic capacity and limited awareness. Hypertension, for example, was only widely recognized after the introduction of the sphygmomanometer in the late 19th century, which made routine blood pressure measurement possible (Carretero and Oparil, 2000). Diabetes, though known in ancient medicine, became more prominent in the mid-20th century as industrialization, dietary shifts, and urbanization increased its prevalence (Tattersall, 2009).

Global data reflect this steady rise. The number of people with diabetes was about 30 million in 1985, rising to more than 150 million by 2000, and over 422 million by 2014. Current projections suggest the number may exceed 800 million by 2045 (WHO, 2016). Hypertension has also grown rapidly: around 600 million adults were affected in 1980, increasing to about 1.28 billion by 2019, with most of the increase occurring in low- and middle-income regions (NCD Risk Factor Collaboration, 2021). Lifestyle changes such as obesity, reduced physical activity, and aging populations are central drivers of these shifts.

Countries like Nigeria shows a similar historical pattern. Surveys from the 1960s and 1970s recorded hypertension rates below 10% (Akinkugbe, 1972). Today, however, over one-third of Nigerian adults are hypertensive, particularly in cities where lifestyle risk factors are more common (Adeloye *et al.,* 2015). Diabetes followed a comparable path: its prevalence was below 1% in the 1960s, but urban studies in the 1980s already revealed a rapid rise in undiagnosed cases (Ohwovoriole *et al.,* 1988). Recent reviews now estimate national rates between 5% and 10%, with obesity and sedentary lifestyles contributing to the increase (Uloko *et al.,* 2018).

Overall, the historical rise in hypertension and diabetes both globally and in Nigeria shows how modernization and lifestyle transitions have turned these conditions into widespread epidemics, creating a major public health challenge.

1.1.3 TYPES OF HYPERTENSION

Hypertension can be grouped into many categories according to the underlying etiology, the degree of blood pressure elevation, and the efficiency of treatment.

1.1.3.3 PRIMARY HYPERTENSION:

Primary (also called essential or idiopathic) hypertension refers to elevated blood pressure that occurs without secondary causes such as renovascular disease, kidney failure, pheochromocytoma, aldosteronism, other secondary hypertension conditions, or monogenic (Mendelian) forms. It represents about 95% of all hypertension cases. This type of hypertension is believed to be caused by several factors such as obesity, insulin resistance, excessive alcohol consumption, and a high salt intake, particularly in salt-sensitive individuals. Other contributing elements include aging, a sedentary lifestyle, psychological stress, and inadequate intake of potassium and calcium (Carretero and Oparil,2000). The condition is influenced by mechanisms including heightened sympathetic nervous system activity, endothelial dysfunction, and an imbalance within the renin-angiotensin-aldosterone system (RAAS).

1.1.3.4 SECONDARY HYPERTENSION: Secondary hypertension refers to elevated blood pressure caused by an identifiable and often reversible underlying condition. It accounts for approximately 5% to 10% of all hypertension cases. The occurrence of secondary hypertension differs across age groups, being notably higher in younger adults—around 30% among individuals aged 18 to 40 who have hypertension (Charles *et al.,* 2017). Among young adults, especially women, renal artery stenosis due to fibromuscular dysplasia is a leading cause of secondary hypertension. This condition can be diagnosed through abdominal magnetic resonance imaging (MRI) or computed tomography (CT), which are also effective for identifying atherosclerotic renal artery stenosis—a common cause of secondary hypertension in older individuals. In middle-aged adults, primary aldosteronism is the most frequent secondary cause, and the initial screening test of choice is the aldosterone-to-renin ratio. In contrast, up to 85% of hypertensive children have an identifiable underlying condition, most

commonly renal parenchymal disease (Viera *et al.,* 2010). The primary approach to treating secondary hypertension typically focuses on addressing its root cause (Messerli *et al*., 2017).

1.1.4 TREATMENT OF HYPERTENSION

The initial approach to managing hypertension involves lifestyle changes, including weight reduction, adopting a balanced diet with reduced sodium and increased potassium, engaging in regular physical activity, and limiting or avoiding alcohol intake. These lifestyle measures have additive effects on lowering blood pressure and complement the benefits of medication.

The decision to start antihypertensive drugs depends on blood pressure levels and the individual's atherosclerotic (Cardiovascular)CVD risk. First-line medications typically include thiazide or thiazide-like diuretics (e.g., hydrochlorothiazide, chlorthalidone), ACE inhibitors or ARBs (e.g., enalapril, candesartan), and calcium channel blockers (e.g., amlodipine). Dosages are adjusted based on office and home (blood pressure) BP readings to achieve a target of less than 130/80 mm Hg in adults younger than 65 and (Systolic Blood Pressure)SBP below 130 mm Hg in those 65 and older. Clinical trials have confirmed that reducing BP significantly lowers the risk of CVD-related and death. A 10 mm Hg decrease in SBP can reduce CVD event risk by about 20% to 30% (Carey *et al.,* 2022).

1.1.5 TYPES OF DIABETES

Gaining insight into the different types of diabetes is vital for enhancing care quality and improving health outcomes.

- **TYPE 1 DIABETES MELLITUS (T1D):** Type 1 diabetes mellitus (T1D) is an autoimmune condition that results in the destruction of pancreatic beta cells, ultimately causing a total absence of insulin (Haller *et al.,* 2005). Both environmental and genetic factors influence this condition. A genetic tendency associated with specific Human Leukocyte Antigen (HLA-DR and HLA-DQ) alleles, along with environmental factors such as viral infections, early exposure to cow's milk, and insufficient vitamin D, contribute to the development of diabetes mellitus (Ziegler *et al*., 2013). Common symptoms include excessive urination, increased thirst, weight loss, and fatigue, often appearing abruptly, particularly during childhood or adolescence.

- **TYPE 2 DIABETES MELLITUS (T2D) :** Type 2 DM (formerly known as non-insulin dependent DM) is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency (Olokoba *et al.,* 2012). T2 D results from interaction between genetic, environmental and behavioral risk factors (Chen *et al.,* 2011). Obesity is considered a major contributing factor to the development of T2D. Excess body fat, especially around the abdomen, leads to insulin resistance, where body cells fail to respond effectively to insulin. This results in increased blood glucose levels, eventually causing T2D. Obesity also triggers chronic low-grade inflammation, further impairing insulin action. Maintaining a healthy weight is one of the key strategies in preventing T2D (Malone *et al.,* 2019).

Other forms of diabetes include ;

- **Gestational Diabetes Mellitus (GDM):** Develops during pregnancy in women who were not previously diabetic. It is caused by hormonal changes leading to insulin resistance and usually resolves after childbirth, but increases the risk of T2D later in life.
- **Prediabetes**: It is a condition where blood glucose levels are higher than normal but not yet diabetes. It increases risk of developing T2D and cardiovascular disease. It is often managed with diet and exercise.
- **Monogenic Diabetes** (e.g., MODY) : Caused by single gene mutations.
- **Secondary Diabetes** : This is cue to other conditions (e.g., pancreatic disease, hormonal disorders) or medications (e.g., steroids).
- **Neonatal Diabetes** : It occurs in infants within first 6 months of life due to genetic factors.

1.1.6 TREATMENT OF DIABETES

Modern insulin therapy is essential in diabetes management, especially for individuals with type 1 diabetes, where it is crucial for survival, and for patients with advanced type 2 diabetes who often require it. Current options include rapid-acting, long-acting, and premixed insulin formulations that aim to mimic the body's natural insulin secretion. Common approaches include the basal-bolus regimen, which combines long-acting insulin with doses at mealtimes, and continuous subcutaneous insulin infusion (CSII) using insulin pumps that deliver insulin steadily and accurately (Davies *et al*., 2018).

Oral medications are a key component in managing type 2 diabetes, providing various options that can be tailored to an individual's condition and disease stage. Metformin is commonly used as the first-line therapy due to its ability to enhance insulin sensitivity and reduce glucose production in the liver, along with its strong safety profile. Other drug classes, such as sulfonylureas, help stimulate insulin release but carry a higher risk of hypoglycemia. Newer options like SGLT2 inhibitors aid in lowering blood sugar by promoting glucose excretion through urine while also offering cardiovascular benefits, and DPP-4 inhibitors improve the activity of incretin hormones to control post-meal glucose levels (Zinman *et al.,* 2015).

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are injectable medications that support weight loss and enhance blood sugar control. They are increasingly prescribed for individuals with type 2 diabetes, particularly those who are overweight or obese (Marso *et al*., 2016).

Spanish researchers attribute the significant rise in obesity within society primarily to the high-calorie content of modern diets and increasingly sedentary lifestyles. Their studies indicate that personalized nutrition plans combined with physical exercise can play a crucial role in effectively preventing or delaying the onset of related diseases. They further emphasize that engaging in regular, moderate physical activity is essential for both prevention and treatment, making it one of the most effective strategies (Suryasa *et al.,*2021).

The choice of medication depends on factors such as blood sugar targets, coexisting health issues, and patient preferences, allowing for individualized treatment plans.

1.1.7 UNDERLYING CHALLENGES ASSOCIATED WITH THE COEXISTENCE OF HYPERTENSION AND DIABETES

1.1.7.1 CARDIOVASCULAR COMPLICATIONS

A patient living with both diabetes and hypertension (CDH) requires exceptional care, as this combination significantly increases the risk of heart attack and stroke. Research indicates that approximately 29% of individuals with coexisting diabetes and hypertension (CDH) are unaware of their elevated blood pressure. Research suggests that managing blood pressure plays a more crucial role in reducing morbidity and mortality among CDH patients than blood glucose control (Taliaferro and Dey, 2017).

1.1.7.2 RENAL DYSFUNCTION

Diabetes is a leading cause of kidney failure, with about 40% of individuals with diabetes developing chronic kidney disease.Hypertension and diabetes mellitus are the primary contributors to end-stage renal disease (ESRD). In the United States, diabetes and hypertension are responsible for approximately 50% and 27% of all ESRD cases, respectively. Elevated blood pressure further increases the risk of developing ESRD. When chronic hypertension occurs alongside diabetes, it accelerates the decline in kidney function. Research indicates that maintaining blood pressure below 130/80 mmHg can slow or prevent kidney damage in diabetic patients (Hezam *et al.,* 2024).

1.1.7.3 NEUROPATHY AND RETINOPATHY

Having both hypertension and diabetes heightens the likelihood and intensity of microvascular complications like neuropathy and retinopathy. Elevated blood pressure aggravates the vascular damage induced by hyperglycemia, speeding up nerve damage and retinal vessel changes, which results in quicker progression of these conditions (American Diabetes Association, 2023).

1.1.7.4 MEDICATION AND MANAGEMENT CHALLENGES

Managing both hypertension and diabetes is challenging due to polypharmacy, adherence issues, and potential drug interactions, requiring strict control of blood pressure and glucose to prevent complications (Cheung *et al.,* 2010).

1.2 LITERATURE REVIEW

1.2.1 EFFICACY OF MEDICINAL PLANTS IN TREATMENT OF THE COEXISTENCE OF HYPERTENSION AND DIABETES

Medicinal plants have long been integral to healthcare systems worldwide and remain essential, especially in developing nations. Reports indicate that nearly 80% of people in these regions rely on traditional remedies, predominantly herbal medicine, to meet their primary healthcare and socio-economic needs (Asafo-Agyei *et al.,* 2023).

The therapeutic effects of these medicinal plants are diverse and multifaceted. One major mechanism is their antioxidant activity, which helps to mitigate oxidative stress, a factor that contributes to vascular damage and disrupted glucose metabolism (Moradi *et al*., 2018).

Certain plants act by inhibiting enzymes such as α-amylase and α-glucosidase, thereby slowing the breakdown of carbohydrates and assisting in blood sugar regulation (Shishu and Aggarwal, 2011). Other plants enhance insulin sensitivity, promoting more efficient glucose uptake by cells, while some exhibit vasodilatory effects that help to reduce blood pressure (Alarcon-Aguilar and Reyes-Chilpa, 2004). The interplay of these mechanisms likely underpins their effectiveness in managing both hypertension and diabetes simultaneously.

Recent clinical studies provide additional support for the potential of these herbal remedies. Systematic reviews indicate that some plants can lower HbA1c levels similarly to standard antidiabetic drugs, although longer-term studies are necessary to confirm these outcomes (Asafo-Agyei *et al*., 2023). Herbal interventions have also been shown to reduce blood pressure in prehypertensive and hypertensive individuals, particularly when combined with lifestyle modifications or conventional antihypertensive therapies (Akinmoladun and Olaleye, 2019).

Despite these encouraging results, challenges remain regarding safety, as inconsistencies in preparation, possible interactions with medications, and a lack of standardized dosing can affect their efficacy and, in some instances, pose health risks.

Overall, medicinal plants offer a promising avenue for addressing coexisting hypertension and diabetes, providing benefits through antioxidant, enzyme-inhibiting, vasodilatory, and insulin-sensitizing effects. Nevertheless, their use should be carefully monitored by healthcare professionals, and further rigorous clinical trials are needed to develop standardized and safe treatment protocols (Moradi *et al*., 2018).

1.2.2 CONDITIONS AND DISEASES ASSOCIATED WITH SIDA ACUTA, *CLEOME RUTIDOSPERMA* AND *HUNTERIA UMBELLATA*

1.2.2.1 *SIDA ACUTA*

Sida acuta, commonly referred to as "Wireweed" or "Bala" in Ayurveda, is a small, perennial shrub belonging to the Malvaceae family. It holds a significant place in traditional medicine systems due to its diverse therapeutic applications and adaptability to different ecological conditions (Kumar *et al*., 2016). The species is widely distributed in tropical and subtropical regions, including Africa, Asia, and the Americas, where it typically grows along roadsides, in open fields, and on disturbed soils (Pradhan *et al*., 2020).

The plant is known by various regional names and has been an important component of indigenous medicinal practices for centuries. In Ayurvedic medicine, S. acuta is recognized for its balya (strength-enhancing) and vedana sthapana (pain-relieving) properties (Patel *et al*., 2018). Its extensive pharmacological potential is attributed to a rich composition of bioactive molecules such as alkaloids (including ephedrine and vasicine), flavonoids, steroids, tannins, and other phenolic compounds (Suresh *et al*., 2019).

This plant demonstrates a wide range of pharmacological activities, including antimicrobial, anti-inflammatory, antipyretic, antidiabetic, hepatoprotective, and wound-healing effects (Okoye *et al*., 2017). Additionally, its extracts have been shown to possess antimalarial and antioxidant properties, making it a valuable candidate for developing herbal-based formulations (Ezeonwumelu *et al*., 2018). The presence of ephedrine-like alkaloids contributes to its stimulant and bronchodilator actions, which are particularly useful in managing respiratory disorders such as asthma and bronchitis (Anjaneyulu *et al*., 2015).

Although S. acuta has a long history of traditional use, its safety and toxicity profile remains insufficiently explored, especially in the context of modern pharmacological validation. With the growing global interest in herbal medicines, comprehensive research on its phytochemical composition and safety evaluation is essential before widespread clinical application. This study aims to investigate the safety and therapeutic potential of *Sida acuta* leaves as an initial step towards their rational and evidence-based utilization in herbal medicine.

Fig 1.1 *Sida acuta* (Source: University of Benin field).

1.2.2.2 *CLEOME RUTIDOSPERMA*

CLEOME RUTIDOSPERMA, commonly known as fringed spider flower or purple cleome, is a small annual herbaceous plant belonging to the family Cleomaceae. Native to tropical

Africa, the species has now naturalized across much of tropical Asia, the Pacific, and the Americas, thriving particularly in disturbed habitats such as roadsides, gardens, agricultural fields, and lawns (Orwa *et al*., 2009). Morphologically, it is characterized by trifoliate leaves, slender stems, violet to purple flowers with elongated stamens, and long seed pods that dehisce to release black seeds (Burkill, 1985). While often considered an invasive weed in many agricultural ecosystems, its traditional and pharmacological significance has drawn considerable attention in ethnobotanical and scientific studies.

Ethnomedicinally, C. rutidosperma has been used for centuries in Africa and Asia to manage a variety of health conditions. The leaves and roots are commonly employed to treat fever, diarrhea, convulsions, ear infections, and skin disorders. Topical applications of crushed leaves serve as poultices for wounds, inflammation, and other dermatological issues, while in certain regions the plant has been reported as a remedy for snakebite (Kpodar *et al*., 2016). Beyond medicinal use, young leaves are consumed as a leafy vegetable, highlighting its nutritional relevance in rural diets. Its widespread availability and ease of growth contribute to its continued use as a readily accessible source of traditional medicine.

Phytochemical investigations of C. rutidosperma reveal a rich profile of bioactive compounds including flavonoids, alkaloids, tannins, saponins, glycosides, and phenolic compounds (N'guessan *et al*., 2009). These secondary metabolites are believed to underlie the plant's diverse pharmacological activities. Experimental studies have demonstrated that extracts of the plant exhibit strong antioxidant activity, antimicrobial effects against pathogenic bacteria and fungi, anti-inflammatory and analgesic properties, and in vitro antiplasmodial activity against Plasmodium species (Kpodar *et al*., 2016). Such findings corroborate the traditional uses of the plant, although most evidence remains limited to in vitro and small animal studies, with clinical validation in humans still lacking.

The ecological adaptability of C. rutidosperma enhances its value both as a resilient weed and as a medicinal resource. Its ability to thrive in low-nutrient soils and disturbed habitats makes it widely available in regions where healthcare resources may be limited.

Fig 1.2 *CLEOME RUTIDOSPERMA* (Source: University of Benin football field).

1.2.2.3 *HUNTERIA UMBELLATA*

Hunteria umbellata is a small tree or shrub in the Apocynaceae family, native to tropical Africa, including Nigeria, Cameroon, Ghana, and Angola. It is locally referred to as "Osu" by the Igbo, "Abeere" by the Yoruba, and "Npokiri" by the Edo people (Adeneye and Adeyemi, 2009). The plant is widely valued for its medicinal properties, with different parts used traditionally to manage numerous health conditions.

Traditionally, the seeds, bark, and leaves are prepared as infusions or decoctions to treat fever, diarrhea, convulsions, ear infections, skin ailments, abdominal colic, and digestive discomfort (Falodun *et al*., 2006). Crushed leaves are applied topically to wounds and inflammation, while seeds are used to manage diabetes. The leaves and pulp are also used in obstetric care to prevent complications such as dystocia and unwanted abortions (Owolabi and Olorunfemi, 2007). Young leaves may be consumed as a vegetable, and the durable, termite-resistant wood is useful for furniture and tools (Orwa *et al*., 2009).

Phytochemical analyses have shown that H. umbellata contains alkaloids, anthraquinones, saponins, tannins, flavonoids, and glycosides (Adegoke and Alo, 1986). GC-MS studies of methanol extracts identified compounds such as 2,2′-Benzylidene Bis(3-methylbenzofuran), caffeine, urs-12-en-24-oic acid, and methyl stearate (Falodun *et al*., 2006). These bioactive compounds contribute to the plant's pharmacological activities, which include antioxidant, anti-inflammatory, analgesic, antimicrobial, anxiolytic, antihyperglycemic, anti-obesity, and potential anticancer effects (Owolabi and Olorunfemi, 2007).

Experimental studies support these traditional applications. Aqueous seed extracts have demonstrated anxiolytic effects and improvements in hematological parameters such as hemoglobin, packed cell volume, and platelet counts in rats (Adeneye and Adeyemi, 2009). Methanol leaf extracts exhibited cytotoxic activity against some cancer cell lines, while seed extracts reduced blood sugar levels and inhibited intestinal glucose absorption in diabetic animal models (Falodun *et al*., 2006). Antimicrobial activity against Escherichia coli and Streptococcus species has also been reported (Owolabi and Olorunfemi, 2007).

Despite these promising findings, caution is necessary regarding prolonged or high-dose use, and further toxicological and clinical studies are required to determine safe and effective dosages (Adeneye and Adeyemi, 2009). Overall, *Hunteria umbellata* is a versatile plant with considerable ethnomedicinal, pharmacological, nutritional, and ecological significance. Continued research could validate its traditional uses and support its development as a therapeutic resource in modern medicine.

Fig 1.3 *Hunteria umbellata seeds* (Source: New Benin Market, Edo State).

1.2.3 AIM OF THE RESEARCH

The primary objective of this research is to assess the pharmacological efficacy of specific medicinal plants; *CLEOME RUTIDOSPERMA*, Sida acuta, and Hunteria umbellata, in addressing hypertension and diabetes, with an emphasis on their potential pancreatic-protective effects in male Wistar rats. In light of the escalating global and national prevalence

of these metabolic conditions, particularly in resource-constrained environments like Nigeria, this study aims to enhance the scientific validation of plants that have been utilized in traditional medicine for centuries. By exploring their antihypertensive and antidiabetic characteristics, this investigation offers valuable insights into their therapeutic significance, safety, and possible incorporation into evidence-based healthcare.

1.2.4 OBJECTIVES OF THE RESEARCH \

\1. To assess the antihypertensive properties of *CLEOME RUTIDOSPERMA*, Sida acuta, and *Hunteria umbellata* extracts in male Wistar rats, with a focus on their capacity to influence blood pressure levels and related cardiovascular metrics.

2. To evaluate the antidiabetic effects of these plant extracts by analyzing their impact on blood glucose control, insulin sensitivity, and lipid metabolism in rats with experimentally induced diabetes.

3. To explore the pancreatic-protective properties of the chosen plant extracts, emphasizing histological examinations of pancreatic tissues to ascertain whether these plants can prevent or alleviate β-cell injury and dysfunction.

4. To compare the effectiveness of the plant extracts from the three species, identifying both similarities and differences in their pharmacological effects.

5. To enhance scientific understanding by substantiating the traditional applications of these plants in the treatment of metabolic disorders, thus bridging the divide between ethnomedicine and contemporary pharmacology.

Through these aims, the research is anticipated to underscore not only the therapeutic potential of *CLEOME RUTIDOSPERMA*, Sida acuta, and *Hunteria umbellata* but also the necessity for additional investigations into their bioactive compounds, mechanisms of action, and clinical relevance.

CHAPTER TWO

MATERIALS AND METHODS

2.1 MATERIALS

Plants: *Sida acuta* and *Cleome rutidosperma* plants were harvested around the Department of Biochemistry environment while the seed plants, Hunteria umbrellate was in Oba Market at ring road and New Benin Market, Benin City, Edo State. The plants were conveyed firstly to the Department of Plant Biology and Biotechnology(PBB) for identification by Prof Akinnibosun Adewale Henry. Voucher Numbers UBH-S454(soda acuta), UBH-C148 (Cleome rutidosperma), and UBH-H637 (*HUNTERIA UMBELLATA*) were given to the individual plants for reference purpose and deposited at the herbarium for a while. Thereafter, the plants were taken to the Department of Biochemistry Laboratory for about 20 days for air-drying and then pulverised at the Department of Pharmacology Laboratory in the University of Benin.

Animals: Thirty-five (35) healthy male Wistar rats were obtained and housed in the animal facility of the Department of Biochemistry, Faculty of Life Sciences, University of Benin. The rats were fed with Happy Chicken Feed Growers Pellet (Nigeria), provided with clean drinking water, and acclimatized using restrainers for a period of two weeks. Their cages were cleaned daily in the morning before feeding.

2.2 DRUGS/CHEMICALS

- L-NAME (Nω-Nitro-L-arginine methyl ester)
- Streptozotocin (STZ)
- Lisinopril
- Glibenclamide
- Formal saline
- Urethane
- Sterile citrate buffer
- Picric acid

Fig 2.1: Glibenclamide (Source: Osagie-Eweka Laboratory)

Fig 2.2 Lisinopril (Source: Osagie-Eweka Laboratory)

2.3 EQUIPMENTS

- Restrainer
- Sensitive weighing balance
- Glucometer and test strips
- Centrifuge
- Hand gloves
- Cotton wool
- Refrigerator
- pH meter
- Syringe
- Set of test tubes
- Pipette
- Sterile water
- Distilled water
- Cholesterol randox
- HDL randox
- Sodium Teco
- Potassium Teco
- Creatinine randox

- Urea Agape
- Agape GGT
- Enzyme Linked Immunosorbent Assay (ELISA) kit

Fig 2.3 Centrifuge (Source: Osagie-Eweka Laboratory)

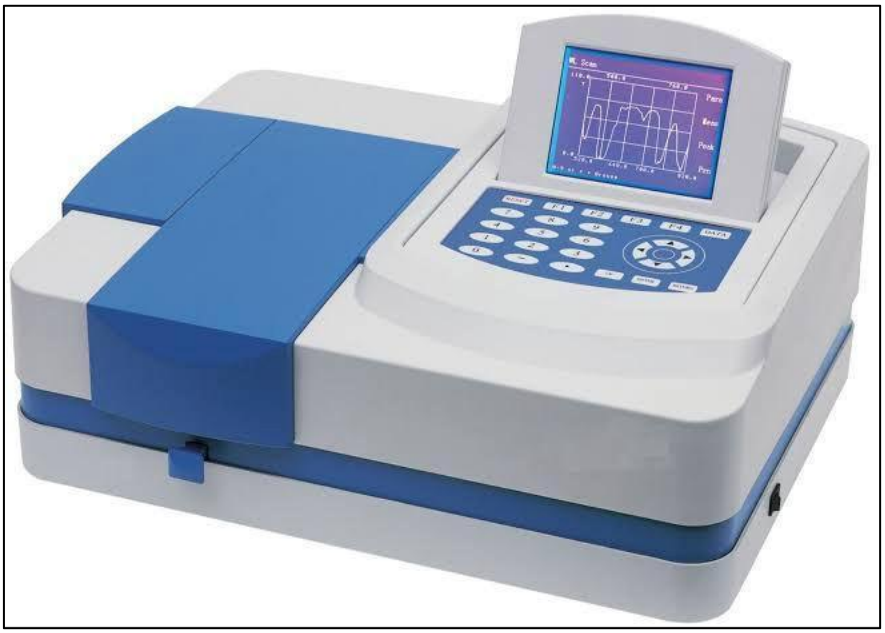

Fig 2.4. Spectrophotometer (Source : Google)

Fig 2.5 Weighing balance (Source: Osagie-Eweka Laboratory)

Fig 2.6 Sterile water (Source: Osagie-Eweka Laboratory)

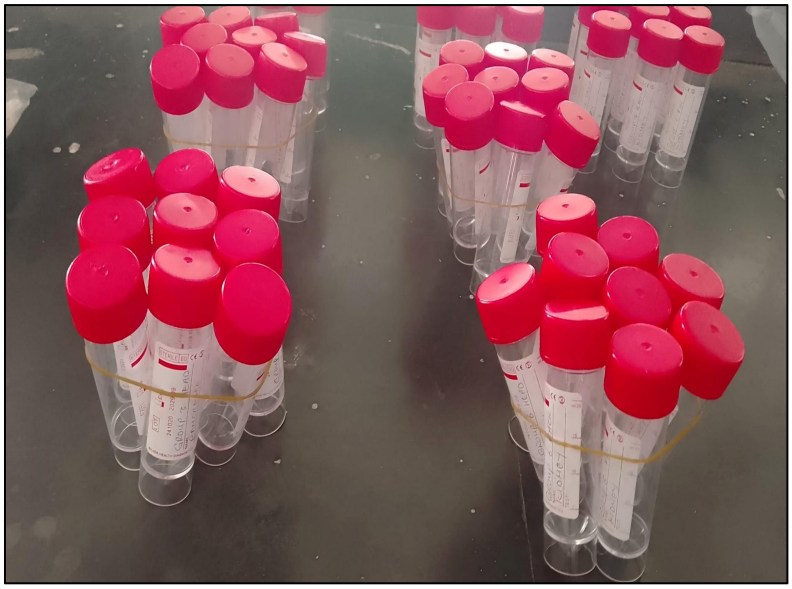

Fig 2.7 Universal Bottle for Histology (Source: Dr. Osagie-Eweka Laboratory)

2.4 PROCEDURE FOR PLANT SAMPLE COLLECTION

Fresh leaves of *Sida acuta* and *CLEOME RUTIDOSPERMA* were collected from the surroundings of the Department of Biochemistry, University of Benin. The seeds of *Hunteria umbellata* were purchased from a local market in New-Benin, Benin City, Edo State. All samples were taken to the Department of Biochemistry Laboratory, where they were kept for about 17 days before being pulverized at the Department of Pharmacognosy Laboratory, University of Benin.

2.5 EXPERIMENTAL DESIGN

The animals were grouped into 7, with 4-6 animals in each group.

Group 1: (Normotensive/ non-diabetic) Positive control; Rats in this group were fed daily with normal feed and tap water without the administration of L-NAME (40 mg/kg)/Streptozotocin (50 mg/kg) and aqueous/methanol extract.

Group 2: (Hypertensive/diabetic) Negative control; Rats in this group were fed with normal feed and tap water daily with administration of L-NAME (40 mg/kg)/Streptozotocin (50mg/kg) and no administration of aqueous/methanol extract.

Group 3: (Hypertensive/Diabetic Group + treated with Lisinopril/Glibenclamide); Rats in this group were fed with normal feed and tap water daily with administration of L-NAME (40 mg/kg)/Streptozotocin (50 mg/kg) and Lisinopril (10 mg/kg)/Glibenclamide (5mg/kg) without the administration of aqueous/methanol extract.

Group 4: (Hypetensive/Diabetic treated with *Sida acuta* and *CLEOME RUTIDOSPERMA*) Aqueous extract; Rats in this group were fed daily with normal feed and tap water with the administration of L-NAME (40 mg/kg)/Streptozotocin (50 mg/kg) and Sida acuta/*CLEOME RUTIDOSPERMA* aqueous extract (50 mg/kg).

Group 5: (Hypetensive/Diabetic treated with *Sida acuta* and *CLEOME RUTIDOSPERMA*) Methanol extract; Rats in this group were fed daily with normal feed and tap water with the administration of L-NAME (40 mg/kg)/Streptozotocin (50 mg/kg) and Sida Acuta/*CLEOME RUTIDOSPERMA* methanol extract (50 mg/kg).

Group 6: (Hypetensive/Diabetic treated with *CLEOME RUTIDOSPERMA* and Hunteria umbellata) Aqueous extract; Rats in this group were fed daily with normal feed and tap water with the administration of L-NAME (40 mg/kg)/Streptozotocin (50 mg/kg) and Cleome rutidosperma/*Hunteria umbellata* aqueous extract (50 mg/kg).

Group 7: (Hypetensive/Diabetic treated with *CLEOME RUTIDOSPERMA* and Hunteria umbellata) Methanol extract; Rats in this group were fed daily with normal feed and tap water with the administration of L-NAME (40 mg/kg)/Streptozotocin (50 mg/kg) and *CLEOME RUTIDOSPERMA*/*Hunteria umbellata* methanol extract (50 mg/kg). The rats were also marked with picric acid in specific parts such as head, back, left hind (LH) limb, right hind (RH) limb, right fore (RF) limb and left fore (LF) limb in each group for identification.

Figure 2.8 Labelling of the Rat Distribution into Groups (Source: Animal House, University of Benin's Biochemistry department).

2.6 MEASUREMENT OF BODY WEIGHT

The body weight of the rats was tracked both prior to and throughout the treatment period. Readings were taken weekly during the period preceding induction and treatment. On average, the rats had an initial body weight of approximately 60 g before the treatment began.

2.7 EXPERIMENTAL INDUCTION OF HYPERTENSION AND DIABETES IN ANIMAL MODELS

Various pharmacological agents such as L-NAME and Streptozotocin are used to model hypertension and diabetes respectively in experimental studies. L-NAME, a nitric oxide synthase inhibitor resulted in elevated systolic blood pressure, accompanied by cardiovascular remodeling, increased oxidative stress, and activation of the renin-angiotensin system, thus inducing Hypertension (Inchan *et al*, 2025). Streptozotocin (STZ) is an antibiotic agent induced type 1 diabetes mellitus (T1DM) by selectively destroying pancreatic islet β-cells (Furman, 2021).

2.8 PREPARATION OF PLANT OF EXTRACTS

2.8.1 *Cleome rutidosperma*

The *Cleome rutidosperma* plant sample was divided into two portions each equally weighing 189g. One of the 189g plant *Cleome rutidosperma* plant sample was submerged in distilled water while the other was submerged in 99.8% methanol. By standardization, 500g of sample is dissolved in 2.5L of solvent. Thus, each 189g *Cleome rutidosperma* plant sample were dissolved in 0.945L (945ml) of distilled water and methanol. The samples were left to dissolve properly after which they were vortexed every 2 hours. They were then extracted using muslim cloth after 24 hours to obtain filtrate and then re-submerged using the same volume of extracts for another 24 hours. The same procedure was carried out to obtain filtrate.

2.8.2 *Sida acuta*

The *Sida acuta* plant sample was divided into two portions each equally weighing 156g. One of the 189g plant *Sida acuta* plant samples was submerged in distilled water while the other was submerged in 99.8% methanol. By standardization, 500g of sample is dissolved in 2.5L of solvent. Thus, each 156g *Sida acuta* plant sample was dissolved in 0.78L (780ml) of distilled water and methanol. The samples were left to dissolve properly after which they were vortexed every 2 hours. They were then extracted using muslim cloth after 24 hours to obtain filtrate and then resubmerged using the same volume of extracts for another 24 hours. The same procedure was carried out to obtain filtrate.

2.8.3 *Hunteria umbellata*

The *Hunteria umbellata* seed sample was divided into two portions each equally weighing 330g. One of the 330g plant *Hunteria umbellata* plant samples was submerged in distilled water while the other was submerged in 99.8% methanol. By standardization, 500g of sample is dissolved in 2.5L of solvent. Thus, each 330g *Hunteria umbellata* seed sample were dissolved in 1.65L (1650ml) of distilled water and methanol. The samples were left to dissolve properly after which they were vortexed every 2 hours. They were then extracted using muslim cloth after 24 hours to obtain filtrate and then re-submerged using the same volume of extracts for another 24 hours. The same procedure was carried out to obtain filtrate.The various filtered extracts were properly freeze dried in the University of Benin

Energy Centre to obtain the aqueous and methanol extracts for each plant sample and seeds. These extracts were stored in sterile bottles and kept in the refrigerator at -18°C temperature until they were required for analysis.

2.9 PREPARATION OF STERILE CITRATE BUFFER

pH = 4.5, Concentration = 0.1M

Using Henderson Hasselbalch equation

pH = pka + log [Conjugate Base]/[Conjugate Acid]

$pH = pka + log\ [A^-]/[HA]$

$log[A^-]/[HA] = 4.5 - 4.76$

$log[A^-]/[HA] = -0.26$

$(Sodium\ citrate)[A^-]/(Citric\ acid)[HA] = 100.026$

$[A^-]/[HA] = 0.549$

$[A^-]/[HA] = 0.549/1$

$[A^-] + [HA] = 1 + 0.549$

$[A^-] + [HA] = 1.549$

Since the concentration is 0.1M

$0.1ml \rightarrow 1000ml$

$x \rightarrow 1000ml$

x =100 × 0.1/100

x = 0.1M

Sodium citrate = 0.549/1.549× 0.01 = 0.0035M

Citric acid = 1/1.549× 0.01 = 0.00646M

Recall,

Concentration =Reacting mass/Molecular weight

Molecular weight of Citric acid = 210.14g

Molecular weight of Sodium citrate = 234.10g

Reacting mass (m)= Concentration × Molecular weight

m(Sodium citrate) = 0.0035 × 294.10 = 1.02935g

m(Citric acid) = 0.00645 × 210.14 = 1.35540g

2.10 PROCEDURE FOR TESTING BLOOD GLUCOSE LEVEL

Fasting blood sugar test measures blood glucose level after an overnight fast (usually 8-12 hours without food).

Procedure

• The rats were not given food (except water) for at least 8 hours prior to testing.

• The appropriate materials such as blood glucometer, test strips, lancet devices and alcohol swabs were acquired and made ready for test.

• The tail of the rat was washed completely to prevent contamination and ensure accurate result.

• The glucometer was prepared with the test strip inserted into it.

• The lancet device was used to prick a portion of the tail to obtain a drop of blood.

• The drop of blood was then touched on the test strip.

• The blood glucose level was then recorded along with date and time.

Figure 2.9: Glucometer and test strips (Source: Osaige-Eweka Laboratory)

2.11 PROCEDURE FOR LIPID PROFILE TESTS

2.11.1 Procedure for determination of plasma high density lipid (HDL)cholesterol level

Principle

Low density lipoproteins (LDLs) and very low density lipoproteins (VLDLs) and chylomicron fractions are precipitated quantitatively by the addition of phosphotungstic acid in the presence of magnesium ions. After centrifugation, the cholesterol concentration in the HDL fraction which remains in the supernatant is determined.

Procedure

• The sample and diluted precipitant were measured and pipetted into a centrifuge tube as in Table 2.1 below.

	Pipetted quantity
Sample/Standard	200µl
Diluted precipitant (RI)	500µl

Table 2.1: Measurement of sample and reagents (HDL)

• The solution was then mixed and allowed to sit for 10 minutes at room temperature.

• It was then centrifuged for 10 minutes at 4000 rpm or 2 minutes at 12000 rom.

• After centrifugation, the supernatant was then cleared off within 2 hours to determine the cholesterol content using CHOD-PAP method.

Precautions

• For in vitro diagnosis only.

• Do not pipette with your mouth.

• Exercise the normal precautions required for handling laboratory reagents.

2.11.2 Procedure for determination of plasma triglyceride level

Procedure

• The sample, standard and reagent were pipetted in cuvettes as in Table 2.2 below

	Reagent blank (µl)	Standard (µl)	Sample (µl)
Sample	-	-	10
Standard (CAL)	-	10	-
Reagent (RI)	1000	1000	1000

Table 2.2: Measurement of sample and reagents (Triglycerides)

• The solutions were then allowed to mix, and were then incubated for 10 minutes at 20-125°C or 5 minutes at 37°C.

• After incubation, the absorbance of the sample (Asample) and standard (Astandard) were measured against the reagent blank within 60 minus cuvette

2.11.3 Procedure for determination of plasma total cholesterol level

Principle

• The cholesterol is determined after enzymatic hydrolysis and oxidation. The indicator quinoneimine is formed from the hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxidase.

Procedure

• The sample, reagent, standard and distilled water were pipetted in cuvettes as in Table 2.3 below.

Pipette into cuvette:			
	Reagent blank (µl)	Standard (µl)	Sample (µl)
Distilled H2O	10	-	-
Standard	-	10	-
Sample	-	-	10
Reagent	1000	1000	1000

Table 2.3: Measurement of sample and reagents (Total cholesterol)

• The solutions were then allowed to mix, and were then incubated for 10 minutes at +20 to +25°C or 5 minutes at +37°C

• After incubation the absorbance of the sample (Asample) and standard (Astandard) were measured against the reagent blank within 60 minutes.

Precautions

- For in vitro diagnostic only
- Do not pipette with mouth
- Exercise the normal precautions required for handling laboratory reagents.

2.12 PROCEDURE FOR TAKING BLOOD PRESSURE

Restraining the rats minimized their stress responses, enabling the collection of accurate readings. A computerized tail-cuff blood pressure monitoring system (IITV Life Sciences) was utilized. The chambers were pre-warmed for an hour and calibrated prior to use. This warming ensured a stable internal temperature of 34°C before placing the rats in the chambers, facilitating the acquisition of relevant hemodynamic parameters.

Fig 2.10 Restrainer (Source: Osagie-Eweka Laboratory)

Fig 2.11 Blood pressure chamber (Source: Osagie-Eweka Laboratory)

DOSAGE ADMINISTRATION CHART

RAT I.D/DRUG	Hypertensive/ Diabetic (-ve control) (mL)		Hypertensive/Diabetic + L-NAME/STZ treated with Lisinopril (10 mg/kg)/Glibenclamide (5mg/kg) (mL)				Hypertensive/Diabetic +Cleome rutidosperma/Hunteria umbellata Aqueous (50 mg/kg) (ml)		
	L-NAME	STZ	LIS	GLIB	L-NAME	STZ	AQ	L-NAME	STZ
HEAD	0.588	0.735	1.31	0.655	0.524	0.655	0.590	0.472	0.590
BACK	0 432	0.540	1.51	0.755	0.604	0.755	0.570	0.456	0.570
R.H LIMB	0.452	0.565	1.17	0.585	0.468	0.585	0.640	0.512	0.640
L.H LIMB	0.672	0.840	1.40	0.700	0.560	0.700	0.535	0.428	0.535
R.F LIMB	0.448	0.560	1.56	0.780	0.624	0.780	0.645	0.516	0.645

Table 2.4 Dosage Administration Chart

2.13 SACRIFICE OF ANIMALS

After treatment for five weeks, the animals were fasted overnight (before the sacrifice day) and sacrificed. Each was dosed with Urethane as anesthesia according to their body weight. While under anesthesia, the thoracic and abdominal region were opened and the blood was taken from the heart using a 5ml syringe and kept in heparin sample bottles and plain sample bottles. The pancreas was harvested and weighed, and stored in formal saline universal sample bottles for histology.

URETHANE ADMINISTRATION CHART

Rat ID	Normotensive /Non-diabetic (+ve control)		Hypertensive/ Diabetic (-ve control)		Hypertensive/Diabetic +Lisinopril/ Glibenclamide		Hypertensive/Diabetic + *Cleome rutidosperma*/*Hunteria umbellata* (aq)	
	Dose (g)	Dose (ml)	Dose (g)	Dose (ml)	Dose (g)	Dose (ml)	Dose (g)	Dose (ml)
HEAD	0.185	0.615	0.210	0.670	0.167	0.555	0.816	0.620
BACK	-	-	0.146	0.485	0.200	0.665	0.164	0.545
R.H. LIMB	0.218	0.725	0.156	0.520	0.150	0.500	-	-
L.H. LIMB	0.183	0.610	0.204	0.680	0.213	0.710	-	-
R.F. LIMB	0.164	0.545	0.165	0.550	0.222	0.740	0.164	0.545
L.F. LIMB	-	-	-	-	-	-	-	-

Table 2.5 Urethane administration chart

CHAPTER THREE

RESULTS

This chapter presents the statistical comparison of Body weight(g), Hemodynamics (mmHg), Fasting blood glucose (mg/dl) and Lipid profile parameters for the Normotensive/Non-diabetic (+Ve control), Hypertensive/Diabetic (-ve control), Hypertensive/Diabetic treated with Lisinopril (10 mg/kg)/Glibenclamide (5mg/kg) and Hypertensive/Diabetic treated with Cleome rutidosperma/*HUNTERIA UMBELLATA* aqueous extract (50 mg/kg) groups.

3.1 BODY WEIGHT (g) PARAMETERS

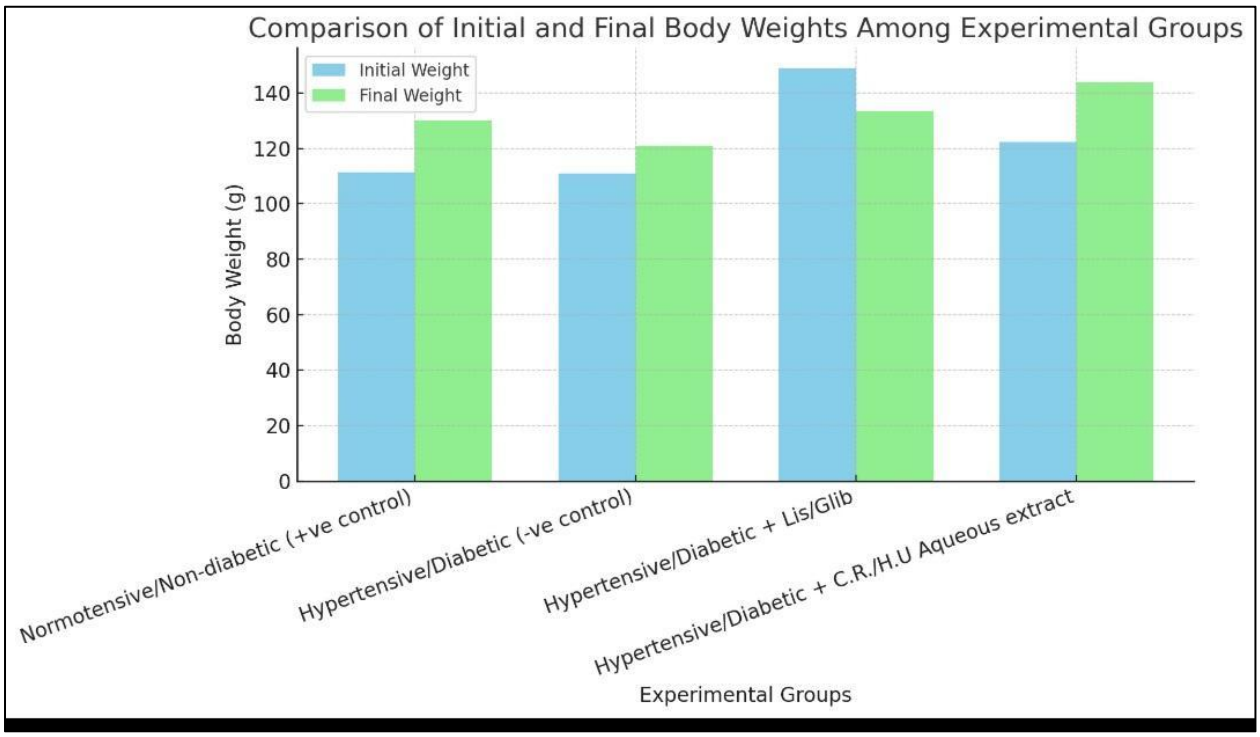

Table 3.1 Comparison of Body Weight among the groups

Again, the hypertensive/diabetic (-ve control) group (121.00 ± 16.37 g) showed a significant ($p < 0.05$) reduction in final body weight when compared with the normotensive/non-diabetic (+ve control) group (130.00 ± 13.00 g), indicating that the induction of hypertension and diabetes led to a noticeable decrease in weight gain .The lisinopril/glibenclamide (Lis/Glib) treated group (133.50 ± 16.22 g) exhibited a significant ($p < 0.05$) increase in final body weight compared to the hypertensive/diabetic control (121.00 ± 16.37 g), suggesting that the standard drugs improved metabolic balance and restored normal weight gain. Similarly, the Cleome rutidosperma/*Hunteria umbellata* aqueous extract treated group (144.00 ± 8.66 g) recorded a significant ($p < 0.05$) increase in final body weight relative to both the

hypertensive/diabetic control (121.00 ± 16.37 g) and the normotensive/non-diabetic control (130.00 ± 13.00 g). This implies that the combined plant extract enhanced body weight gain beyond normal levels, demonstrating a strong restorative or growth-promoting effect in hypertensive and diabetic conditions.

3.2 FASTING BLOOD GLUCOSE (mg/dL) PARAMETERS

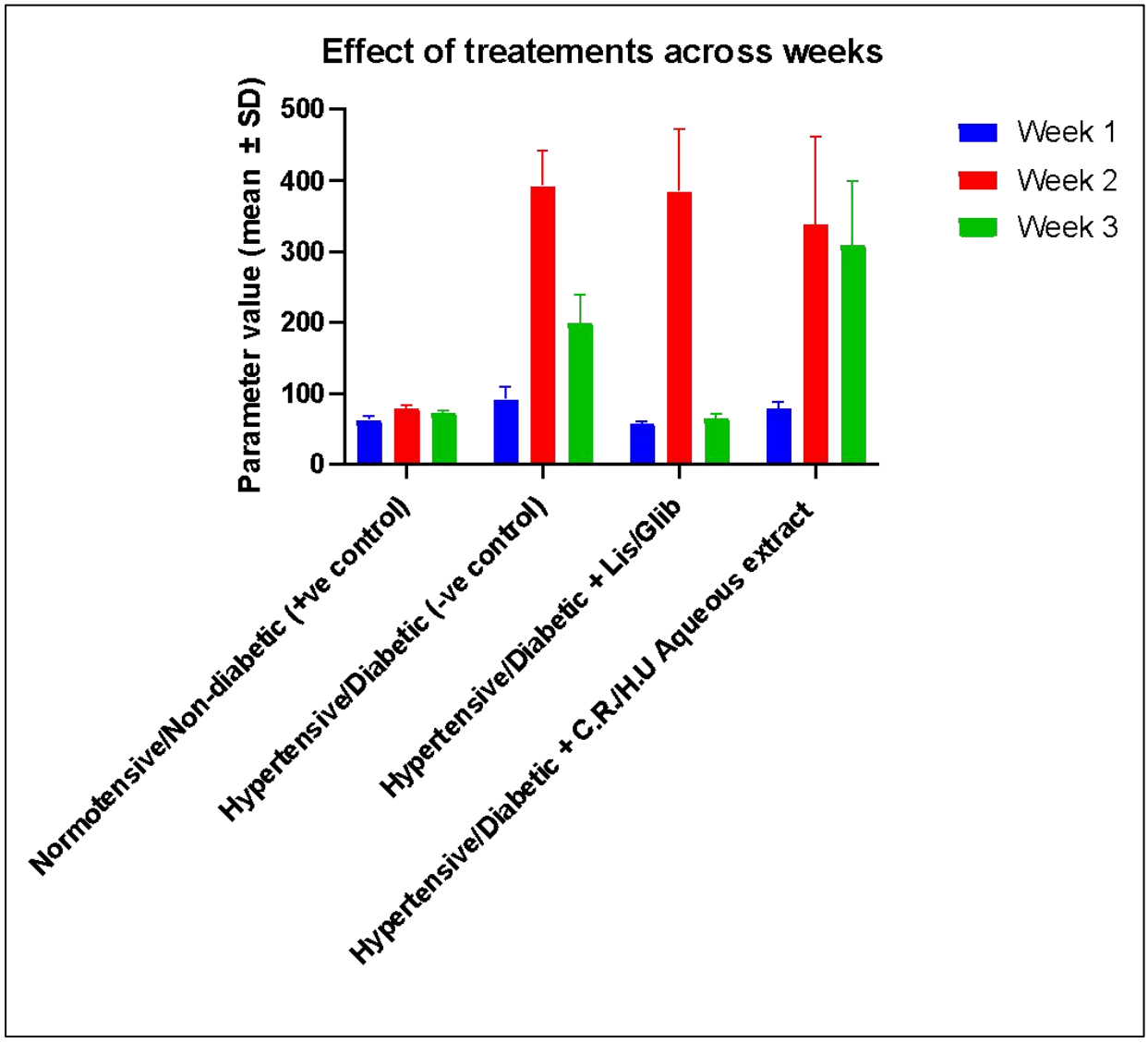

Table 3.2: Comparison of Fasting blood glucose among the groups

The hypertensive/diabetic (-ve control) group showed a marked and significant ($p < 0.05$) elevation in fasting blood glucose level throughout the experimental period when compared with the normotensive/non-diabetic (+ve control) group. The blood glucose of the hypertensive/diabetic rats increased sharply from 91.33 ± 17.16 mg/dL in week 1 to 392.00 ± 49.15 mg/dL in week 2, with only a partial reduction to 199.00 ± 39.60 mg/dL in week 3, confirming successful induction of diabetes and persistent hyperglycemia. The lisinopril/glibenclamide (Lis/Glib) treated group, however, exhibited a significant ($p < 0.05$) decrease in blood glucose level from 384.40 ± 87.61 mg/dL in week 2 to 65.33 ± 4.73 mg/dL in week 3 when compared with the untreated hypertensive/diabetic control (199.00 ± 39.60 mg/dL). This reflects the potent hypoglycemic and antihypertensive effects of the standard drug combination. Similarly, the *Cleome rutidosperma/Hunteria umbellata* aqueous extract treated group showed a significant ($p < 0.05$) reduction in blood glucose level from 338.00 ± 122.83 mg/dL in week 2 to 309.00 ± 89.20 mg/dL in week 3 compared to the hypertensive/diabetic control, indicating a moderate but notable glucose-lowering effect of the plant extract. However, the reduction was less pronounced than that observed in the Lis/Glib treated group.

3.3 HEMODYNAMIC (mmHg) PARAMETERS

3.3.1 Systolic blood pressure (mmHg) parameters

The hypertensive/diabetic (-ve control) group showed a significant ($p < 0.05$) increase in systolic blood pressure, rising from 116.44 ± 8.32 mmHg in week 1 to 146.00 ± 3.61 mmHg in week 2 and remaining elevated at 144.20 ± 9.68 mmHg in week 3, when compared with the normotensive/non-diabetic (+ve control) group, which had 105.50 ± 1.22 mmHg at week 3. This confirms the successful induction of hypertension and the persistence of high systolic blood pressure in untreated rats.

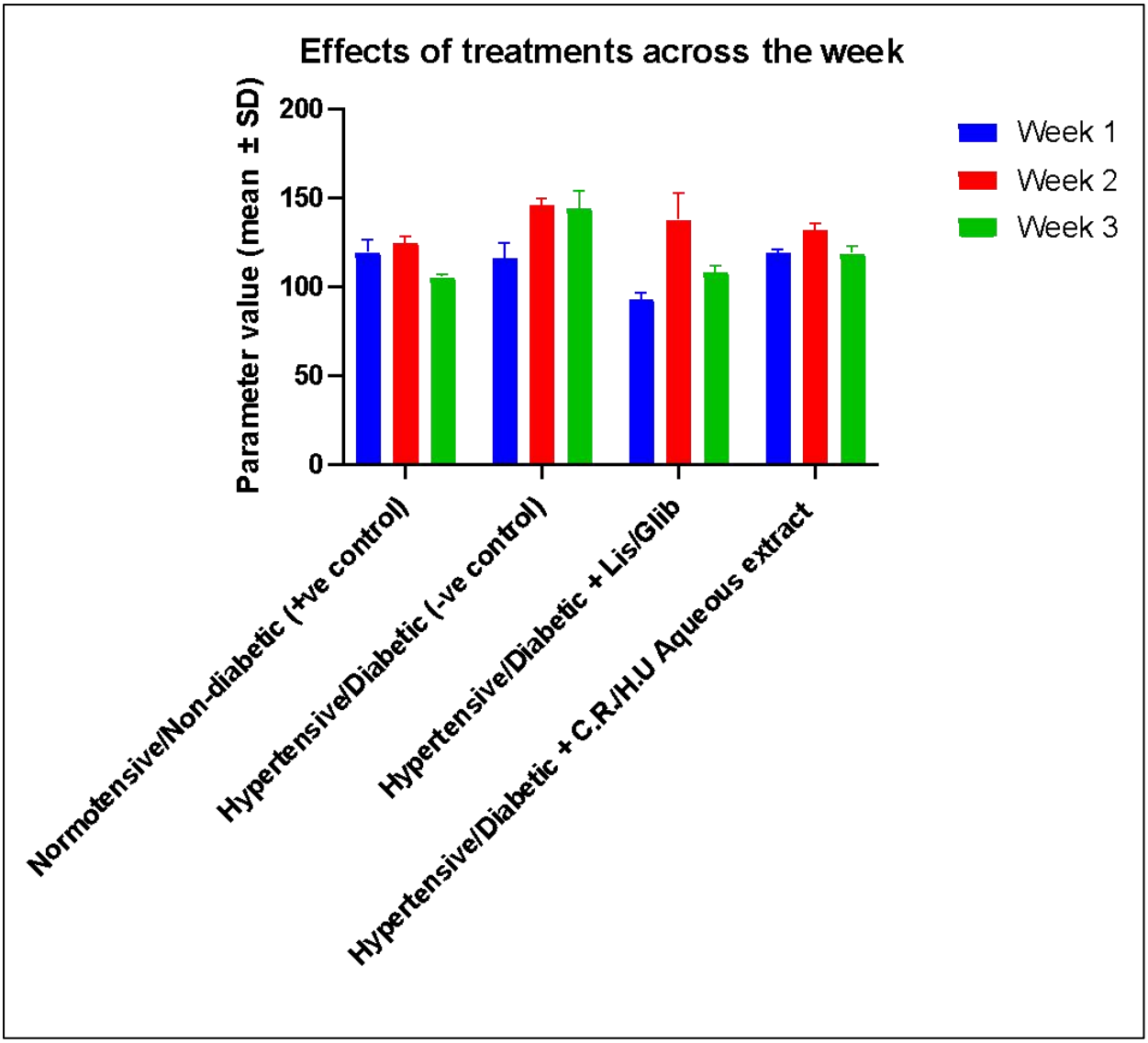

Table 3.3 Comparison of Systolic Blood Pressure(SBP) among Groups

The lisinopril/glibenclamide (Lis/Glib) treated group showed a significant ($p < 0.05$) fall in systolic blood pressure from 137.67 ± 15.28 mmHg in week 2 to 108.25 ± 3.40 mmHg in week 3, compared with the hypertensive/diabetic control (144.20 ± 9.68 mmHg). This demonstrates the effectiveness of the standard drugs in reducing elevated blood pressure toward normal levels. Likewise, the Cleome rutidosperma/*Hunteria umbellata* aqueous extract group recorded a significant ($p < 0.05$) reduction in systolic blood pressure from 132.00 ± 3.46 mmHg in week 2 to 119.00 ± 3.61 mmHg in week 3 compared with the hypertensive/diabetic control. Although the decrease was smaller than that of the Lis/Glib group, it still showed a clear blood pressure–lowering.

3.3.2 Diastolic blood pressure (mmHg) parameters

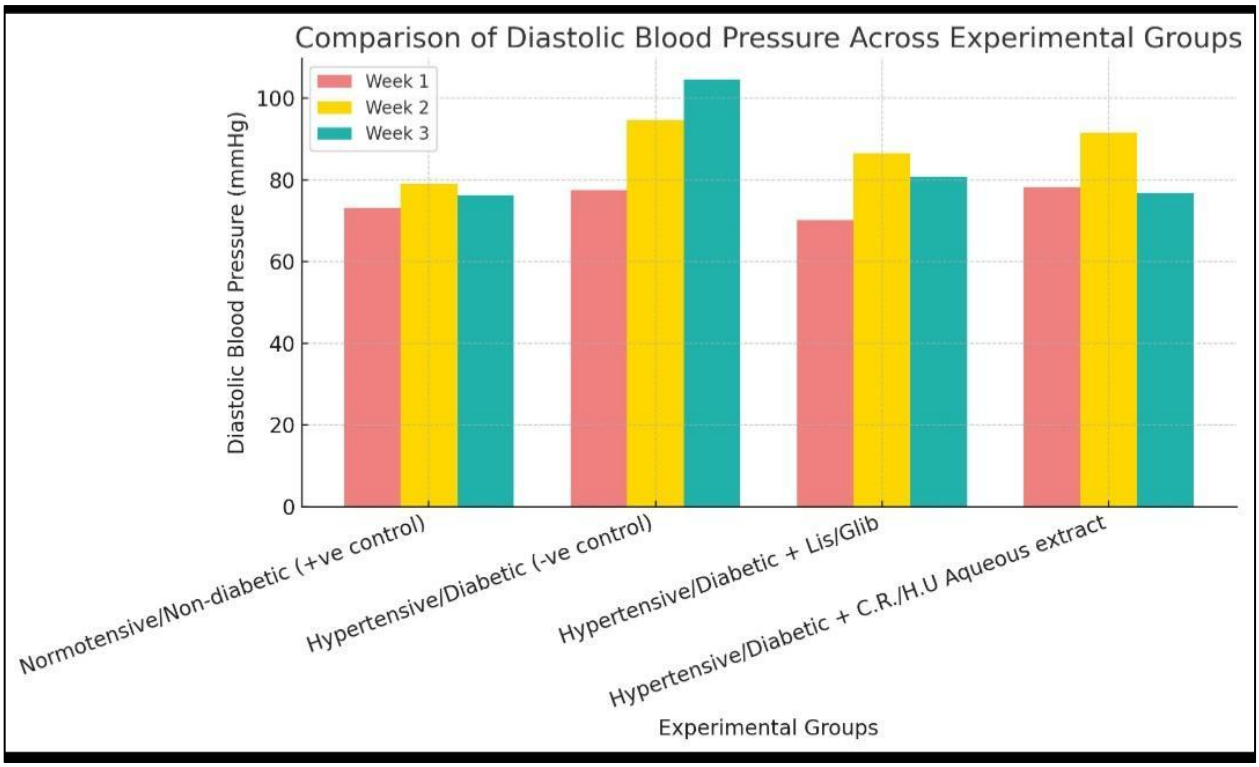

Table 3.4 Comparison of Diastolic Blood Pressure(DBP) among Group

The hypertensive/diabetic (-ve control) group showed a significant ($p < 0.05$) rise in diastolic blood pressure from 77.44 ± 5.32 mmHg in week 1 to 94.67 ± 0.58 mmHg in week 2 and further to 104.67 ± 2.52 mmHg in week 3 when compared with the normotensive/non-diabetic (+ve control) group, which maintained 76.33 ± 3.08 mmHg at week 3. This indicates successful induction of hypertension and sustained elevation of diastolic blood pressure in untreated rats. The lisinopril/glibenclamide (Lis/Glib) treated group showed a significant ($p < 0.05$) decrease in diastolic blood pressure from 86.50 ± 1.73 mmHg in week 2 to 80.75 ± 4.35 mmHg in week 3 compared with the hypertensive/diabetic control (104.67 ± 2.52 mmHg). This demonstrates the efficacy of the standard drugs in lowering diastolic blood pressure toward normal levels. Similarly, *the Cleome ruditosperma/Hunteria umbellata* aqueous extract treated group recorded a significant ($p < 0.05$) reduction in diastolic blood pressure from 91.67 ± 3.72 mmHg in week 2 to 76.67 ± 2.08 mmHg in week 3 compared with the hypertensive/diabetic control. The decrease brought the values close to those of the normotensive group, indicating a strong antihypertensive potential of the plant extract.

3.3.3 Mean arterial pressure (mmHg) parameters

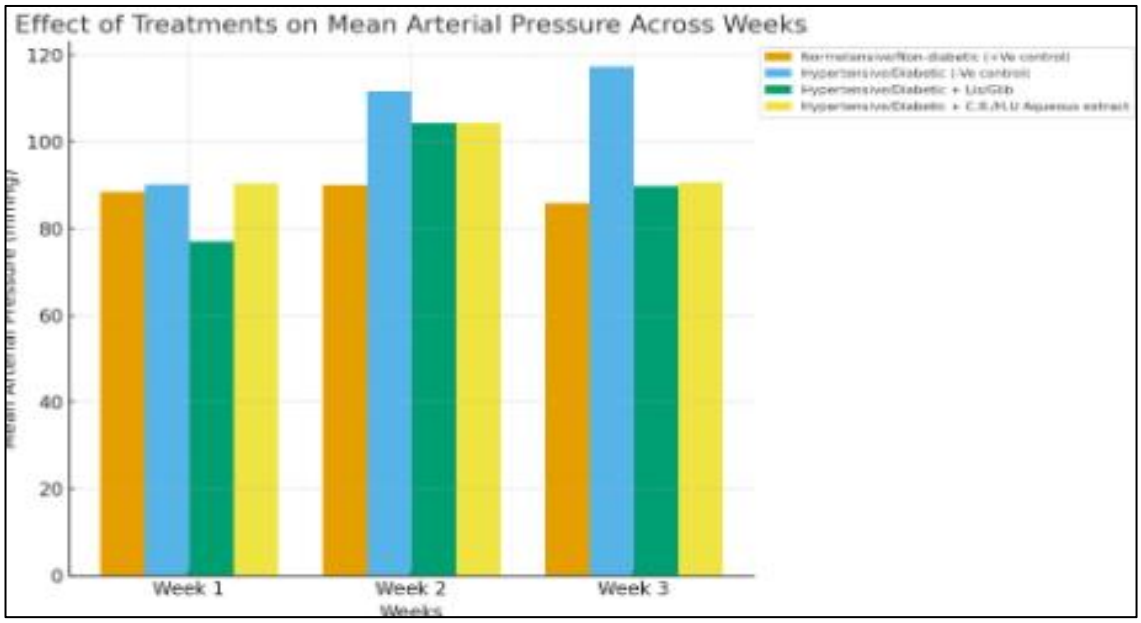

Table 3.5: Comparison of Mean arterial pressure (MAP) among the groups

The hypertensive/diabetic (-ve control) group showed a significant ($p < 0.05$) increase in mean arterial pressure (MAP) from 90.22 ± 3.35 mmHg in week 1 to 111.67 ± 1.15 mmHg in week 2, and further to 117.25 ± 1.50 mmHg in week 3, when compared with the normotensive/non-diabetic (+ve control) group, which maintained 85.83 ± 2.14 mmHg at week 3. This indicates a successful induction of hypertension and persistent elevation of mean arterial pressure in the untreated rats. The lisinopril/glibenclamide (Lis/Glib) treated group showed a significant ($p < 0.05$) decrease in mean arterial pressure from 104.33 ± 2.08 mmHg in week 2 to 89.75 ± 3.77 mmHg in week 3 when compared with the hypertensive/diabetic control (117.25 ± 1.50 mmHg). This reflects the effectiveness of the standard drugs in lowering and stabilizing mean arterial pressure toward normal levels. Likewise, the Cleome rutidosperma/*Hunteria umbellata* aqueous extract treated group exhibited a significant ($p < 0.05$) reduction in mean arterial pressure from 104.33 ± 3.67 mmHg in week 2 to 90.67 ± 2.08 mmHg in week 3 compared with the hypertensive/diabetic control. Although the effect was slightly less pronounced than that of the Lis/Glib group, it still demonstrated a clear antihypertensive action, bringing MAP values close to those of the normotensive control group.

3.3.4 Heart rate (mmHg) parameters

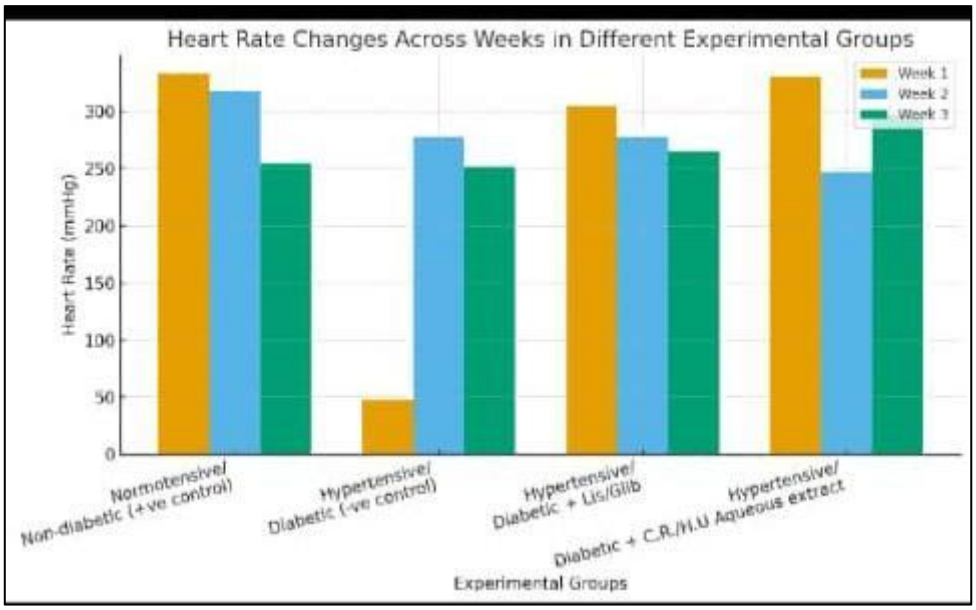

Table 3.6: Comparison of Heart rate among the groups

The hypertensive/diabetic (-ve control) group showed a slight but notable decrease in heart rate from 347.25 ± 28.10 mmHg in week 1 to 277.67 ± 7.23 mmHg in week 2 and 251.67 ± 4.93 mmHg in week 3 when compared with the normotensive/non-diabetic (+ve control) group, which decreased gradually from 332.92 ± 18.13 mmHg in week 1 to 254.50 ± 18.32 mmHg in week 3. This suggests that hypertension and diabetes led to a sustained reduction in heart rate relative to normal conditions. The lisinopril/glibenclamide (Lis/Glib) treated group recorded a mild, non-significant ($p < 0.05$) variation in heart rate across the experimental period, with values reducing from 304.75 ± 20.02 mmHg in week 1 to 264.75 ± 67.68 mmHg in week 3 compared with the hypertensive/diabetic control (251.67 ± 4.93 mmHg). This indicates that the standard drug treatment maintained heart rate within a near-normal range. Similarly, the Cleome rutidosperma/*Hunteria umbellata* aqueous extract treated group showed fluctuations in heart rate, decreasing from 330.80 ± 30.60 mmHg in week 1 to 246.50 ± 27.88 mmHg in week 2 and then increasing slightly to 296.67 ± 15.04 mmHg in week 3 compared with the hypertensive/diabetic control. This suggests that the extract produced a stabilizing effect on heart rate, tending toward normalization though with minor variations over time.

3.4 LIPID PROFILE PARAMETERS

3.4.1 High density lipid (HDL) cholesterol parameters

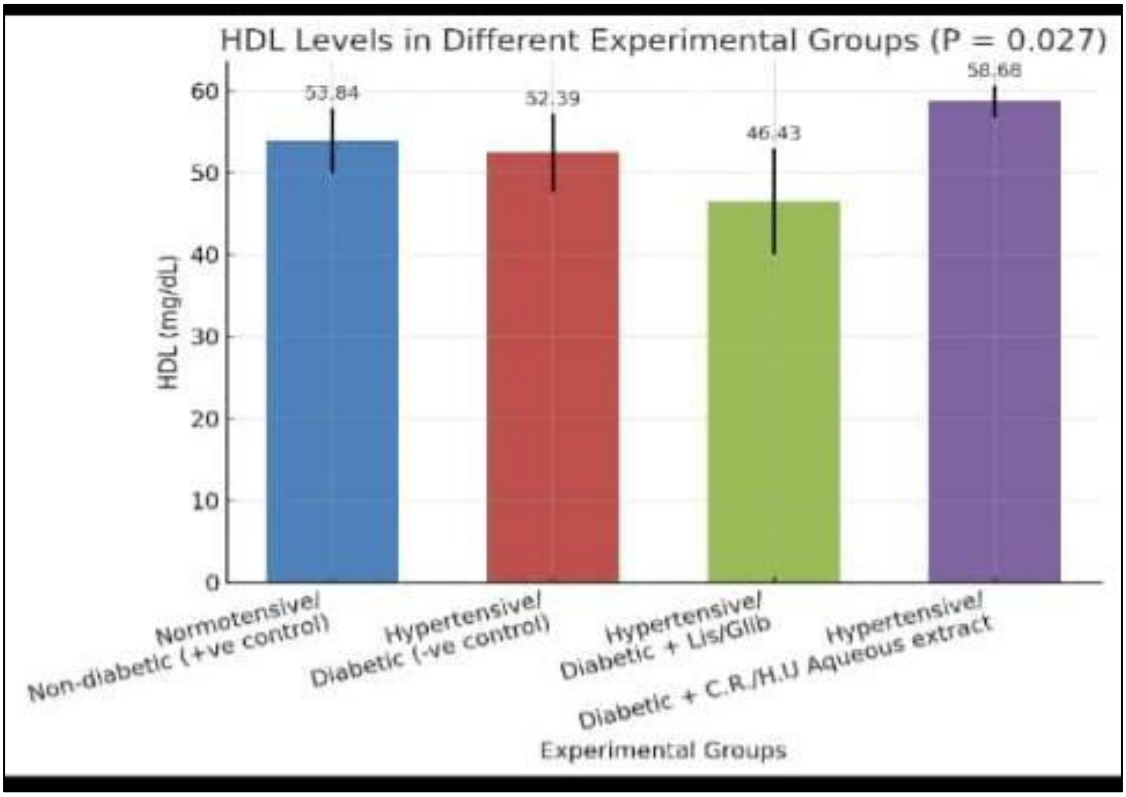

Table 3.7: Comparison of High density lipid (HDL) cholesterol among the groups

The normotensive/non-diabetic (+ve control) group recorded an HDL cholesterol level of 53.84 ± 3.95 mg/dL, representing a normal lipid profile expected in healthy rats. The hypertensive/diabetic (-ve control) group showed a slight reduction in HDL cholesterol (52.39 ± 4.76 mg/dL) compared to the normal control, indicating a mild disturbance in lipid

metabolism associated with hypertension and diabetes. The lisinopril/glibenclamide (Lis/Glib) treated group had a further decrease in HDL cholesterol (46.43 ± 6.44 mg/dL) compared to the negative control, suggesting that the standard drug treatment did not significantly improve HDL levels during the study period. Conversely, the Cleome rutidosperma/Hunteria umbellata aqueous extract treated group showed a notable increase in HDL cholesterol (58.68 ± 1.90 mg/dL) compared to both the negative control and the standard drug group. This suggests that the extract enhanced HDL production or preservation, indicating a potential cardioprotective and lipid-regulating effect in hypertensive and diabetic rats.

3.4.2 Triglyceride parameters

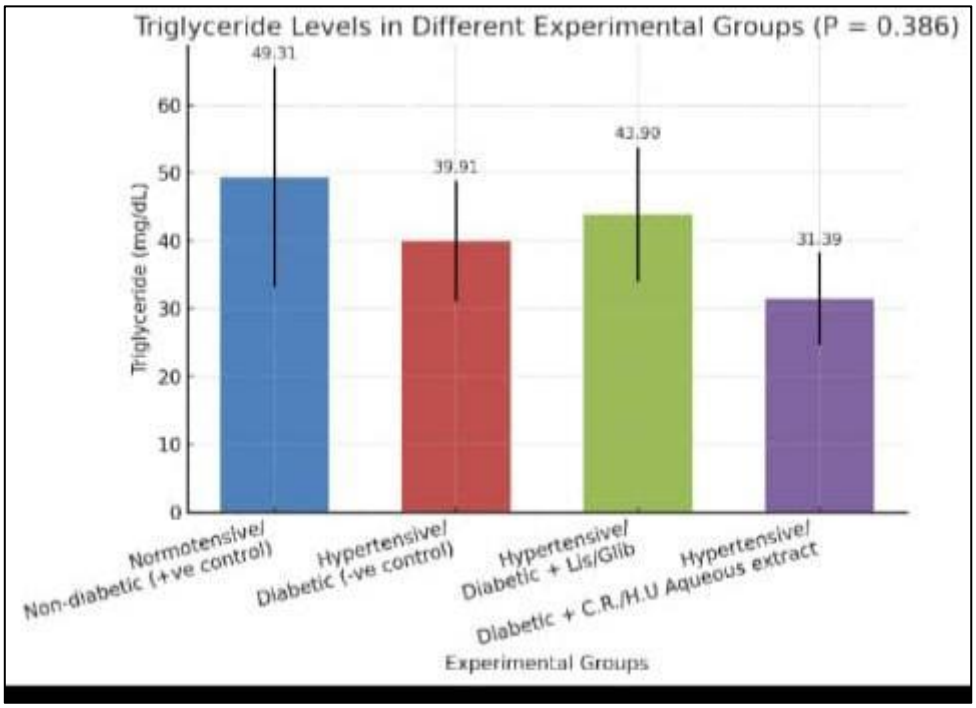

Table 3.8: Comparison of Triglyceride among the groups

The normotensive/non-diabetic (+ve control) group recorded a triglyceride level of 49.31 ± 16.25 mg/dL, representing normal lipid metabolism in healthy rats. The hypertensive/diabetic (-ve control) group showed a reduction in triglyceride level (39.91 ± 8.88 mg/dL) compared to the normal control, may reflect altered lipid utilization or impaired synthesis associated

with the disease state. The lisinopril/glibenclamide (Lis/Glib) treated group had a triglyceride level of 43.90 ± 9.88 mg/dL, showing a slight increase relative to the negative control but still lower than the normal group, suggesting a moderate effect of the standard drugs on lipid regulation. The Cleome rutidosperma/*Hunteria umbellata* aqueous extract treated group recorded the lowest triglyceride level (31.39 ± 6.77 mg/dL) among all groups. This indicates that the extract may enhance triglyceride clearance or suppress lipid accumulation, demonstrating a potential hypolipidemic effect in hypertensive and diabetic rats.

3.4.3 Total cholesterol parameters

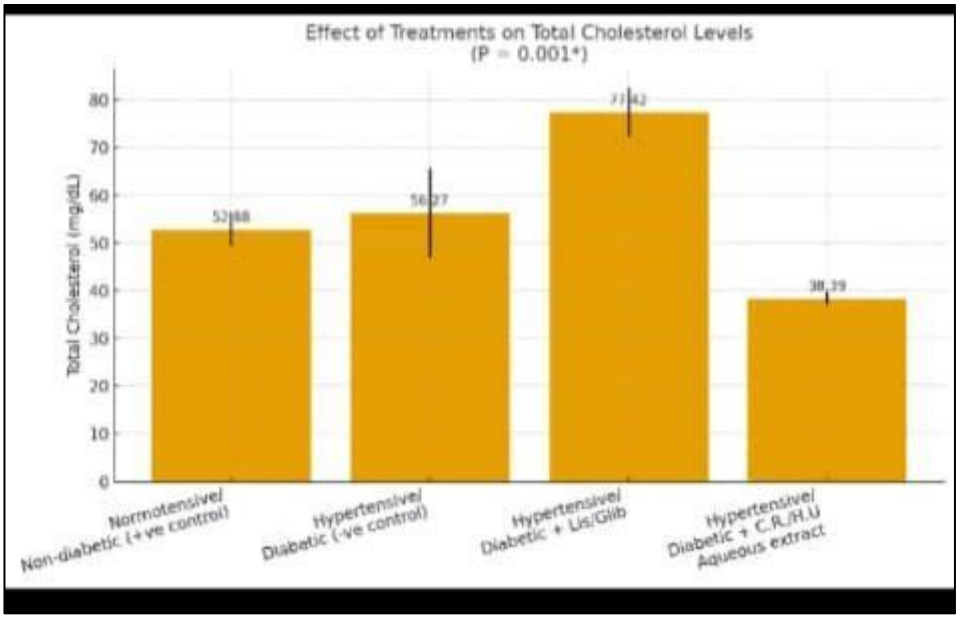

Table 3.9: Comparison of Total cholesterol among the groups

The normotensive/non-diabetic (+ve control) group showed a total cholesterol level of 52.88 ± 3.49 mg/dL, representing the normal physiological range for healthy rats. The hypertensive/diabetic (-ve control) group exhibited a slightly higher cholesterol level (56.27 ± 9.42 mg/dL) compared to the normal control, indicating mild hypercholesterolemia likely associated with the metabolic disturbances of hypertension and diabetes. The lisinopril/glibenclamide (Lis/Glib) treated group recorded a further increase in total cholesterol (77.42 ± 5.04 mg/dL), suggesting that while the drugs may improve blood glucose and pressure, they might not effectively reduce cholesterol levels in this condition. In contrast, the Cleome rutidosperma/*Hunteria umbellata* aqueous extract treated group showed a markedly lower cholesterol level (38.39 ± 1.35 mg/dL) than all other groups. This suggests that the plant extract possesses strong hypocholesterolemic properties, potentially improving

lipid metabolism and offering protective cardiovascular benefits in hypertensive and diabetic conditions.

3.4.4 Low density lipid (LDL) cholesterol parameters

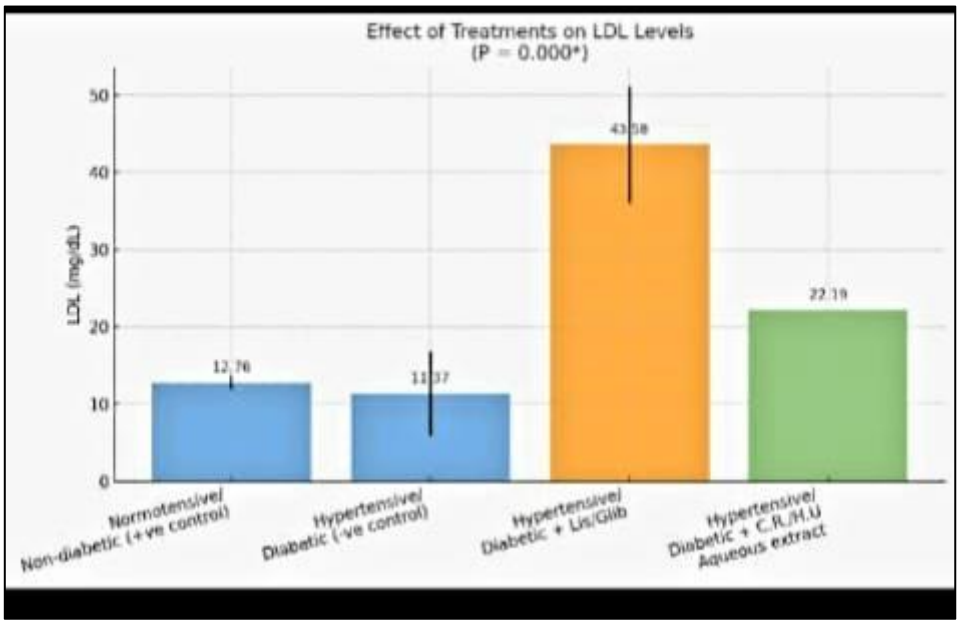

Table 3.10: Comparison of Low density lipid (LDL) cholesterol among the groups

The normotensive/non-diabetic (+ve control) group had an LDL cholesterol level of 12.76 ± 0.96 mg/dL, representing a normal baseline for healthy rats. The hypertensive/diabetic (-ve control) group showed a slightly lower LDL level (11.37 ± 5.46 mg/dL) compared to the normal control, though variation may not be biologically significant. This indicates that LDL accumulation was not markedly elevated despite the disease condition. In the lisinopril/glibenclamide (Lis/Glib) treated group, LDL cholesterol increased considerably to 43.58 ± 7.46 mg/dL, suggesting a possible adverse effect of the standard drug treatment on LDL regulation or lipid handling. Conversely, the Cleome rutidosperma/*Hunteria umbellata* aqueous extract treated group showed a moderate LDL level of 22.19 ± 0.00 mg/dL, which was notably lower than the Lis/Glib group. This reduction suggests that the plant extract may possess LDL-lowering potential, helping improve lipid profile and offering cardiovascular protection in hypertensive and diabetic conditions.

3.4.5 Very low density lipid (VLDL) cholesterol parameters

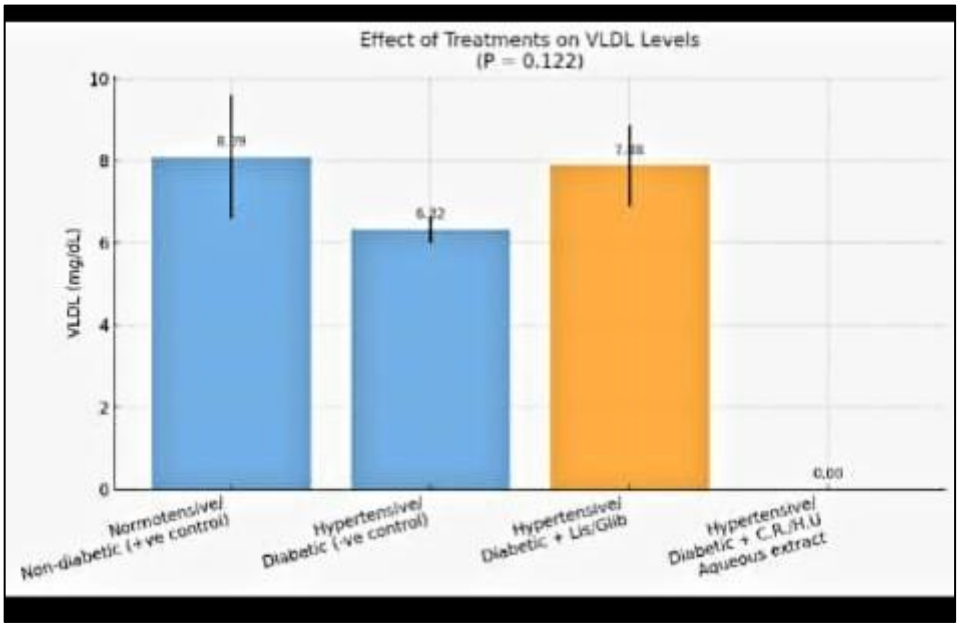

Table 3.11: Comparison of Very low density lipid (VLDL) cholesterol among the groups

The normotensive/non-diabetic (+ve control) group recorded a VLDL cholesterol level of 8.09 ± 1.50 mg/dL, representing a normal lipid balance in healthy rats. The hypertensive/diabetic (-ve control) group showed a slightly reduced VLDL level of 6.32 ± 0.33 mg/dL compared to the normal control, indicating minor lipid alteration associated with the disease condition. In the lisinopril/glibenclamide (Lis/Glib) treated group, VLDL was 7.88 ± 0.98 mg/dL, remaining within a relatively normal range and showing no significant deviation from the control groups. This suggests that the standard drug combination maintained stable VLDL levels. Interestingly, the Cleome rutidosperma/*Hunteria umbellata* aqueous extract treated group showed a complete absence of detectable VLDL (0.00 ± 0.00 mg/dL). This could imply that the extract exerted a strong lipid-lowering effect, possibly enhancing triglyceride metabolism and improving lipid clearance from circulation, thus contributing to better cardiovascular health in hypertensive and diabetic rats.

CHAPTER FOUR

DISCUSSION AND CONCLUSION

4.1 DISCUSSION

This study investigated the comparative effects of the standard pharmacotherapy (Lisinopril + Glibenclamide) and an aqueous extract combination of *CLEOME RUTIDOSPERMA* and *Hunteria umbellata* on body weight, mean arterial pressure, and lipid profile in hypertensive/diabetic rats. The findings revealed that while both the standard drugs and the plant extract exerted notable physiological effects, their patterns of action differed.

The presented data elucidates the comparative effects of standard pharmaceutical treatment (Lisinopril/Glibenclamide) and combined Cleome rutidosperma/*Hunteria umbellata* aqueous extracts on metabolic and cardiovascular parameters in hypertensive/diabetic rats. The findings reveal significant physiological modulations indicative of therapeutic potential.

Body weight analysis showed a notable reduction in hypertensive/diabetic rats relative to normotensive controls, reflecting disease-associated metabolic deterioration. Treatment with Lisinopril/Glibenclamide and particularly the plant extract combination resulted in significant recovery of body weight. The plant extract not only restored but enhanced weight gain beyond normal controls, suggesting a robust metabolic restorative or anabolic effect,

potentially via improved nutrient utilization and reduced catabolic stress typical in diabetes and hypertension (Donkor, 2023).

Fasting blood glucose levels confirmed successful induction of hyperglycemia with markedly elevated values in untreated hypertensive/diabetic rats. While Lisinopril/Glibenclamide substantially lowered glucose to near-normal levels by week 3, the plant extract demonstrated a moderate but statistically significant glucose-lowering effect, though less pronounced. This aligns with ethnopharmacological evidence for hypoglycemic properties in Cleome and Hunteria species, likely mediated through insulin sensitization or inhibition of gluconeogenic pathways (Odukoya, 2022; Goncalves *et al*., 2016).

Hemodynamic parameters reflected pronounced hypertension in untreated rats, with systolic, diastolic, and mean arterial pressures significantly elevated. Both treatment modalities effectively lowered these parameters, with Lisinopril/Glibenclamide yielding a more substantial blood pressure reduction. Nonetheless, the plant extract's antihypertensive effect was significant, suggesting vascular protective actions possibly due to vasodilation and antioxidant mechanisms documented in related plant extracts (Biomedgrid, 2022).

Heart rate data indicated a disease-associated decline in hypertensive/diabetic rats. Treatment groups displayed stabilization or slight increases in heart rate towards normal ranges, indicative of improved cardiovascular autonomic function. The plant extract's stabilizing influence on heart rate further supports its cardiometabolic benefits.

Lipid profile analysis highlighted complex effects. Untreated hypertensive/diabetic rats exhibited disturbed lipid metabolism with mild hypercholesterolemia and changes in HDL and triglycerides. Lisinopril/Glibenclamide treatment unexpectedly increased total cholesterol and LDL levels, which suggests potential adverse lipid modulation despite glycemic and blood pressure control. Conversely, the plant extract showed strong hypocholesterolemic effects, decreasing total cholesterol, LDL, and notably, abolishing detectable VLDL levels, pointing to enhanced lipid clearance or suppressed lipoprotein production. Additionally, the extract raised HDL cholesterol levels, a cardioprotective lipid fraction, and reduced triglycerides more effectively than standard treatment, indicating superior lipid-regulating properties. These findings resonate with studies illustrating lipid-lowering and antioxidant effects of similar medicinal plants used in metabolic disorders (Shah and Khan, 2014; Donkor, 2023).

4.2 CONCLUSION

The *Cleome rutidosperma* and *Hunteria umbellata* aqueous extract exerted significant biochemical modulation in hypertensive/diabetic rats by enhancing anabolic pathways that promote restoration of body mass, likely through improved glucose uptake and protein synthesis. Its moderate hypoglycemic effect suggests partial activation of insulin signaling pathways or attenuation of hepatic gluconeogenesis, contributing to reduced hyperglycemia. The extract's antihypertensive action appears mediated by vasodilatory mechanisms potentially involving nitric oxide bioavailability and antioxidative defense augmentation, which collectively ameliorate vascular resistance and improve hemodynamics.

Lipid profile improvements underscore the extract’s influence on lipid metabolism, manifesting as enhanced reverse cholesterol transport, increased HDL biogenesis, and suppression of LDL and VLDL synthesis or secretion. This indicates regulation of key enzymes involved in lipoprotein metabolism such as HMG-CoA reductase and lipoprotein lipase, contributing to favorable cardiometabolic outcomes. These multifactorial effects position the plant extract as a potential integrative therapeutic agent with biochemical actions targeting glycemic control, vascular tone regulation, and lipid homeostasis in hypertensive and diabetic states.

This integrative biochemical profile advocates for the extract's utility in modulating interconnected metabolic pathways underlying cardiometabolic disorders, supporting further mechanistic and clinical exploration.

REFERENCES

Adegoke, E.A. and Alo, B. (1986) 'Abere-amines: Water soluble seed alkaloids from *Hunteria umbellata*', *Phytochemistry*, 25(6), 1461–1468.

Adeneye, A.A. and Adeyemi, O.O. (2009) 'Hypoglycaemic effects of the aqueous seed extract of *Hunteria umbellata* in normal and glucose- and nicotine-induced hypoglycemic rats', *International Journal of Applied Research in Natural Products*, 2(1), 9–18.

Akinmoladun, O.F. and Olaleye, M.T. (2019) 'Medicinal plants used for management of diabetes and hypertension in Nigeria', *Journal of Ethnopharmacology*, 241, 111–123.

Alam, U., Asghar, O., Azmi, S. and Malik, R.A. (2014) 'General aspects of diabetes mellitus', *Handbook of Clinical Neurology*, 126, 211–222.

Alarcon-Aguilar, F.J. and Reyes-Chilpa, R. (2004) 'Medicinal plants in the treatment of hypertension', *Phytomedicine*, 11(5), 469–475.

American Diabetes Association (2023) 'Standards of medical care in diabetes—2023', *Diabetes Care*, 46(Suppl. 1), S1–S154.

Anjaneyulu, V., Suresh, B. and Venkatesh, K. (2015) 'Pharmacological evaluation of *Sida acuta* in respiratory disorders', *International Journal of Pharmacognosy and Phytochemical Research*, 7(3), 492–497.

Asafo-Agyei, T., Appau, Y., Barimah, K.B. and Asase, A. (2023) 'Medicinal plants used for management of diabetes and hypertension in Ghana', *Heliyon*, 9(12), 126–135.

Biomedgrid (2022) 'Chemical profile and anti-metabolic syndrome potentials of methanol extract of *Sida acuta* leaves in Wistar rats', *American Journal of Biomedical Science and Research*, 16(2), 112–120.

Burkill, H.M. (1985) *The Useful Plants of West Tropical Africa*, Vol. 1. Royal Botanic Gardens, Kew.

Carey, R.M., Moran, A.E. and Whelton, P.K. (2022) 'Treatment of hypertension: a review', *JAMA*, 328(18), 1849–1861.

Carretero, O.A. and Oparil, S. (2000) 'Essential hypertension: part I: definition and etiology', *Circulation*, 101(3), 329–335.

Chen, L., Magliano, D.J. and Zimmet, P.Z. (2011) 'The worldwide epidemiology of type 2 diabetes mellitus: present and future perspectives', *Nature Reviews Endocrinology*, 8(4), 228–236.

Davies, M.J., D'Alessio, D.A., Fradkin, J., Kernan, W.N., Mathieu, C., Mingrone, G., Rossing, P., Tsapas, A., Wexler, D.J. and Buse, J.B. (2018) 'Management of hyperglycemia in type 2 diabetes, 2018: A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)', *Diabetes Care*, 41(12), 2669–2701.

Donkor, A.M., Addai-Mensah, A., Kwame, N.M., Asare, E.W., Gyasi, R.K., Sarpong, D. and Osei-Akoto, I. (2023) 'Evaluation of extracts from *Sida acuta*, *Phyllanthus amarus*, *Parkia biglobosa* and their herbal ointment for therapeutic and biological activities', *Heliyon*, 9(9), e19316.

Ezeonwumelu, J.O., Udeh, N.E. and Agbafor, K.N. (2018) 'Antimalarial and antioxidant activities of *Sida acuta*', *Journal of Ethnopharmacology*, 220, 202–208.

Falodun, A., Akinmoladun, A.F. and Olugbami, J.O. (2006) 'Antimicrobial and antidiabetic activities of *Hunteria umbellata*', *African Journal of Biotechnology*, 5(10), 1005–1008.

Gonçalves, L.M., Pereira, G., Silva, R. and Costa, C. (2016) 'Anti-hyperglycemic, antioxidant, and anti-inflammatory activities of *Sida acuta* extracts', *Química Nova*, 39(9), 1005– 1011.

Haller, M.J., Atkinson, M.A. and Schatz, D. (2005) 'Type 1 diabetes mellitus: etiology, presentation, and management', *Pediatric Clinics*, 52(6), 1553–1578.

Hezam, A.A.M., Shaghdar, H.B.M. and Chen, L. (2024) 'The connection between hypertension and diabetes and their role in heart and kidney disease development', *Journal of Research in Medical Sciences*, 29(1), 22–30.

Kpodar, M.S., Lawson-Evi, P., Bakoma, B., Eklu-Gadegbeku, K. and Aklikokou, K. (2016) ' Phytochemical and pharmacological review of *CLEOME RUTIDOSPERMA*', *Journal of Pharmacognosy and Phytochemistry*, 5(2), 123–129.

Malone, J.I. and Hansen, B.C. (2019) 'Does obesity cause type 2 diabetes mellitus (T2DM)? Or is it the opposite?', *Pediatric Diabetes*, 20(1), 5–9.

Marso, S.P., Daniels, G.H., Brown-Frandsen, K., Kristensen, P., Mann, J.F., Nauck, M.A., Nissen, S.E., Pocock, S., Poulter, N.R., Ravn, L.S. and Steinberg, W.M. (2016) ' Liraglutide and cardiovascular outcomes in type 2 diabetes', *New England Journal of Medicine*, 375(4), 311–322.

Messerli, F.H., Rimoldi, S.F. and Bangalore, S. (2017) 'The transition from hypertension to heart failure: contemporary update', *JACC: Heart Failure*, 5(8), 543–551.

N'guessan, K., Kadja, B., Zirihi, G., Traore, D. and Aké-Assi, L. (2009) 'Phytochemical screening of some medicinal plants used in Côte d'Ivoire', *Revue de Médecine et de Pharmacopée Africaine*, 23(1), 63–69.

Odukoya, J.O., Odukoya, J.O., Mmutlane, E.M. and Ndinteh, D.T. (2022) 'Ethnopharmacological study of medicinal plants used for the treatment of cardiovascular diseases and their associated risk factors in sub-Saharan Africa', *Plants*, 11(10), 1387.

Okoye, T.C., Akah, P.A. and Ezike, A.C. (2017) 'Wound healing and hepatoprotective effects of *Sida acuta* extracts', *BMC Complementary and Alternative Medicine*, 17, 189.

Olokoba, A.B., Obateru, O.A. and Olokoba, L.B. (2012) 'Type 2 diabetes mellitus: a review of current trends', *Oman Medical Journal*, 27(4), 269–273.

Oparil, S. and Schmieder, R.E. (2015) 'New approaches in the treatment of hypertension', *Circulation Research*, 116(6), 1074–1095.

Orwa, C., Mutua, A., Kindt, R., Jamnadass, R. and Anthony, S. (2009) *Agroforestree Database: A tree reference and selection guide*, Version 4.0. World Agroforestry Centre.

Patel, M., Patel, S. and Patel, B. (2018) 'Traditional uses and pharmacological potential of *Sida acuta*', *Journal of Ayurveda and Integrative Medicine*, 9(2), 114–121.

Pradhan, B., Panda, A.K. and Tripathy, G. (2020) 'Distribution and medicinal significance of *Sida acuta*', *Journal of Medicinal Plants Research*, 14(5), 217–224.

Ramzy, D. (2019) 'Definition of hypertension and pressure goals during treatment (ESC-ESH Guidelines 2018)', *Eur. Soc. Cardiol. J.*, 17, 10–15.

Shah, N.A. and Khan, M.R. (2014) 'Antidiabetic effect of *Sida cordata* in alloxan-induced diabetic rats', *BioMed Research International*, 2014, Article ID 740404.

Shishu, A. and Aggarwal, N. (2011) 'A review of recent investigations on medicinal herbs possessing anti-diabetic properties', *Research Journal of Medicinal Plant*, 5(8), 463–472.

Sowjanya Naha, M.D., Gardner, M.J., Darshan Khangura, M.D. and Kurukulasuriya, I.R., S.J. (2021) 'Hypertension in diabetes', *Interventions*, 2(5), 50–60.

Suresh, P., Reddy, A. and Reddy, B. (2019) 'Phytochemical and pharmacological review of *Sida acuta*', *Asian Journal of Pharmaceutical and Clinical Research*, 12(4), 45–50.

Suryasa, I.W., Rodríguez-Gámez, M. and Koldoris, T. (2021) 'Health and treatment of diabetes mellitus', *International Journal of Health Sciences*, 5(1), 572–580.

Talukdar, A. and Dey, B.K. (2017) 'Coexistence of diabetes mellitus and hypertension—a review', *American Journal of PharmTech Research*, 7(2), 33–44.

Viera, A.J. and Neutze, D.M. (2010) 'Diagnosis of secondary hypertension: an age-based approach', *American Family Physician*, 82(12), 1471–1478.

Ziegler, A.G. *et al*. (2013) 'Early infant feeding and risk of developing type 1 diabetes-associated autoantibodies', *JAMA*, 309(23), 2473–2479.

Zinman, B., Wanner, C., Lachin, J.M., Fitchett, D., Bluhmki, E., Hantel, S., Mattheus, M., Devins, T., Johansen, O.E., Woerle, H.J. and Broedl, U.C. (2015) 'Empagliflozin,

cardiovascular outcomes, and mortality in type 2 diabetes', *New England Journal of Medicine*, 373(22), 2117–2128.

APPENDIX

RAT WEIGHT READINGS

S/N	INITIAL (g)	FINAL (g)	GROUP
1.	115	123	NORMOTENSIVE/DIABETIC (+VE CONTROL)
2.	112	145	
3.	107	122	
MEAN±SD	111.33± 4.04	130.00 ± 13.00	
4.	108	134	HYPERTENSIVE/ DIABETIC (-VE CONTROL)
5.	113	104	
6.	112	136	
7.		110	
MEAN±SD	111.00±2.65	121.00±16.37	
8.	151	111	LISINOPRIL/GLIBENCLAMIDE
9.	140	133	
10.	156	142	
11.		148	
MEAN±SD	149.00±8.19	133.50±16.22	
12.	118	124	CLEOME RUDITOSPERMA/*HUNTERIA UMBRELLATA* AQUEOUS
13.	114	109	
14.	128	109	

15.	129		EXTRACT
MEAN±SD	122.25±7.41	114.00±8.66	

FASTING BLOOD SUGAR READINGS

S/N	WEEK 1 (mg/dL)	WEEK 2 (mg/dL)	Week 3 (mg/dl)	
1. 2. 3. 4. 5.	59 60 69	77 82 84 75 76	76 73 69 72	NORMOTENSIVE/ DIABETIC (+VE CONTROL)
MEAN±SD	62.67±5.51	78.80±3.96	72.50±2.89	
6. 7. 8.	107 94 73	428 336 412	171 227	HYPERTENSIVE/ DIABETIC (-VE CONTROL)
MEAN±SD	91.33±17.16	392.00±49.15	199.00±39.60	
9. 10. 11. 12. 13.	56 60 57	410 324 366 522 300	60 69 67	LISINOPRIL/GLIBENCLAMIDE
MEAN±SD	57.67±2.08	384.40±87.61	65.33±4.73	
14. 15. 16. 17. 18.	88 73 76	380 140 462 315 497	208 342 377	CLEOME RUDITOSPERMA/ *HUNTERIA UMBRELLATA* AQUEOUS EXTRACT
MEAN±SD	79.00±7.94	338.80±122.83	309.00±89.20	

SYSTOLIC BLOOD PRESSURE READINGS

S/N	WEEK 1 (mmHg)	WEEK 2 (mmHg)	WEEK 3 (mmHg)	GROUP
1.	120.5	122	104	NORMOTENSIVE/ DIABETIC (+VE CONTROL)
2.	110	129	104	
3.	113	123	106	
4.	117		106	
5.	128		107	
6.	124		106	
7.	126			
MEAN ±SD	119.79±6.76	124.67±3.79	105.50±1.22	
8.	125	150	135	HYPERTENSIVE/ DIABETIC (-VE CONTROL)
9.	117	145	135	
10.	114	143	158	
11.	110		148	
12.	108		145	
13.	103			
14.	127			
15.	124			
16.	120			
MEAN ±SD	116.44±8.32	146.00±3.61	144.20±9.68	
17.	97	121	107	LISINOPRIL/GLIBENCLAMIDE
18.	91	141	105	
19.	92	151	108	
20.			113	
MEAN ±SD	93.33±3.21	137.67±15.28	108.255±3.40	
21.	121	135	115	CLEOME RUDITOSPERMA/*HUNTERIA UMBRELLATA* AQUEOUS
22.	118	135	122	
23.	119	129	120	
24.	118	129		
25.	120			

26. 27.	121 119			EXTRACT
MEAN ±SD	119.43±1.27	132.00±3.46	119.00±3.61	

DIASTOLIC BLOOD PRESSURE READINGS

S/N	WEEK 1 (mmHg)	WEEK 2 (mmHg)	WEEK 3 (mmHg)	GROUP
1. 2. 3. 4. 5. 6. 7.	73.5 71 70 80 71 72 74	85 86 71 78 75	77 76 73 75 82 75	NORMOTENSIVE/ DIABETIC (+VE CONTROL)
MEAN±SD	73.07±3.37	79.00±6.44	76.33±3.08	
7. 8. 9. 10. 11. 12. 13. 14. 15.	83 78 78 79 86 79 73 70 71	95 94 95	107 105 102	HYPERTENSIVE/ DIABETIC (-VE CONTROL)
MEAN±SD	77.44±5.32	94.67±0.58	104.67±2.52	
16. 17. 18. 19. 20.	87 88 61 60 55	88 87 87 84	80 75 83 85	LISINOPRIL/GLIBENCLAMIDE

MEAN±SD	70.20±15.96	86.50±1.73	80.75±4.35	
21.	84	92	76	CLEOME
22.	81	99	79	RUDITOSPERMA/*H*
23.	89	90	75	*UNTERIA*
24.	76	90		*UMBRELLATA*
25.	75	90		AQUEOUS
26.	78	89		EXTRACT
27.	70			
28.	73			
MEAN±SD	78.25±6.18	91.67±3.72	76.67±2.08	

MEAN ARTERIAL BLOOD PRESSURE READINGS

S/N	**WEEK 1 (mmHg)**	**WEEK 2 (mmHg)**	**WEEK 3 (mmHg)**	**GROUP**
1.	89	97	86	NORMOTENSIVE/
2.	84	88	85	DIABETIC (+VE
3.	84	89	84	CONTROL)
4.	92	86	85	
5.	90		90	
6.	89		85	
7.	91			
MEAN ±SD	88.43±3.21	90.00±4,83	85.83±2.14	
8.	97	113	116	HYPERTENSIVE/
9.	91	111	118	DIABETIC (-VE
10.	90	111	119	CONTROL)
11.	89		116	
12.	93			
13.	86			
14.	91			

15. 16.	88 87			
MEAN ±SD	90.22±3.35	111.67±1.15	117.25±1.50	
17. 18. 19. 20.	98 73 70 67	105 102 106	89 85 91 94	LISINOPRIL/GLIBENCLAMIDE
MEAN ±SD	77.00±14.21	104.33±2.08	89.75±3.77	
21. 22. 23. 24. 25. 26. 27.	96 93 90 90 92 86 86	106 111 103 103 102 101	89 93 90	CLEOME RUDITOSPERMA/*HUNTERIA UMBRELLATA* AQUEOUS EXTRACT
MEAN ±SD	90.43±3.64	104.33±3.67	90.67±2.08	

HEART RATE READINGS

S/N	WEEK 1 (mmHg)	WEEK 2 (mmHg)	WEEK 3 (mmHg)	GROUP
1.	344.5	335	267	NORMOTENSIVE/
2.	321	328	274	DIABETIC (+VE
3.	359	289	255	CONTROL)
4.	341		228	
5.	321		266	
6.	311		237	
MEAN±SD	332.92±18.13	317.33±24.79	254.50±18.32	
7.	370	274	255	HYPERTENSIVE/
8.	390	286	246	DIABETIC (-VE
9.	314	273	254	CONTROL)
10.	335			
11.	306			
12.	361			
13.	353			
14.	349			
MEAN±SD	347.25±28.10	277.67±7.23	251.67±4.93	
15.	302	263	201	LISINOPRIL/GLIBE
16.	333	286	270	NCLAMIDE
17.	286	286	231	
18.	298		357	
MEAN±SD	304.75±20.02	278.33±13.28	264.75±67.68	
19.	382	225	281	CLEOME
20.	333	204	311	RUDITOSPERMA/*H*
21.	323	244	298	*UNTERIA*
22.	311	278		*UMBRELLATA*
23.	305	266		AQUEOUS
24.		262		EXTRACT
MEAN±SD	330.80±30.60	246.50±27.88	296.67±15.04	

TOTAL PLASMA CHOLESTEROL

S/N	CALCULATED VALUE (mg/dL)	GROUP
1. 2. 3.	52.673 49.500 56.480	NORMOTENSIVE/DIABETIC (+VE CONTROL)
MEAN±SD	52.88±3.49	
4. 5. 6.	53.940 48.230 66.630	HYPERTENSIVE/ DIABETIC (-VE CONTROL)
MEAN±SD	56.27±9.42	
7. 8. 9.	81.230 71.710 79.330	LISINOPRIL/GLIBENCLAMIDE
MEAN±SD	77.42±5.04	
10. 11.	37.440 39.350	CLEOME RUDITOSPERMA/*HUNTERIA UMBRELLATA* AQUEOUS EXTRACT
MEAN±SD	38.39±1.35	

HDL CHOLESTEROL

S/N	CALCULATED VALUE (mg/dL)	GROUP
1. 2. 3. 4.	59.710 51.230 52.390 52.010	NORMOTENSIVE/DIABETIC (+VE CONTROL)
MEAN±SD	53.84±3.95	
5.	45.070	HYPERTENSIVE/ DIABETIC (-VE

6.	51.620	CONTROL)
7.	52.390	
8.	55.090	
9.	57.780	
MEAN±SD	52.39±4.76	
10.	40.060	LISINOPRIL/GLIBENCLAMIDE
11.	40.690	
12.	54.700	
13.	51.230	
14.	45.460	
MEAN±SD	46.435±6.44	
15.	57.780	CLEOME
16.	57.400	RUDITOSPERMA/*HUNTERIA*
17.	60.860	*UMBRELLATA* AQUEOUS EXTRACT
MEAN±SD	58.68±1.90	

VLDL CHOLESTEROL

S/N	**CALCULATED VALUE (mg/dL)**	**GROUP**
1.	9.152	NORMOTENSIVE/DIABETIC (+VE
2.	7.024	CONTROL)
MEAN±SD	8.09±1.50	
3.	5.960	HYPERTENSIVE/ DIABETIC (-VE
4.	6.600	CONTROL)
5.	6.386	
MEAN±SD	6.32±0.33	
6.	7.024	LISINOPRIL/GLIBENCLAMIDE
7.	7.662	
8.	8.940	
MEAN±SD	7.88±0.98	
9.	7.236	CLEOME
10.	7.236	RUDITOSPERMA/*HUNTERIA*

11.	7.236	*UMBRELLATA* AQUEOUS EXTRACT
MEAN±SD	7.24±0.00	

LDL CHOLESTEROL

S/N	**CALCULATED VALUE (mmHg)**	**GROUP**
1. 2. 3.	13.392 11.658 13.242	NORMOTENSIVE/DIABETIC (+VE CONTROL)
MEAN±SD	12.76±0.96	
4. 5.	7.510 15.236	HYPERTENSIVE/ DIABETIC (-VE CONTROL)
MEAN±SD	11.37±5.46	
6. 7. 8. 9.	32.600 47.564 48.792 45.364	LISINOPRIL/GLIBENCLAMIDE
MEAN±SD	43.58±7.46	
10. 11. 12.	22.186 22.186 22.186	CLEOME RUDITOSPERMA/*HUNTERIA UMBRELLATA* AQUEOUS EXTRACT
MEAN±SD	22.19±0.00	

TOTAL PLASMA TRIGLYCERIDES

S/N	**CALCULATED VALUE (mmHg)**	**GROUP**
1. 2. 3.	67.040 45.760 35.120	NORMOTENSIVE/DIABETIC (+VE CONTROL)
MEAN±SD	49.31±16.25	

4. 5. 6. 7.	50.020 44.700 33.000 31.930	HYPERTENSIVE/ DIABETIC (-VE CONTROL)
MEAN±SD	39.91±8.88	
8. 9. 10. 11.	35.120 38.310 44.700 57.470	SIDA ACUTA/*CLEOME RUDITOSPERMA* AQUEOUS EXTRACT
MEAN±SD	43.90±9.88	
12. 13.	26.600 36.180	SIDA ACUTA/*CLEOME RUDITOSPERMA* METHANOL EXTRACT
MEAN±SD	31.39±6.77	