THE EVALUATION OF THE ANTI-HYPERLIPIDEMIA, ANTI-ATHEROSCLEROSIS, EFFECT OF THE POLYHERBAL FORMULATED TEA ON ATHEROGENIC DIET INDUCED HYPERLIPIDEMIA AND ATHEROSCLEROSIS IN WISTAR RATS.

BY

Blessing Julius IMAFIDON (Miss)

LSC2009745

(PHYSIOLOGY AND PHARMACOLOGY TECHNIQUES)

DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY

FACULTY OF LIFE SCIENCE

UNIVERSITY OF BENIN

BENIN CITY

NOVEMBER, 2025.

THE EVALUATION OF THE ANTI-HYPERLIPIDEMIA, ANTI-ATHEROSCLEROSIS, EFFECT OF THE POLYHERBAL FORMULATED TEA ON ATHEROGENIC DIET INDUCED HYPERLIPIDEMIA AND ATHEROSCLEROSIS IN WISTAR RATS.

BY

Blessing Julius IMAFIDON (Miss)
LSC2009745

A PROJECT WORK SUBMITTED TO THE DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY, FACULTY OF LIFE SCIENCE, UNIVERSITY OF BENIN, BENIN CITY, EDO STATE, NIGERIA. IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE BACHELOR DEGREE (BSc.) IN SCIENCE LABORATORY TECHNOLOGY DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY (PHYSIOLOGY AND PHARMACOLOGY TECHNIQUES) FACULTY OF LIFE SCIENCES, UNIVERSITY OF BENIN, BENIN CITY

NOVEMBER, 2025

CERTIFICATION

This is to certify that this project work, titled "**The Evaluation Of The Anti-Hyperlipidemia, Anti-Atherosclerosis, Effect Of The Polyherbal Formulated Tea On Atherogenic Diet Induced Hyperlipidemia And Atherosclerosis In Wistar Rats.**'' was carried out by Blessing Julius IMAFIDON (Miss) with matriculation number LSC2009745 of the Department of Science Laboratory Technology (Physiology and Pharmacology Techniques), Faculty of Life Sciences, University of Benin, Benin City, Edo State, under the supervision of Dr Dickson O. Uwaya.

__________________ __________________

Dr Dickson O. Uwaya **Date**

(*Project Supervisor*)

__________________ __________________

Dr. P. O. Alonge **Date**

(*Project Coordinator*)

__________________ __________________

Prof J.O. Osarumwese **Date**

(*Head of Department*)

__________________ __________________

(*External Examiner*) **Date**

DEDICATION

I dedicate this project work to God Almighty, to my beloved family for their unwavering support, and to my amazing friends whose love and encouragement have carried me through every step of the journey.

ACKNOWLEDGEMENT

I give all glory and utmost appreciation to God Almighty, whose grace, provision, and unwavering love have sustained me throughout this journey. My profound gratitude goes to my father, Mr. Imafidon Oscar Julius; my mother, Mrs. Patience Imafidon; and my amazing big sisters, Miss Imafidon Mirabel and Miss Imafidon Daniella. Thank you for your steadfast support, understanding, money, and constant motivation. Your love and belief in me have been my greatest strength.

I also want to appreciate my ever-intellectual and vibrant supervisor, Dr. Dickson O. Uwaya, for his invaluable mentorship, patience, and consistent guidance. His constructive feedback, encouragement, and dedication played an important role in shaping the quality of this work. I also wish to sincerely thank my friends (Sandra, Faith, Stella, Destiny, Queen, and Esther) and my roommate (Miss Christiana Thomas), whose companionship and encouragement have made this academic journey both meaningful and memorable so far.

A special thanks to my pastor, Rev. Isaiah Ehijie, for being a support system, motivation, and spiritual backup. My gratitude goes to Mr. John Osifo and the staff of Benin Medical Care Diagnostics and Laboratory for their input in my academic success. To Success, Princessa, Abieyuwa, Divine, Grace, Akachi and the rest of my project group members, I love you guys, and I am grateful to you all for making this research journey a success.

I really want to thank my late friend Mr. Kelly Osemen Oriarewo; your death still hurts my heart every minute of the day, but I know you're in a better place. Thank you very much for kickstarting my university journey with me. Thank you for the genuine kindness you showed me, and I pray you keep on resting well, my friend.

Finally, I extend my heartfelt appreciation to the entire staff of the Department of Science Laboratory Technology for their dedication and the essential roles they have played in my academic development.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF PLATES

LIST OF TABLES

ABSTRACT

Medicinal plants are presently in demand, and their acceptance is increasing progressively; hence, plants with ethnomedicinal values are currently screened for their therapeutic potential and safety profile. This study evaluated the effects of a polyherbal-formulated tea (*Ageratum conyzoides*, *Anthocleista djalonensis, Zingiber officinale, Allium sativum,* and *Thespesia garckeana*) on atherogenic diet-induced hyperlipidaemia and atherosclerosis in male albino Wistar rats. Twenty-five rats were divided into five groups of five: group 1 as normal control, group 2 as cholesterol control, groups 3 and 4 received polyherbal tea at 20 and 40 mg/kg, respectively, and group 5 was treated with atorvastatin (5 mg/kg). Hyperlipidaemia was induced in groups 2 to 5 by administering 10 mg/kg of 1% cholesterol and 0.5% cholic acid. Treatments and a cholesterol diet were given orally for 28 days. The results indicated that polyherbal tea at both doses of 20 mg/kg and 40 mg/kg prevented weight gain and reduced organ-to-body weight ratios when compared to the cholesterol control ($P < 0.05$). Polyherbal tea treatment decreased total cholesterol, triglycerides, low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) levels, while elevating high-density lipoprotein (HDL) levels ($P < 0.05$). Polyherbal tea had a reduction in aortic wall thickness and ALT and AST levels compared to the cholesterol control ($p<0.05$). Histological examination revealed normal aortic and hepatic features in treated groups compared with the cholesterol control. In conclusion, the polyherbal-formulated tea demonstrated antihyperlipidemic, anti-atherosclerotic, and hepatoprotective properties and may reduce cardiovascular risk.

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF STUDY

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide, accounting for nearly one-third of global deaths each year (World Health Organization [WHO], 2021). Among the various risk factors associated with CVDs, hyperlipidaemia and atherosclerosis are particularly significant (Ference et al., 2017). Hyperlipidaemia is characterised by an abnormal elevation of blood lipids, specifically high levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C), along with reduced levels of high-density lipoprotein cholesterol (HDL-C) (Ference et al., 2017). This lipid imbalance disrupts normal vascular function and promotes cholesterol accumulation within blood vessel walls (Taskinen and Borén, 2015). Over time, persistent hyperlipidaemia leads to the progression of atherosclerosis, a chronic disease that affects the arteries (Libby et al., 2019). Atherosclerosis is marked by lipid accumulation, inflammatory cell infiltration, and smooth muscle cell proliferation within the arterial walls (Libby et al., 2019). These pathological changes result in the formation of fatty streaks and fibrous plaques, which gradually thicken the vessel wall and narrow the arterial lumen (Libby et al., 2019).

Statins, fibrates, and bile acid binders are some of the most common drugs used to lower blood lipids (Banach et al., 2017). They work by lowering cholesterol levels and decreasing the risk of heart disease (Banach et al., 2017). However, side effects, high costs, and limited availability in low-income regions often constrain their long-term use (Banach et al., 2017). As a result, many researchers are looking into plant-based alternatives, such as polyherbal formulations that combine several medicinal plants to make them more effective, cause fewer side effects, and have more health benefits. Medicinal plants have been used in traditional medicine for hundreds of years and are still an important source of treatment for many people (Adedapo et al., 2015). According to the World Health Organization (2021), over 80% of the global population still depends on plant-based remedies for their healthcare needs. Prominent plants such as *Camellia sinensis* (green tea), *Allium sativum* (garlic), and *Zingiber officinale* (ginger) have shown the ability to lower blood lipids and protect cardiovascular health (Adedapo et al., 2015). The synergistic effects of these plants, when combined with a polyherbal formulation, can enhance their therapeutic benefits, potentially including a reduction in cholesterol synthesis, an increase in bile acid excretion, an enhancement of the body's antioxidant defences, and a decrease in vascular inflammation (Azantsa et al., 2022). Polyherbal teas amalgamate various medicinal plants with lipid-lowering, antioxidant, and anti-inflammatory properties, positioning them as potential natural alternatives for managing hyperlipidaemia and preventing atherosclerosis (Akinmoladun et al., 2020).

1.2 AIM OF STUDY

The aim of this study is to evaluate the Anti-Hyperlipidemia, Anti-Atherosclerosis Effect Of The Polyherbal Formulated Tea On Atherogenic Diet Induced Hyperlipidemia And Atherosclerosis In Wistar Rats.

1.3 SPECIFIC OBJECTIVES OF THE STUDY

The specific objectives of the study are:

1. To induce hyperlipidemia and atherosclerosis in Wistar rats using cholesterol and cholic acid dissolved in arachis oil.

2. To analyze the lipid profiles, such as cholesterol, triglycerides, LDL, VLDL, and HDL, using the colorimetric method.

3. To assess atherosclerotic lesions through histopathological examination of vascular tissues using a microscope.

4. To monitor changes in body weight of Wistar rats across the different groups, including Normal Control (NC), Cholesterol Control (CC), Polyherbal Tea (PHT), and Atorvastatin (ATV), in order to assess the effect of treatments on weight gain or reduction.

5. To compare the overall effectiveness of the polyherbal tea with that of a standard lipid-lowering drug (atorvastatin).

CHAPTER TWO

LITERATURE REVIEW

2.1 Description of *Ageratum conyzoides* (Goat Weed)

Ageratum conyzoides L., commonly known as goat weed, billy-goat weed, or chick weed, is an annual aromatic herb belonging to the family Asteraceae. It is native to tropical and subtropical regions but has spread widely across Asia, Africa, and South America due to its adaptability and ability to colonize disturbed soils. It thrives in open grasslands, roadsides, and agricultural fields and is often regarded as an invasive species in many regions. The plant is characterized by a soft, erect stem and a relatively short growth cycle, usually completing its lifespan within a single season. Mature plants typically range from 30 to 100 cm in height, though under favorable conditions, they may grow slightly taller. The leaves are opposite, ovate, and serrated, usually measuring about 5–7 cm long, and when crushed, they emit a strong and characteristic odor due to the release of volatile oils (Chahal et al., 2021). The flowers of A. conyzoides are small, delicate, and grouped in dense clusters known as corymbose capitula. These clusters give the inflorescences a tufted or filamentous appearance. Their color varies from white to pinkish-lilac, making the plant easy to identify in the field. The stem is often covered with fine hairs, which protect the plant from herbivores and water loss. The seeds are lightweight and easily dispersed by wind, contributing to the species' invasive potential. Phytochemical studies have revealed that *Ageratum conyzoides* contain a wide variety of secondary metabolites. The most notable include precocene I and II (chromene derivatives), flavonoids such as quercetin and luteolin, alkaloids, terpenoids, coumarins, and phytosterols. These compounds are believed to be largely responsible for the plant's medicinal properties (Kato-Noguchi et al., 2024).

2.1.2 Distribution of *Ageratum conyzoides* (Goat Weed)

Although originally native to tropical America, *Ageratum conyzoides* has spread widely across the globe and is now considered one of the most aggressive invasive weeds in tropical and subtropical regions. Today, it is found in sub-Saharan Africa, South and Southeast Asia, and parts of Oceania, where it grows abundantly along farm margins, roadsides, gardens, fallow lands, abandoned fields, and disturbed soils. One major reason for its successful spread is its high seed production capacity. A single mature plant can produce thousands of very small and lightweight seeds, which are easily dispersed by the wind over long distances. These seeds can also stick to animal fur, clothing, or farm equipment, making unintentional human and animal activity another factor aiding its spread. Once dispersed, the seeds germinate rapidly under favorable conditions such as warm temperatures and moderate rainfall, allowing the plant to establish quickly and outcompete native vegetation (Kaur et al., 2023). Another important factor behind the weed's invasiveness is its allelopathic properties. *Ageratum conyzoides* is capable of releasing chemical compounds into the soil that suppress the germination and growth of surrounding plants. This natural chemical warfare gives goat weed a competitive advantage, enabling it to dominate fields and open lands while reducing biodiversity in the areas it invades. Ecological studies further show that the weed is highly adaptable to diverse environments. It thrives in arid, semi-arid, and humid climates and is capable of growing at altitudes of up to 1,800 meters above sea level. This wide tolerance for environmental conditions makes it extremely difficult to contain. In addition, its aggressive competition with crops leads to serious agricultural problems. It competes with cultivated plants for sunlight, water, and soil nutrients, often resulting in reduced crop yields and soil depletion. In natural ecosystems, its spread can displace native plant species, alter soil chemistry, and disrupt ecological balance (Kaur et al., 2023).

2.1.3 Ethnomedicinal Properties of *Ageratum conyzoides* (Goat Weed)

Despite being regarded mainly as an invasive weed, *Ageratum conyzoides* have long held an important place in traditional medicine systems across different regions of the world. Many communities in Africa, Southeast Asia, and South America have used this plant for centuries to manage a variety of health problems. Local healers often prepare remedies from its leaves, stems, and roots, which remain popular where access to conventional medicine is limited (Chahal et al., 2021). Traditional applications of *Ageratum conyzoides* are diverse, including treatments for fever, colds, headaches, diarrhea, rheumatism, stomachaches, and skin wounds. In Nigeria, ethnobotanical surveys show that poultices from crushed leaves are applied to burns, wounds, and skin infections. Decoctions or infusions prepared from the leaves or roots are also consumed to relieve gastrointestinal complaints such as dysentery, stomach upset, and abdominal pain (Chahal et al., 2021). These practices highlight the plant's deep-rooted role in local healing traditions. Recent scientific studies have validated many of these traditional uses. Animal studies show that extracts of *Ageratum conyzoides* promote faster wound closure, stimulate collagen formation, and support skin regeneration, also helping prevent bacterial contamination (Putri et al., 2021). Both leaf and root extracts have demonstrated anti-inflammatory and analgesic effects by reducing swelling and relieving pain, believed to be linked to the inhibition of inflammatory mediators such as prostaglandins and cytokines (Chahal et al., 2021). The plant also contains compounds with strong antimicrobial activity, inhibiting the growth of harmful bacteria like Staphylococcus aureus and Escherichia coli, which supports its traditional use for skin and gastrointestinal issues (Chahal et al., 2021). Furthermore, flavonoids and chromenes act as effective antioxidants, neutralizing free radicals, and also exhibit antispasmodic actions on smooth muscles, explaining their use for relieving gastrointestinal cramps (Chahal et al., 2021).

2.2 *Anthocleista djalonensis* (Cabbage tree)

2.2.1 Description of *Anthocleista djalonensis* (Cabbage tree)

Anthocleista djalonensis A. Chev. is a medium-sized tropical African tree belonging to the Gentianaceae (gentian) family. It is widely recognized by its straight trunk (bole), which often supports a rounded and spreading crown. The leaves are among its most striking features as they are simple, entire, and conspicuously large, often measuring 20–30 cm or more in length. The leaves are arranged oppositely and borne on short petioles with a clearly visible midrib. In younger plants or newly sprouting branches, the leaves form tight whorls at the shoot tips, giving the canopy a "cabbage-like" appearance (Anyanwu et al., 2015). This characteristic explains its popular common name, "cabbage tree." The flowers are tubular, showy, and creamy white, borne in terminal clusters (inflorescences). The fruit is also an ovoid capsule as it contains many tiny seeds, which facilitates wide dispersal (Kouakou et al., 2023). According to World Flora Online (WFO, 2024), *Anthocleista djalonensis* is an accepted species name, first published by Auguste Chevalier in 1908. Taxonomic records confirm its inclusion as part of the Anthocleista genus, which comprises several African species valued in local medicine and ethnobotany. The tree typically occurs in moist, lowland areas, forest margins, and riverine environments across West and Central Africa, where it has both ecological and medicinal importance (Kouakou et al., 2023).

2.2.2 Distribution of *Anthocleista djalonensis* (Cabbage tree)

Anthocleista djalonensis is native to West Tropical Africa and is well adapted to the ecological conditions of the region. Floristic surveys and plant guides indicate that its natural range extends from Guinea and Guinea-Bissau eastward to Cameroon, covering countries such as Sierra Leone, Liberia, Ivory Coast, Ghana, Togo, Benin, Nigeria, and parts of Cameroon (World Flora Online, 2024). Within this belt, the species thrives in several types of habitats, including savanna woodlands, forest margins, thickets, and moist riparian zones. The tree is most commonly found at low elevations below 500 meters, but it can also occur along gallery forests and riverbanks where soils are consistently moist. Such environments provide favorable conditions for its growth, as the plant prefers well-drained but fertile soils with moderate to high humidity. Field records from the Central African Plants Photo Guide document populations in Guinea and Mali, giving visual evidence of its habitat preferences and confirming its presence in both semi-open savanna and moister forest-edge areas (Kouakou et al., 2023). From a broader taxonomic perspective, the genus Anthocleista is widely distributed across tropical Africa, including Madagascar and the Comoros Islands. Many species within the genus share overlapping ranges and ecological niches. For example, A. vogelii and A. nobilis are often reported in similar habitats, sometimes co-occurring with *Anthocleista djalonensis*. This close ecological overlap explains why several Anthocleista species are frequently cited in ethnobotanical surveys and traditional medicine reports across West and Central Africa (Anyanwu et al., 2015).

2.2.3 Ethnomedicinal properties of *Anthocleista djalonensis* (Cabbage tree)

Anthocleista djalonensis is widely utilized in traditional medicine across West Africa for treating metabolic, infectious, inflammatory, and febrile conditions. Practitioners commonly prepare decoctions or macerations using the root bark, stem bark, or leaves (Anyanwu et al., 2015). A recent nationwide analysis of Nigerian ethnobotanical data (1964–2024) lists *Anthocleista djalonensis* as a remedy for hypertension, diabetes, gastrointestinal disorders, malaria, jaundice, skin infections, and wound care. Preparations are administered orally, applied topically, or used in therapeutic body baths (Rafiu et al., 2025). Scientific studies have also provided evidence supporting many traditional uses. Antioxidant, anti-inflammatory, and neuroprotective activity was demonstrated when fractionated root bark extracts protected mice from pentylenetetrazole-induced seizures and neuronal loss. These extracts restored antioxidant balance (e.g., lowering MDA, improving GSH and SOD), enhanced GABAergic signaling, and provided mechanistic evidence for traditional CNS uses. Bioactive fractions rich in djalonensin, lichexanthone, sweroside, and ursolic acid were identified, and acceptable acute-toxicity profiles were reported in mice within tested ranges (Kouakou et al., 2023). Furthermore, in adult rats, methanolic and aqueous-ethanolic root extracts showed reproductive/testicular protection and anti-inflammatory effects by mitigating LPS-induced testicular inflammation (e.g., reducing interleukin-6 and nitrite) and protecting against busulfan-induced depletion of germ cells, with histological evidence of seminiferous tubule recovery. These outcomes align with the anti-inflammatory and antioxidant phytochemicals reported for the species. The synthesizing of traditional claims concluded that *Anthocleista djalonensis* shows strong evidence for antidiabetic and antibacterial effects, consistent with iridoids/secoiridoids and phenolic constituents known to affect glucose handling, microbe growth, and inflammatory pathways. Such activity profiles rationalize folk uses for diabetes, typhoid-like fevers, diarrhea/dysentery, and skin/wound infections (Anyanwu et al., 2015). Ethnobotanical sources routinely mention root bark and stem bark decoctions for internal use and leaf poultices or washes for skin and wounds (Anyanwu et al., 2015; Rafiu et al., 2025). However, safety likely depends on the plant part, dose, solvent, and chemotype. Acute-toxicity observations in murine models suggest a reasonable safety margin for certain fractions, but comprehensive chronic toxicity, mutagenicity, and reproductive-toxicity evaluations remain limited and should precede clinical translation. Given the potent iridoids/xanthones present, standardized extraction, quality control, and dose-response studies are recommended (Anyanwu et al., 2015).

2.3 *Zingiber officinale* (Ginger)

2.3.1 Description of *Zingiber officinale* (Ginger)

Zingiber officinale Roscoe, commonly known as ginger, is a perennial herb that belongs to the Zingiberaceae family. It is one of the most widely used spices and medicinal plants in the world, cultivated mainly for its aromatic rhizome (underground stem). Ginger grows by producing leafy stems called pseudostems that rise from the rhizome. Each pseudostem carries narrow, lance-shaped leaves and produces flower clusters that are usually pale yellow or greenish in color. While the plant as a whole is useful, the rhizome is the most important part because it serves as both a cooking spice and a traditional remedy. Phytochemically, ginger contains a wide variety of active compounds. The most abundant are gingerols, particularly 6-gingerol, which is responsible for its distinctive pungent taste and many of its health benefits. When ginger is dried or heated, gingerols can change into shogaols, such as 6-shogaol, which are often more potent in certain biological activities. Other compounds include paradols, zingerone, volatile oils like zingiberene, flavonoids, and phenolic acids. The balance of these compounds can change depending on the variety of ginger, where it is grown, and how it is processed (fresh vs dried). For instance, dried ginger tends to have higher levels of shogaols, which can make it stronger for medicinal purposes. Beyond its culinary use as a flavoring agent in food and drinks, ginger is highly valued for its medicinal properties. Studies have shown that it possesses antioxidant and anti-inflammatory effects, can reduce nausea and vomiting (antiemetic), has antimicrobial activity, and may help regulate metabolism. These broad activities explain why ginger is widely used in both traditional medicine systems, such as Ayurveda and Chinese medicine, and modern clinical settings (Mao et al., 2019).

2.3.2 Distribution of *Zingiber officinale* (Ginger)

Ginger (*Zingiber officinale*) is believed to have originated in Southeast Asia, where it has been cultivated and used for both food and medicine for thousands of years. Historical records show its long-standing role in Indian, Chinese, and Middle Eastern cultures, where it was traded as a valuable spice and healing plant. Over time, ginger spread through trade routes and colonial exchange, eventually becoming a globally recognized crop. Today, ginger is grown widely in tropical and subtropical regions around the world. The major producers include India, China, Indonesia, Nigeria, Nepal, Bangladesh, and Thailand. India alone contributes a large percentage of global production, followed by China, making both countries leaders in ginger farming and export. In Africa, Nigeria stands out as one of the main sources, particularly for local consumption and export to nearby countries (Mao et al., 2019). The plant requires warm climates with consistent rainfall or irrigation, high humidity, and well-drained soils to thrive. Cultivation usually begins with planting pieces of rhizome rather than seeds. These rhizome segments sprout into new plants, which grow into leafy pseudostems. The crop is typically ready for harvest 7 to 10 months after planting, once the aboveground stems and leaves start to turn yellow, signaling that the rhizomes have matured. Beyond agriculture, ginger is widely distributed in global markets in many forms, such as fresh rhizomes, dried slices, powdered spice, essential oil, and standardized extracts. These are used in traditional medicine systems such as Ayurveda and Traditional Chinese Medicine, as well as in modern herbal products and nutraceuticals. In addition, ginger remains a staple in culinary practices worldwide, valued for its strong aroma, spicy taste, and health-promoting properties (Mao et al., 2019).

2.3.3 Ethnomedicinal properties of *Zingiber officinale* (Ginger)

Ginger (*Zingiber officinale*) has a long history of traditional use across many cultures for healing. It’s been a common remedy for nausea and vomiting (especially during pregnancy or after surgery), digestive problems (like bloating or indigestion), common colds, and pain from arthritis or menstruation (Mao et al., 2019). Modern scientific research has confirmed these traditional uses and also pointed to benefits for the heart and metabolism. Ginger's power comes from compounds like gingerols, shogaols, and paradols. These chemicals act as strong antioxidants and anti-inflammatories, fighting cell damage and calming inflammation (Mao et al., 2019; Pourmasoumi et al., 2018). Scientific studies strongly support ginger's ability to settle the stomach and stop nausea and vomiting, which is one of its most reliable traditional uses (Mao et al., 2019). Ginger also helps reduce pain in people with osteoarthritis and menstrual cramps, likely by slowing down the production of pain-causing chemicals (Mao et al., 2019). Research on ginger's effects on blood fats (lipids) has been mixed. Early studies suggested it could lower bad cholesterol (LDL-C) and triglycerides (Pourmasoumi et al., 2018), but later research showed these results weren't consistent, likely due to differences in the dose (usually 1–3 grams per day), the form of ginger used, and the people studied (Pourmasoumi et al., 2018; Ebrahimzadeh et al., 2022). However, several trials have shown ginger can cause a small drop in blood pressure and improve inflammation markers. This, combined with its antioxidant action, suggests it may help protect against heart disease (Ebrahimzadeh et al., 2022). Ginger may protect blood vessels by preventing the oxidation of LDL, an early step in the development of heart issues (Mao et al., 2019; Pourmasoumi et al., 2018). Ginger is generally considered safe when consumed in the typical amounts used for cooking. Doses in clinical studies range from 500 mg to 3 grams daily. Side effects are minor, usually just heartburn or stomach upset. However, because ginger can act as a blood thinner, high doses might increase the risk of bleeding in people already taking anti-clotting medications. Therefore, it's important to use standardized extracts and monitor for any interactions with other drugs (Mao et al., 2019). While lab and animal studies show clear benefits, the results in human trials still vary depending on how the ginger is used (Pourmasoumi et al., 2018; Ebrahimzadeh et al., 2022; Salih et al., 2023).

2.4 *Allium sativum* (Garlic)

2.4.1 Description of *Allium sativum* (Garlic)

Allium sativum L., commonly known as garlic, is a bulbous perennial plant that belongs to the Amaryllidaceae family. It has been cultivated for centuries across the world, both as a spice in cooking and as a medicinal plant. The garlic plant develops a short stem above the ground and a bulb underground. This bulb is made up of multiple smaller segments called cloves, each covered by a thin, papery skin. When crushed or chopped, the bulb produces a very strong odor and flavor that are easily recognized. This characteristic smell is due to the presence of sulfur-containing compounds, especially alliin, which is converted into allicin by the enzyme alliinase when the tissue is damaged (Pourreza et al., 2022). Phytochemical studies reveal that garlic is rich in bioactive compounds. These include organosulfur compounds such as allicin, diallyl disulfide, and diallyl trisulfide, as well as S-allyl cysteine, which is more common in aged garlic preparations. In addition, garlic contains flavonoids, saponins, and several polyphenols that contribute to its therapeutic effects (Du et al., 2024; Sleiman et al., 2024). These compounds are responsible for garlic's broad range of biological activities. Allicin, for instance, is strongly antimicrobial, helping to fight bacteria, fungi, and some viruses. Organosulfur compounds also show antioxidant and anti-inflammatory effects, which support cardiovascular health and protect tissues from damage. Furthermore, garlic is known for its lipid-lowering and antiplatelet actions, which explain why it is often recommended in relation to heart health and blood circulation (Du et al., 2024).

2.4.2 Distribution of *Allium sativum* (Garlic)

Garlic (*Allium sativum*) is believed to have originated in Central Asia, particularly in regions that are now parts of Iran and Turkmenistan. From there, it spread through trade and migration and has been cultivated for thousands of years. Historical records show that garlic was used in ancient Egypt, Greece, Rome, India, and China, both as food and as medicine. Because of its long history of human use, wild forms of garlic are rare today, and most of the species exist only in cultivation (Asgharpour et al., 2021). At present, garlic is grown widely around the world. The largest producers are China and India, which together supply most of the global market. Other major producers include Bangladesh, Egypt, South Korea, Spain, and some African countries such as Nigeria and Ethiopia. Garlic grows well in temperate and subtropical climates, thriving in well-drained soils with moderate rainfall and plenty of sunlight. Farmers usually propagate it using cloves rather than seeds, and the crop is harvested after several months once the leaves begin to yellow and dry (Asgharpour et al., 2021). In addition to being an important agricultural crop, garlic is widely available in commercial markets in different forms. These include fresh bulbs, dried or powdered garlic, garlic oil, and aged garlic extract (AGE). Each preparation has its own chemical profile, which influences its flavor, strength, and medicinal properties. For this reason, research and clinical studies emphasize the need to clearly state the form of garlic used and its standardization (e.g., allicin or S-allyl cysteine content) to ensure accuracy and comparability (Du et al., 2024; Zhao et al., 2024).

2.4.3 Ethnomedicinal properties of *Allium sativum* (Garlic)

Garlic (*Allium sativum*) is one of the world's most widely used medicinal plants, with a long history stretching back thousands of years across ancient civilizations like the Egyptians and Greeks, who used it for treating infections, fatigue, and circulation problems. Today, both traditional use and modern research agree that garlic is valuable for its strong effects on the heart, blood vessels, metabolism, and immunity, making it highly relevant for conditions like high blood fat levels (hyperlipidemia) and artery plaque buildup (atherosclerosis). Garlic is best known for its lipid-lowering effects, a property supported by modern clinical research. Many studies have shown that garlic supplements can significantly reduce total cholesterol (TC), triglycerides (TG), and "bad cholesterol" (LDL-C), and sometimes slightly increase "good cholesterol" (HDL-C) (Zhao et al., 2024). These effects are primarily due to garlic's organosulfur compounds, such as allicin, which are thought to lower cholesterol production in the liver by inhibiting the key enzyme HMG-CoA reductase (Sleiman et al., 2024). Results can vary depending on the type of garlic preparation used, dosage, and study length. A major benefit is garlic's powerful antioxidant action. It helps protect the body by fighting harmful free radicals and boosting natural antioxidant enzymes (like SOD, CAT, and GPx) (Sleiman et al., 2024). This is critical in atherosclerosis, as garlic slows down plaque formation by preventing the oxidation of LDL cholesterol, an essential early step in the disease. Garlic also has strong anti-inflammatory properties, lowering markers like C-reactive protein (CRP) and IL-6, which helps calm blood vessel walls and slow plaque progression (Zhao et al., 2024). Garlic has also been shown to reduce blood pressure, particularly in people with hypertension (Sleiman et al., 2024). It does this by increasing nitric oxide (NO) availability, which relaxes blood vessels, and by protecting the vessel lining (endothelial cells). Furthermore, garlic exhibits mild anti-platelet activity, reducing the risk of blood clot formation on existing plaques, a common cause of heart attacks and strokes (Sleiman et al., 2024). This anti-clotting effect, however, means its use must be monitored in patients taking blood thinners. Garlic is a valuable component for polyherbal mixtures aiming to treat hyperlipidemia because it offers multiple benefits: it directly lowers lipids (Zhao et al., 2024), provides antioxidant defense to protect vessels (Sleiman et al., 2024), and calms inflammation (Sleiman et al., 2024). In animal studies, garlic extracts have consistently improved lipid profiles and reduced oxidative stress, strongly supporting its use in testing polyherbal tea formulations for hyperlipidemia in Wistar rats (Asgharpour et al., 2021). Garlic is generally safe at food-level doses (0.5–5 g/day), with mild side effects like odor or stomach discomfort. However, researchers must carefully standardize the preparation and dose and monitor for increased bleeding risk and drug interactions (Zhao et al., 2024).

2.5 *Thespesia garckeana* (Snot Apple)

2.5.1 Description of *Thespesia garckeana* (Snot Apple)

Thespesia garckeana F. Hoffm., also known by its synonym Azanza garckeana, is a small to medium-sized tree that belongs to the Malvaceae family. The tree usually grows between 3 and 10 meters tall and often develops a single or just a few trunks, which support a rounded and spreading canopy. Its leaves are broad, heart-shaped to oval (cordate to ovate), and can sometimes have slightly toothed edges. The plant is quite attractive when in bloom, producing bright hibiscus-like flowers that range from yellow to orange. These flowers later develop into rounded or oval-shaped fruits. The fruits are especially distinctive because of their sticky, mucilaginous pulp. When the pulp is chewed, it forms a gummy and elastic mass, which is why the fruit is popularly called "snot apple" or "African chewing gum." In many African communities, people eat the fruit pulp as a snack, while in some areas it also has cultural and traditional uses (Kafunda et al.,2017). Phytochemical studies show that *Thespesia garckeana* is rich in several bioactive compounds. These include flavonoids, phenolics, terpenoids, fatty acids, and other polyphenols. Among these, luteolin and related flavones are often identified as key components, particularly through modern analyses such as HPLC and LC-MS. These compounds are thought to play a major role in the plant's antioxidant activity and its ability to modulate enzymes (Yusuf et al., 2023). The seeds, bark, leaves, and fruit pulp have all been studied, and results show that the chemical composition can vary depending on which part of the plant is used, how it is extracted, and even the region where the plant is grown. (Yusuf et al., 2023).

2.5.2 Distribution of *Thespesia garckeana* (Snot Apple)

Thespesia garckeana is native to sub-Saharan Africa and has a very wide distribution across the continent. It is commonly found in savanna woodlands, open bushlands, and dry deciduous thickets, making it an important species of semi-arid and sub-humid regions. The tree grows naturally in West Africa, including countries like Guinea and Nigeria, and extends through Central Africa into Southern Africa, where it is especially common in Botswana, Zimbabwe, Mozambique, and South Africa (Kafunda et al., 2017). This tree usually prefers well-drained soils and can adapt to a variety of local conditions. It often grows near termite mounds, along old farmlands, and sometimes around homesteads where it is encouraged because of its usefulness. The ability of *Thespesia garckeana* to survive in harsh, dry environments shows its resilience and ecological importance in African landscapes (Kafunda et al., 2017). Beyond its natural growth, the tree holds significant value for local communities. The sticky fruit pulp is eaten as food, often enjoyed as a natural snack, while other parts of the tree are used in traditional medicine. It also serves as fuelwood, provides timber for construction, and contributes to household needs in rural areas (Mgalula et al., 2024).

2.5.3 Ethnomedicinal properties of *Thespesia garckeana* (Snot Apple)

Thespesia garckeana, also known as snot apple or African bubblegum, is highly valued across Africa for both its nutritional and medicinal roles. Traditional healers use the fruit, seeds, bark, and leaves to prepare remedies for a wide range of issues, including stomach pain, diarrhea, coughs, fever, wounds, and liver conditions. Notably, the fruit pulp is also traditionally used to boost fertility and libido, and as a tonic for postpartum women (Nutraceutical Review, 2022; Mgalula et al., 2024). The sticky fruit pulp is often eaten or made into drinks, while the other plant parts are processed into decoctions or poultices (Nutraceutical Review, 2022). Recent laboratory and animal studies are now confirming many of these traditional uses, linking the effects to the plant's rich mix of phytochemicals, especially flavonoids like luteolin and polyphenols. A key finding is its potent antioxidant and anti-inflammatory action. Extracts, particularly those rich in luteolin, boost the body's natural antioxidant enzymes (like SOD and catalase) and reduce inflammation in various experimental models, which scientifically supports its use for metabolic and inflammatory conditions (Yusuf et al., 2023). Several studies have confirmed the antidiabetic and hypoglycemic actions of *Thespesia garckeana* extracts. They appear to lower blood sugar by enhancing insulin release and protecting the insulin-producing cells of the pancreas from damage, which aligns with its use in managing diabetes (Yusuf et al., 2023). Furthermore, experimental evidence suggests hepatoprotective and nephroprotective effects, meaning the extracts can shield the liver and kidneys from chemical injury by reducing elevated liver enzymes and improving kidney function markers. These protective actions are attributed to its antioxidant and anti-inflammatory properties, supporting its traditional use for liver ailments (Yusuf et al., 2023). Additionally, laboratory tests confirm antimicrobial activity against common bacteria (like Staphylococcus aureus and E. coli) and fungi (Candida albicans), justifying its traditional use in wound care and treating infections (Kafunda et al., 2017). Findings on its effects on lipid profile are mixed. Some animal studies, particularly in diabetic models, show that extracts can improve lipid profiles by reducing total cholesterol and LDL levels (Yusuf et al., 2023). However, other research reports contradictory or insignificant effects, with one study noting increased cholesterol at a high dose (Obia et al., 2024; Iloabuchi et al., 2024). This variability likely depends on the plant part, extraction method, and dose. Overall, the plant's strong antioxidant effects, largely due to luteolin, provide a strong mechanistic reason for its potential in preventing heart disease by protecting against cell damage and reducing inflammation (Yusuf et al., 2023). Nutritionally, the fruit is valuable, containing proteins, vitamins, minerals, and various polyphenols (Nutraceutical Review, 2022). Regarding safety, acute toxicity tests suggest *Thespesia garckeana* has low immediate toxicity (LD_{50} values greater than 2000 mg/kg for some extracts). However, the potential for unintended metabolic consequences, such as increased cholesterol at high doses (Obia et al., 2024), means researchers urge caution and call for more detailed long-term safety studies before the plant is widely recommended for medicinal use (Obia et al., 2024).

Plate 1: *Ageratum conyzoides*

(Chahal et al., 2021)

Plate 2: *Anthocleista djalonensis*

(Yusuf et al., 2023)

Plate 3: *Zingiber officinale*

(Kouakou et al., 2023)

Plate 4: *Allium sativum*

(Dhanik et al., 2017)

Plate 5: *Thespesia garckeana*

(Mgalula et al., 2024)

2.6 Atorvastatin

2.6.1 Overview of Atorvastatin

Atorvastatin belongs to the drug class known as statins, or more specifically, HMG-CoA reductase inhibitors. It is one of the most commonly prescribed medicines in the world for lowering cholesterol levels and reducing the risk of cardiovascular disease. At the molecular level, atorvastatin works by blocking the enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. This enzyme is very important in the liver because it controls the rate-limiting step of cholesterol production. When atorvastatin inhibits this enzyme, the liver produces less cholesterol. As a result, the liver cells respond by increasing the number of LDL receptors on their surface. These receptors pull more low-density lipoprotein cholesterol (LDL-C, often called "bad cholesterol") out of the bloodstream. The final outcome is a significant reduction in blood LDL-C levels, which lowers the risk of atherosclerosis and heart disease. Apart from lowering cholesterol, atorvastatin also has what are called "pleiotropic effects." These are additional benefits not directly related to cholesterol lowering. For example, it improves endothelial function, helps stabilize atherosclerotic plaques, reduces oxidative stress, decreases vascular inflammation, and provides mild antithrombotic (anti-clotting) effects. These actions are linked to its influence on isoprenoid intermediates, inflammatory pathways such as NF-κB, and its ability to increase nitric oxide availability in blood vessels (Toth et al., 2019).

2.6.2 History of Atorvastatin

The history of atorvastatin is closely tied to the discovery of the statin drug class. The journey began in the 1970s when Japanese scientist Akira Endo and his team identified certain fungal metabolites that were able to block the enzyme HMG-CoA reductase. This enzyme plays a central role in cholesterol production, so its inhibition opened a new path for treating high cholesterol and preventing heart disease. Early statins were natural compounds or their derivatives, but scientists later developed synthetic statins with stronger effects and better safety profiles. Atorvastatin, a fully synthetic statin, was developed by Pfizer during the late 1980s and early 1990s. It was approved by the U.S. Food and Drug Administration (FDA) in 1996 under the brand name Lipitor®. Once launched, it quickly became one of the most prescribed medicines worldwide. The reason for its success was its ability to significantly lower LDL cholesterol (often called "bad cholesterol") at doses that were convenient and well tolerated. Compared to earlier statins, atorvastatin has a longer half-life, greater potency, and allows for once-daily dosing. These advantages, along with its proven role in preventing cardiovascular disease, made it a cornerstone therapy (Chester et al., 2021).

2.6.3 Indications

Atorvastatin is one of the most commonly prescribed medicines for managing cholesterol problems and reducing the risk of heart disease. Doctors use it to treat a wide range of lipid disorders and to lower the chance of developing serious cardiovascular events. One major use of atorvastatin is in people with primary hypercholesterolemia, which means having very high cholesterol either because of inherited causes (familial) or lifestyle and diet (nonfamilial). In these cases, atorvastatin helps reduce levels of low-density lipoprotein cholesterol (LDL-C), often referred to as "bad cholesterol." It is also prescribed for mixed dyslipidemia, a condition where patients may have high triglycerides (TG), high LDL, and low high-density lipoprotein cholesterol (HDL). In such cases, atorvastatin works as an add-on to lifestyle changes like diet and exercise (Grundy et al., 2018). Beyond lowering cholesterol, atorvastatin is important in the prevention of atherosclerotic cardiovascular disease (ASCVD). It is given to people who already have heart problems such as coronary artery disease, stroke, or peripheral arterial disease (secondary prevention), and also to those at high risk of developing these conditions (primary prevention). Certain groups, like patients with diabetes or familial hypercholesterolemia, benefit greatly from atorvastatin because they need to reach strict LDL-C goals to reduce risk. Clinical guidelines from major health organizations (AHA/ACC, ESC) recommend atorvastatin as either moderate- or high-intensity therapy. High doses (40–80 mg) can reduce LDL-C by 50% or more, making it especially useful for very high-risk patients (Arnett et al., 2019).

2.6.4 Side Effects

Atorvastatin is generally well tolerated, but important adverse effects and safety concerns include:

Myopathy and myalgia: Muscle-related problems are the most widely recognized side effects of statins. These can range from mild muscle pain (myalgia) to more serious conditions such as myopathy or rhabdomyolysis, which is severe muscle breakdown. The risk is higher at larger doses, in older patients, in those with kidney disease, or when atorvastatin is combined with drugs that interfere with its metabolism, especially CYP3A4 inhibitors (Newman et al., 2019; Turner et al., 2019).

Transaminase elevations and rare severe liver injury: Some patients develop mild and usually temporary increases in liver enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST). These elevations often resolve on their own, even while treatment continues. True cases of significant liver injury are very rare but have been documented in post-marketing reports (Averbukh et al., 2022).

New-onset diabetes mellitus (small absolute risk increase): High-intensity statins, including atorvastatin, are associated with a slightly increased risk of developing type 2 diabetes.

However, the overall risk is small, and the benefits in reducing cardiovascular events such as heart attack and stroke are considered much greater (Grundy et al., 2018; Arnett et al., 2019).

Cognitive complaints and other reported adverse effects: Rare cases of memory loss, confusion, or other cognitive complaints have been reported. Current research has not confirmed a clear or consistent link between statin use and these symptoms, and evidence of causation is limited (Ward et al., 2019).

General safety perspective: Most adverse effects improve with dose adjustment or discontinuation. Serious side effects are uncommon, and overall, atorvastatin remains highly beneficial for reducing the risk of atherosclerotic cardiovascular disease (Turner et al., 2019; Averbukh et al., 2022).

2.6.5 Contraindications

Contraindications and cautions for atorvastatin include:

Known hypersensitivity: Atorvastatin should not be used in people who have a history of allergy or hypersensitivity to the drug or any of its components. Allergic reactions may include skin rash, swelling, or difficulty breathing (FDA label) (Ward et al., 2019).

Active liver disease or unexplained persistent liver enzyme elevation: Because atorvastatin is metabolized in the liver, it must not be given to patients with active liver disease or those showing unexplained increases in liver enzymes such as ALT or AST. Regular monitoring of liver function before and during therapy is advised (Averbukh et al., 2022).

Pregnancy and lactation: Statins, including atorvastatin, are contraindicated during pregnancy since cholesterol is essential for fetal development, and possible teratogenic risks cannot be ruled out. Similarly, use during breastfeeding is avoided because the drug may pass into breast milk. Although some newer guidelines allow clinician judgment in rare cases, standard practice is to avoid statins during pregnancy and lactation (Ward et al., 2019).

Concomitant use of strong CYP3A4 inhibitors: Drugs such as certain antifungals, macrolide antibiotics, and HIV protease inhibitors can significantly increase atorvastatin levels in the blood, raising the risk of myopathy and rhabdomyolysis. In such cases, dose adjustment or an alternative therapy is recommended (Arnett et al., 2019).

Other considerations: Clinicians also take into account kidney function, possible drug–drug interactions, and individual patient risk factors before prescribing or adjusting atorvastatin (Arnett et al., 2019).

2.6.6 Role as the Gold Standard and Rationale for Comparison with Polyherbal Tea

Atorvastatin is considered the gold standard drug for the treatment of hyperlipidemia and prevention of cardiovascular disease. This reputation comes from several key factors. First, there is strong scientific evidence from large randomized controlled trials and meta-analyses showing that atorvastatin not only lowers LDL cholesterol effectively but also reduces the risk of major cardiovascular events such as heart attacks, strokes, and cardiovascular-related deaths (Toth et al., 2019; Arnett et al., 2019). Second, atorvastatin has a well-understood pharmacology. Its mechanism of action, metabolism, and dose–response effects are clearly established, which means clinicians can predict how much LDL reduction to expect at different doses. Third, atorvastatin is endorsed by major clinical guidelines worldwide as a first-line therapy for both primary prevention (in high-risk individuals) and secondary prevention (in patients with existing cardiovascular disease) (Grundy et al., 2018). Because of these factors, atorvastatin is not only effective but also a trusted benchmark in both research and clinical settings. In preclinical studies, including those using Wistar rats, atorvastatin is often chosen as a positive control drug. This allows researchers to confirm that the hyperlipidemia or atherosclerosis model is working correctly and to have a reliable standard for comparison. For example, atorvastatin provides a measurable reduction in serum cholesterol and LDL, improvement in lipid ratios, and reduction in aortic plaque formation. These outcomes create a baseline standard against which new therapies, such as polyherbal teas, can be measured (Grundy et al., 2018; Arnett et al., 2019). Comparing a polyherbal tea with atorvastatin is scientifically valuable for several reasons. First, atorvastatin gives a clear reference point for lipid-lowering effects, so researchers can quantify how effective the herbal tea is in comparison. Second, atorvastatin has pleiotropic effects; it reduces inflammation and oxidative stress and stabilizes plaques, and these are mechanisms that overlap with many phytochemicals found in herbal preparations. Third, if the polyherbal tea demonstrates comparable or complementary effects, such as strong antioxidant activity with potentially lower side effects, this strengthens its case as a safe and effective alternative or adjunct (Toth et al., 2019). In summary, using atorvastatin as a comparison ensures scientific rigor. If the polyherbal tea shows benefits similar to atorvastatin in terms of lipid profile, inflammation markers, antioxidant defense, and tissue protection, it would provide convincing preclinical evidence to move forward with further safety testing and eventual clinical trials (McIver et al., 2020; Averbukh et al., 2022).

2.7 Hyperlipidemia

2.7.1 Definition of Hyperlipidemia

Hyperlipidemia is a health condition where the levels of fats (lipids) in the blood are higher than normal. The main lipids involved are cholesterol and triglycerides, which are important for normal body functions such as building cell membranes, producing hormones, and storing energy. However, when these lipids become too high, they start to harm the body instead of helping it. This condition is one of the major risk factors for cardiovascular diseases, including coronary artery disease, stroke, and peripheral vascular disease (Mach et al., 2020). High lipid levels, especially low-density lipoprotein cholesterol (LDL-C), can accumulate on the walls of blood vessels, forming fatty deposits called plaques. Over time, these plaques harden and narrow the arteries, a process known as atherosclerosis, which restricts blood flow and increases the risk of heart attack or stroke (Grundy et al., 2019). Hyperlipidemia may show up in different ways: high total cholesterol, high LDL-C, low high-density lipoprotein cholesterol (HDL-C) (the "good" cholesterol), or high triglycerides. Many people with hyperlipidemia do not have any symptoms for years, which is why it is often called a silent condition. Regular blood lipid testing is very important for early detection and prevention of serious health problems (Ference et al., 2017).

2.7.2 Types of Hyperlipidemia (Primary vs Secondary)

Hyperlipidemia can be broadly classified into primary (genetic) and secondary (acquired) forms.

Primary Hyperlipidemia:

Primary hyperlipidemia is usually inherited and caused by genetic mutations that interfere with how the body processes lipids. The most well-known condition is familial hypercholesterolemia (FH). In this disorder, mutations affect genes such as the LDL receptor, apolipoprotein B, or PCSK9, which are responsible for removing LDL cholesterol ("bad cholesterol") from the blood. Because of this defect, LDL remains in circulation, leading to very high cholesterol levels even from childhood. People with FH have a much higher risk of developing atherosclerosis and heart disease at a young age. If not managed, this condition can cause premature heart attacks or strokes (Nordestgaard et al., 2013).

Secondary Hyperlipidemia:

Secondary hyperlipidemia develops later in life due to lifestyle choices or other medical conditions. Factors that can contribute include obesity, diabetes, hypothyroidism, chronic kidney disease, and excessive alcohol use (Goldberg et al., 2020). Certain medications, such as corticosteroids, antiretroviral drugs, and diuretics, may also raise lipid levels. In addition, poor diet, especially eating large amounts of saturated fats and trans fats is a key modifiable cause (Grundy et al., 2019). While primary hyperlipidemia is less common, secondary hyperlipidemia is far more widespread worldwide, mainly due to rising obesity and metabolic syndrome. This highlights the importance of lifestyle interventions like healthy diet, exercise, and weight control, alongside medications, in reducing risk (Toth et al., 2022).

2.7.3 Causes of Hyperlipidemia

Hyperlipidemia occurs when there are too many lipids, such as cholesterol and triglycerides, in the bloodstream. The causes can be grouped into genetic factors, lifestyle choices, medical conditions, and medications.

Genetic causes (primary):

Some individuals inherit genetic changes that disrupt lipid metabolism. A common example is familial hypercholesterolemia (FH), caused by mutations in LDLR, APOB, or PCSK9 genes. This leads to very high LDL cholesterol from childhood and a strong risk of early cardiovascular disease (Berberich and Hegele, 2019; Raal and Santos, 2023).

Lifestyle factors:

Eating foods rich in saturated fats, trans fats, and refined carbohydrates increases LDL cholesterol and triglycerides. Physical inactivity also reduces HDL (good cholesterol) and raises LDL (bad cholesterol). In addition, obesity, especially abdominal obesity, is strongly linked with high triglycerides and low HDL levels. Excessive alcohol consumption is another major contributor (Mach et al., 2020).

Medical conditions (secondary causes):

Certain health conditions can cause hyperlipidemia. These include type 2 diabetes, hypothyroidism, chronic kidney disease, and liver disease, all of which interfere with normal lipid metabolism (Grundy et al., 2019; Ference et al., 2017).

Medications:

Some drugs can increase lipid levels as a side effect. Examples include corticosteroids, antiretroviral therapy, thiazide diuretics, and some antipsychotic drugs. In summary, hyperlipidemia can be inherited or acquired. Lifestyle changes remain the most important preventive step, while genetic and disease-related forms often need long-term medical treatment (Goldberg et al., 2020; Toth et al., 2022).

2.7.4 Pathophysiology of Hyperlipidemia

The pathophysiology of hyperlipidemia is closely linked to how the body manages lipids through processes such as synthesis, absorption, transport, and clearance. When any of these steps are disrupted, blood lipid levels become abnormal, leading to disease.

Lipid metabolism:

Lipids from food are absorbed in the small intestine and packaged into chylomicrons, which enter the lymphatic system before reaching the bloodstream. At the same time, the liver produces cholesterol and triglycerides, which are released into circulation as very low-density lipoproteins (VLDL). Through the action of enzymes, VLDL is progressively broken down to intermediate-density lipoproteins (IDL) and finally low-density lipoproteins (LDL). LDL carries most of the cholesterol in the blood and delivers it to tissues, while high-density lipoproteins (HDL) collect excess cholesterol and return it to the liver for recycling or removal (Rosenson et al., 2020).

Role of LDL in disease:

LDL cholesterol is the main “bad” lipoprotein because high levels cause cholesterol to build up inside arteries. This deposition creates fatty streaks, which progress into atherosclerotic plaques. Over time, plaques harden and narrow the arteries, impair blood flow, and trigger inflammation. These changes increase the risk of coronary artery disease, stroke, and peripheral artery disease (Ference et al., 2017).

Role of HDL in protection:

HDL cholesterol is known as the “good cholesterol.” Its protective function comes from reverse cholesterol transport, where it removes cholesterol from tissues and arterial walls and sends it back to the liver for elimination. Low levels of HDL reduce this protective mechanism and are strongly linked with higher rates of atherosclerosis (Rosenson et al., 2020).

Role of Triglycerides:

Triglycerides, carried by chylomicrons and VLDL, are an important source of energy. However, when levels are high, they contribute to cardiovascular disease. Elevated triglycerides are associated with small dense LDL particles, which are highly atherogenic, as well as endothelial dysfunction and chronic vascular inflammation (Toth et al., 2022). Very high triglyceride levels (above 500 mg/dL) also increase the risk of acute pancreatitis, which can be life-threatening. Hyperlipidemia develops when there is too much LDL and VLDL or too little HDL. This imbalance drives plaque formation, vascular damage, and systemic inflammation. Ultimately, it accelerates atherosclerosis, leading to increased morbidity and mortality from cardiovascular diseases (Mach et al., 2020).

2.8 Atherosclerosis

2.8.1 Definition of Atherosclerosis

Atherosclerosis is a long-term and progressive disease that affects medium- and large-sized arteries. It is mainly caused by the buildup of lipids (fats), inflammatory cells, and connective tissue inside the arterial wall. Over time, these substances form plaques (also called atheromas), which make the arteries narrower, less flexible, and harder. Narrowing of the artery reduces blood flow, and in severe cases, the plaques can rupture or form blood clots (thrombosis). These events are the main causes of heart attack, ischemic stroke, and peripheral artery disease (Libby et al., 2019). Modern understanding of atherosclerosis shows that it is not just the passive storage of cholesterol but rather an active inflammatory process involving many types of cells. The disease usually begins with endothelial dysfunction when the inner lining of the artery becomes damaged by risk factors such as high cholesterol, hypertension, diabetes, or smoking. This dysfunction allows LDL cholesterol to enter and accumulate in the arterial wall. Immune cells, especially macrophages, then engulf the lipids, turning into foam cells that contribute to fatty streaks. Over time, smooth muscle cells and connective tissue form a fibrous cap over the plaque. If this cap ruptures, platelets gather, leading to clot formation and potentially life-threatening complications (Libby, 2021).

2.8.2 Pathophysiology of Atherosclerosis (plaque formation, oxidative stress, endothelial dysfunction)

The development of atherosclerosis is not a single-step event but a long, complex process that involves the interaction of blood lipids, the vessel wall, and the immune system. It begins early in life and can progress silently for many years before causing serious disease.

Initiation—Endothelial Dysfunction and Lipid Retention

The first noticeable step is *endothelial dysfunction*. The endothelium is the thin inner lining of blood vessels, and when healthy, it regulates blood flow and prevents unnecessary clotting or inflammation. However, certain risk factors like high blood pressure, smoking, diabetes, and high LDL cholesterol can damage or stress the endothelium. A dysfunctional endothelium becomes more "leaky," allowing LDL cholesterol particles to pass through into the vessel wall. At the same time, it expresses adhesion molecules (such as VCAM-1 and ICAM-1), which act like "Velcro," pulling white blood cells, especially monocytes and T cells, into the arterial wall (Libby et al., 2019). Once trapped, LDL particles can undergo oxidation, turning into *oxidized LDL (oxLDL)*. This oxidized form is toxic and highly inflammatory. Immune cells, particularly macrophages, recognize oxLDL and engulf it through scavenger receptors, turning themselves into *foam cells*. Foam cells are the hallmark of early atherosclerotic lesions and contribute to fatty streak formation (Ference et al., 2017; Borén et al., 2020).

Role of Oxidative Stress

Oxidative stress plays a central role in this process. It happens when the production of harmful reactive oxygen species (ROS) overwhelms the body's natural antioxidant defenses. ROS damages the endothelium, reduces nitric oxide (NO), which normally helps vessels relax, and makes the vessels prone to spasm and inflammation. ROS also directly promotes LDL oxidation and activates inflammatory pathways, including NF-κB, which drives the release of more cytokines and adhesion molecules (Batty et al., 2022; Daiber et al., 2020). Normally, antioxidant systems such as superoxide dismutase, catalase, and glutathione peroxidase provide protection, but when they fail, oxidative stress accelerates plaque growth (Daiber et al., 2020).

Inflammation and Cellular Interplay

Atherosclerosis is now recognized as a chronic inflammatory disease. Immune cells release inflammatory messengers like TNF-α, IL-1β, and IL-6, which attract more cells and worsen tissue injury. Meanwhile, smooth muscle cells (SMCs) migrate from deeper layers of the artery into the intima, where they multiply and produce structural proteins such as collagen and proteoglycans. These form a *fibrous cap* over the plaque. The stability of the plaque depends on this cap. If macrophages release too many matrix-degrading enzymes (MMPs), the cap becomes thin and fragile, increasing the chance of rupture (Libby et al., 2019; Libby, 2021).

Plaque Progression and Complications

As the disease advances, plaques develop a *necrotic core* due to foam cell death and poor clearance of dead cells. They may also show neovascularization (growth of new fragile blood vessels), intraplaque bleeding, and calcium deposits. When plaques rupture, the exposed core triggers blood clotting. A large clot can suddenly block blood flow, causing heart attack or stroke. In other cases, plaque erosion without rupture can also lead to thrombosis, especially in younger patients (Libby et al., 2019).

2.8.3 Link between Hyperlipidemia and Atherosclerosis

Hyperlipidemia and atherosclerosis are closely connected, and this relationship is central to the development of cardiovascular diseases. Elevated levels of circulating lipids, especially low-density lipoprotein cholesterol (LDL-C) and triglyceride-rich lipoproteins (TRLs), are considered the main causes of atherosclerosis. Evidence from genetics, population studies, and clinical trials all confirm that the higher and longer the body is exposed to LDL-C, the greater the risk of developing cardiovascular diseases. On the other hand, lowering LDL-C levels consistently reduces the progression of atherosclerotic plaque and lowers the chance of heart attack or stroke (Ference et al., 2017; Borén et al., 2020). Mechanistically, when LDL and TRLs are elevated in the blood, more of these lipoproteins enter the inner layer of arteries (the intima). Once inside, they bind to extracellular matrix proteoglycans, where they can undergo oxidative changes. Oxidized LDL (oxLDL) is highly inflammatory and stimulates immune cell recruitment, foam cell formation, and further plaque development (Libby et al., 2019). Besides LDL, high triglycerides and remnant cholesterol also play an important role in atherosclerosis. They increase inflammation, worsen endothelial dysfunction, and lead to the formation of small, dense LDL particles. These particles are even more dangerous because they penetrate arterial walls more easily and are more prone to oxidation (Sandesara et al., 2019). Therefore, managing lipid imbalance by lowering LDL-C, reducing triglycerides, and supporting healthy HDL function is a key target for preventing and treating atherosclerosis. This is why lipid-lowering drugs such as statins, ezetimibe, and PCSK9 inhibitors are strongly recommended. It also explains why plant-based compounds with lipid-lowering or antioxidant properties are now being studied as promising alternatives or complementary options (Borén et al., 2020).

2.9 Role of Medicinal Plants in Hyperlipidemia Management

Medicinal plants help manage blood fats and slow down atherosclerosis (the buildup of plaque in arteries) through several important actions. First, plants help by reducing cholesterol production in the liver. They do this by blocking a main enzyme called HMG-CoA reductase, or by activating a key regulatory protein known as AMPK (Eqbal et al., 2022; Cai et al., 2023). They also improve how the body clears cholesterol from the blood by increasing the number of LDL receptors (which pull "bad cholesterol" out of circulation) and by reducing the protein PCSK9 (Cai et al., 2023; Ataei et al., 2022). Second, plant compounds limit the amount of fat you absorb from food. Phytosterols compete with dietary cholesterol in the gut, effectively blocking its entry into the bloodstream. Other compounds block special fat transporters, like NPC1L1, further reducing absorption (Weerawatanakorn et al., 2024). Third, certain plant compounds, including those found in ginger, help the body get rid of cholesterol by increasing the production and removal of bile acids, which are made from cholesterol in the liver (Kiyama et al., 2021). Plants also protect blood vessels from damage. Their antioxidant activity is important because it stops LDL from being oxidized (damaged), a key early step in plaque formation (Laka et al., 2022; Weerawatanakorn et al., 2024). Their anti-inflammatory effects calm down the blood vessel walls by reducing inflammatory signals, which helps stabilize existing plaques (Gonfa et al., 2023; Liu et al., 2022). Lastly, some plants improve the balance of gut bacteria, which indirectly helps regulate lipid profiles and reduces the risk of atherosclerosis (Weerawatanakorn et al., 2024). Scientific evidence backs up the effects of certain plant compounds: Phytosterols/Stanols reliably lower LDL-C by 8–12% in studies (Barkas et al., 2023; Han et al., 2016). Berberine effectively lowers LDL and triglycerides by influencing the receptor pathway and activating AMPK (Cai et al., 2023; Ataei et al., 2022). Green Tea Catechins and Ginger components also offer benefits for cholesterol and triglyceride levels (Cui et al., 2020; Kiyama et al., 2021). Garlic modestly reduces total cholesterol, LDL, and triglycerides (Zhao et al., 2024). Despite these promising effects, challenges remain. Standardization is difficult because the amount of active compounds in a plant can vary widely (Weerawatanakorn et al., 2024). There are also safety risks like drug interactions (e.g., berberine and drug-metabolizing enzymes; garlic and blood thinners) and potential toxicity, meaning careful testing is required (Cai et al., 2023). More high-quality, long-term human studies are needed to confirm these benefits consistently (Barkas et al., 2023; Liu et al., 2022).

Medicinal plants are a promising complementary option, but they need careful safety testing and clinical proof before being widely recommended (Zhao et al., 2024).

CHAPTER THREE

MATERIALS AND METHODS

3.1. Apparatus and Equipments Used

The apparatus and equipment used in this study are as follows:

The apparatus and equipment utilised in this study include the following: a spectrophotometer (Model Number: 752+UV/VIS, Wincom, China), a centrifuge, an industrial blender (KENWOOD Model: KCB239K) an analytical weighing balance (Ohaus Corp., Pine Brook, NJ, USA, China), a water bath (HH-S6, China), Automated haematological analyser (Model: PCE – 2100, Japan) a rat cage, a dissecting set, a mortar and pestle, a conical flask (500 ml), beakers (50 ml and 250 ml), a measuring cylinder (100 ml), a plain bottle, universal bottles (10 ml), syringes and needles (1 ml, 2 ml, and 5 ml), hand gloves, cotton wool, Distilled water, an ethylenediaminetetraacetic acid (EDTA) bottle, a strainer, a stirrer, a chopping board, masking tape, and methylated spirit.

3.2. Chemicals and Reagents

The following chemicals and reagents were utilised in this study: ethanol, ketamine, cholic acid, normal saline, distilled arachis oil, fructose, cholesterol, distilled water, a cholesterol assay kit, a triglyceride assay kit, and HDL and LDL reagents. All chemicals and reagents employed were of analytical grade.

3.3 Plant Collection

Ageratum conyzoides (goat weed) and *Anthocleista djalonensis* were sourced from Ikpoba Okha Local Government Area, Edo State, Nigeria. *Thespesia garckeana* fruits were obtained from Tula village in Kaltungo Local Government Area, Gombe State. *Zingiber officinale* (ginger) and *Allium sativum* (garlic) were purchased fresh from Kurmi Market in Kano Municipal, Kano State, Nigeria. The plants were identified and authenticated by a plant taxonomist in the Department of Plant Biology and Biotechnology, University of Benin, and voucher specimens were deposited for reference.

3.4 Preparation of Plant Materials

Fresh samples of *Zingiber officinale* (rhizomes), *Allium sativum* (bulbs), and *Thespesia garckeana* (seeds) were washed, peeled (where necessary), and chopped into smaller pieces. *Anthocleista djalonensis* leaves were removed from the stalk, washed, and air-dried under shade to preserve phytochemicals. *Ageratum conyzoides* leaves were also washed and shade-dried. The chopped materials (ginger, garlic, and Gordon Tula seeds) were dehydrated using a dehydrator (Model: SF-4006 China) at 50°C for 48 hours, while Anthocleista djalonensis and *Ageratum conyzoides* were air-dried. After drying, all plant samples were ground separately into fine powder using an industrial blender (KENWOOD Model: KCB239K) and stored in airtight containers until use.

3.5 Formulation of Polyherbal Tea

The polyherbal tea was formulated using the method outlined by Uwaya and Effiong (2024) with slight modifications. The formulation consisted of *Ageratum conyzoides, Anthocleista djalonensis*, *Zingiber officinale, Allium sativum,* and *Thespesia garckeana* in the ratio 1:1:1:1:1, respectively.

3.6 Polyherbal Tea Extraction

Formulated polyherbal tea (324 g) was placed in an extraction jar, and 2.5 litres of distilled water were added. The mixture was stirred and allowed to macerate for 72 hours. Subsequently, the mixture was filtered through a strainer into a lidded storage container. The filtrate was then concentrated using a water bath. Finally, the extract was stored in a container in the refrigerator at 4°C until required.

3.7 Experimental Animals

Twenty-five (25) healthy Wistar rats of both sexes were purchased from a commercial farm in Ibadan, Oyo State. The animals were housed within the animal facility of the Phytomedicine unit in the Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin. The animals were given two weeks of acclimatisation under normal laboratory conditions in a 12-hour light/dark cycle. They were fed with normal animal pellets and water spontaneously, and the cages were cleaned regularly. All procedures adhered to the National Institutes of Health (NIH) guidelines for the care and use of laboratory animals. This study was approved by the Faculty of Science Laboratory Technology Research Ethical Committee with reference number UNIBEN/FSLT/00016.

3.8 Experimental Design

This study was carried out using atherogenic diet-induced hyperlipidaemia in rats according to Aziza et al. (2015)

The 25 rats were randomly divided into five groups (n = 5 per group):

Group 1 (Normal control): Received 2 ml/kg of distilled water only.

Group 2 (Low dose polyherbal): Received 20 mg/kg aqueous extract of the polyherbal tea.

Group 3 (High dose polyherbal): Received 40 mg/kg aqueous extract of the polyherbal tea.

Group 4 (Standard drug): Received 5 mg/kg Atorvastatin.

Group 5 (Negative control): Received cholesterol diet only (10 mg/kg of 0.5% cholesterol suspension).

Hyperlipidaemia and atherosclerosis were induced by administering 10 mg/kg of 1% cholesterol and 0.5% cholic acid orally for five consecutive days. On the fifth day, both the extract and the standard drug were given, alongside a cholesterol-rich diet, for a duration of 28 days. After 28 days, the animals were sacrificed using ketamine (100 mg/kg) as anaesthesia. They were then dissected through the abdominal region, and blood was collected from the abdominal aorta using a 5 ml syringe. One millilitre of blood was placed in an EDTA bottle for haematological analysis, while the remaining blood was transferred to a lithium heparin bottle for lipid profile testing. The organs were subsequently isolated, weighed, and fixed in a 10% formalin saline solution.

3.9 Procedures for Biochemical and Histological Analysis

3.9.1 Lipid Profile Analysis

Serum levels of total cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) were assessed using enzymatic colorimetric methods. This analysis employed commercial Agappe® diagnostic kits, following the manufacturer's instructions meticulously.

Determination of Total Cholesterol

Total cholesterol levels were measured using an enzymatic colorimetric method with the Agappe Test Kit. In brief, 10 μL of serum sample was combined with 1 mL of cholesterol reagent in a clean test tube. The mixture was then incubated at 37°C for 10 minutes, after which the absorbance was recorded at 500 nm using a spectrophotometer (Model Number: 752+UV/VIS, Wincom China). Cholesterol concentration was determined from a calibration curve prepared with a standard cholesterol solution (Khera et al., 2017).

Determination of Triglycerides

Serum triglyceride levels were estimated using the GPO-PAP method, in accordance with the Agappe Test Kit protocol. Specifically, 10 µL of the serum sample was combined with 1 mL of the working reagent and incubated at 37°C for 10 minutes. The absorbance was then measured at 520 nm against a reagent blank using a spectrophotometer (Model Number: 752+UV/VIS, Wincom, China). The concentration of triglycerides was calculated relative to the standard (Sniderman et al., 2019).

Determination of High-Density Lipoprotein (HDL)

HDL cholesterol was determined using a precipitation method. Specifically, 200 µL of serum was combined with 500 µL of the HDL precipitating reagent, which consists of phosphotungstic acid and magnesium chloride. The resulting mixture was allowed to stand for 10 minutes before being centrifuged at 4000 rpm for another 10 minutes. The clear supernatant was then separated, and HDL cholesterol was measured enzymatically, following the method outlined for total cholesterol (Cole and Jeyaraj, 2015).

Determination of Low-Density Lipoprotein (LDL) and Very Low-Density Lipoprotein (VLDL)

LDL and VLDL levels were determined using Friedewald's formula as outlined by Martin et al. (2013).

3.9.2 Liver Function Tests

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were assayed using Reitman-Frankel method kits.

Determination of Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT)

AST and ALT activities were measured using the colorimetric method with Randox diagnostic kits (Randox Laboratories Ltd, UK). For each enzyme, 100 µL of serum was combined with 1 mL of substrate solution and incubated at 37°C. Following incubation, 1 mL of colour reagent (2,4-dinitrophenylhydrazine) was added, and the mixture was left for 10 minutes at room temperature. Subsequently, 10 mL of 0.4 N sodium hydroxide was introduced, and the absorbance was recorded at 546 nm using a spectrophotometer(Model Number: 752+UV/VIS, Wincom, China). The enzyme activities were reported in IU/L (Mohammed et al., 2019).

3.9.3 Body Weight and Organ Indices

The body weights of all experimental rats were recorded weekly using an electronic balance (Ohaus Corp, Pine Brook, NJ, USA). At the conclusion of the experimental period, the animals were sacrificed, and the spleen, liver, kidney, and heart were meticulously excised, washed with saline, blotted dry, and weighed. The organ-to-body weight ratios were calculated using the following formula:

Organ-to-body weight ratio = Organ weight / Body weight (Organisation for Economic Co-operation and Development, 2022).

3.9.4 Histopathological Examination

Tissue samples from the liver and aorta were fixed in 10% neutral buffered formalin for a duration of 24 hours. Following fixation, the tissues underwent processing by standard paraffin embedding techniques, after which sections measuring 5 µm in thickness were cut using a microtome. The sections were subsequently stained with haematoxylin and eosin (H&E) and examined under a light microscope (Olympus CX23, Japan) at various magnifications. Photomicrographs were captured using a digital camera attached to the microscope. Pathological changes, including lipid deposition, atheroma formation, and hepatocellular injury, were scored by a qualified histopathologist (Suvarna, 2019).

3.10 Statistical Analysis

The data are shown as the mean ± standard error of the mean (SEM), and "n" stands for the number of rats in each experimental group. A one-way analysis of variance (ANOVA) was performed, followed by the Tukey test for post-hoc analysis. All data analyses were conducted using GraphPad Prism software version 9, obtained from the UK. A significance level of $p < 0.05$ was established to indicate statistically significant differences between the compared groups.

CHAPTER FOUR

RESULTS

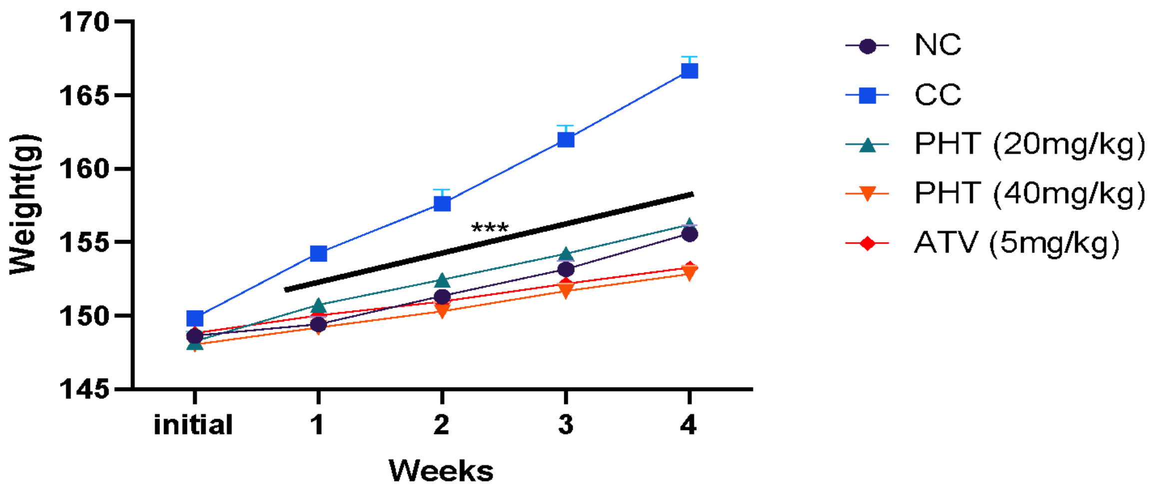

Figure 1: The effect of polyherbal tea on the body weight in cholesterol induced hyperlipidemia and atherosclerosis in Wistar rats.

The aqueous extract of polyherbal tea (20 and 40mg/kg) and artovastatin (5mg/kg) prevented weight gain in cholesterol induced hyperlipidemia and atherosclerosis when compared to Cholesterol Control ($p<0.001$). NC: Normal Control, CC:Cholesterol Control, PHT: Polyherbal Tea, ATV:Artovastatin. The data is represented as±S.E.M, n=5.

Table 1: The effect of polyherbal tea on organ to body weight ratio in cholesterol induced hyperlipidemia and arteriosclerosis in Wistar rats

TREATMENT	L:BW (10^{-2})	K:BW (10^{-3})	S:BW (10^{-3})	H:BW (10^{-3})
NC	3.85±0.16	6.92±0.06	4.12±2.29	3.46±0.24
CC	4.62±0.43	8.34±0.59	5.99±0.83	3.89±0.32
PHT (20mg/kg)	4.16±0.05 *	7.35±0.12 **	5.06±0.10	3.47±0.01 *
PHT (40mg/kg)	3.97±0.01 ***	7.48±0.44 **	4.67±0.11	3.34±0.04 **
ATV (5mg/kg)	3.85±0.04 ***	6.99±0.05 ****	3.73±0.17 *	3.22±0.03***

The organ to body weight ratios were increased in the Cholesterol Control group (CC) compared to the Normal Control (NC), indicating organ hypertrophy. Treatment with polyherbal tea (PHT) at both 20mg/kg and 40mg/kg reduced these ratios, with the 40mg/kg group showing a more pronounced effect. Atorvastatin (ATV 5mg/kg), the standard drug, also significantly reduced organ to body weight ratios compared to CC group, confirming its known antihyperlipidemic action ($p<0.05$). NC: Normal Control, CC: Cholesterol Control, PHT: Poly Herbal Tea, ATV: Artovastatin, L:BW: Liver to Body Weight ratio, K:BW: Kidney to Body Weight ratio, S:BW: Spleen to Body Weight ratio, H:BW: Heart to Body Weight ratio. The data is represented as ±S.E.M, n=5.

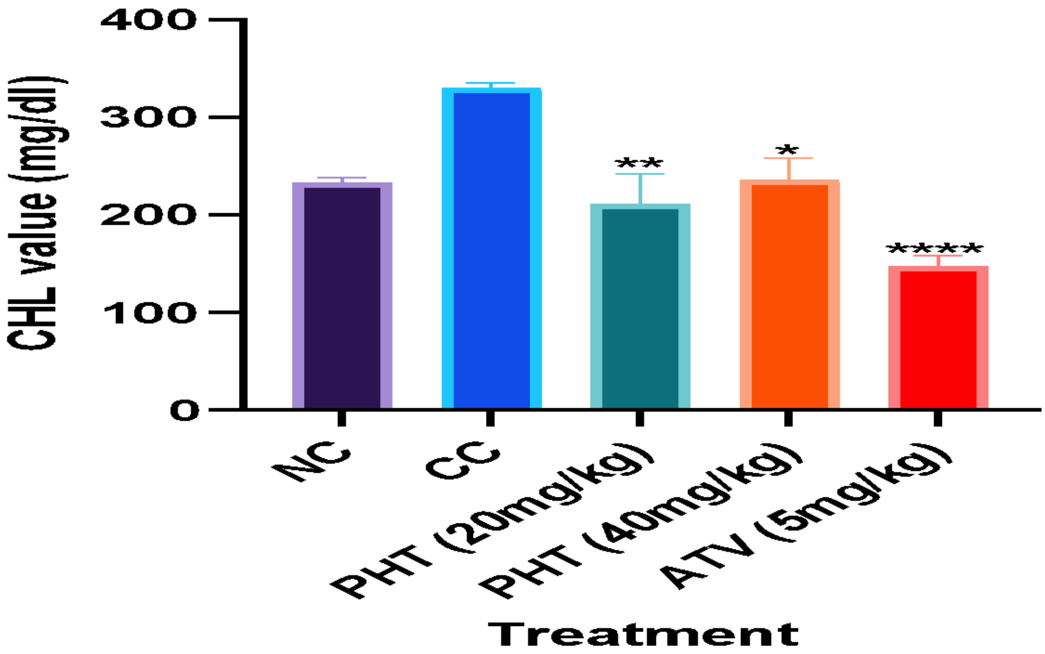

Figure 2: The effect of polyherbal tea on cholesterol in cholesterol induced hyperlipidemia and atherosclerosis in Wistar rats.

The aqueous extract of polyherbal tea (20mg/kg and 40mg/kg) and Artovastatin (5mg/kg) reduced cholesterol levels in cholesterol induced hyperlipidemia and atherosclerosis when compared to Cholesterol Control ($p<0.05$; $p\leq0.001$). NC: Normal Control, CC: Cholesterol Control, PHT: Polyherbal Tea, ATV: Artovastatin. The data is represented as ± S.E.M, n=5.

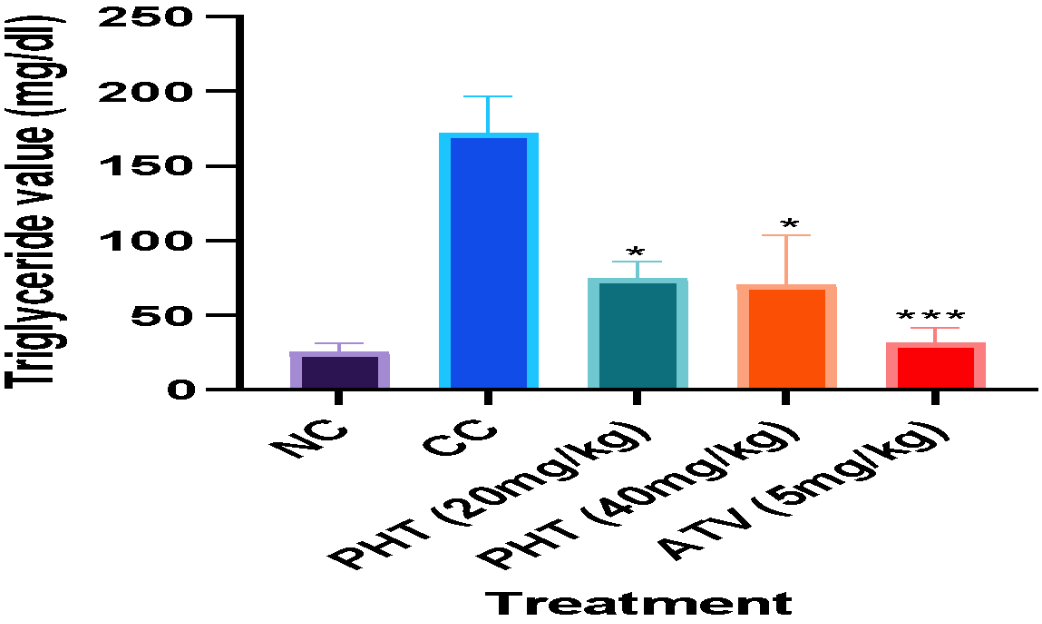

Figure 3: The effect of polyherbal tea on triglycerides in cholesterol induced hyperlipidemia and atherosclerosis in Wistar rats.

The aqueous extract of polyherbal tea (20mg/kg and 40mg/kg) and Artovastatin (5mg/kg) reduced triglyceride levels in cholesterol induced hyperlipidemia and atherosclerosis when compared to Cholesterol Control ($p<0.05$; $p\leq0.001$). NC: Normal Control, CC: Cholesterol Control, PHT: Polyherbal Tea, ATV: Artovastatin. The data is represented as ±S.E.M, n=5.

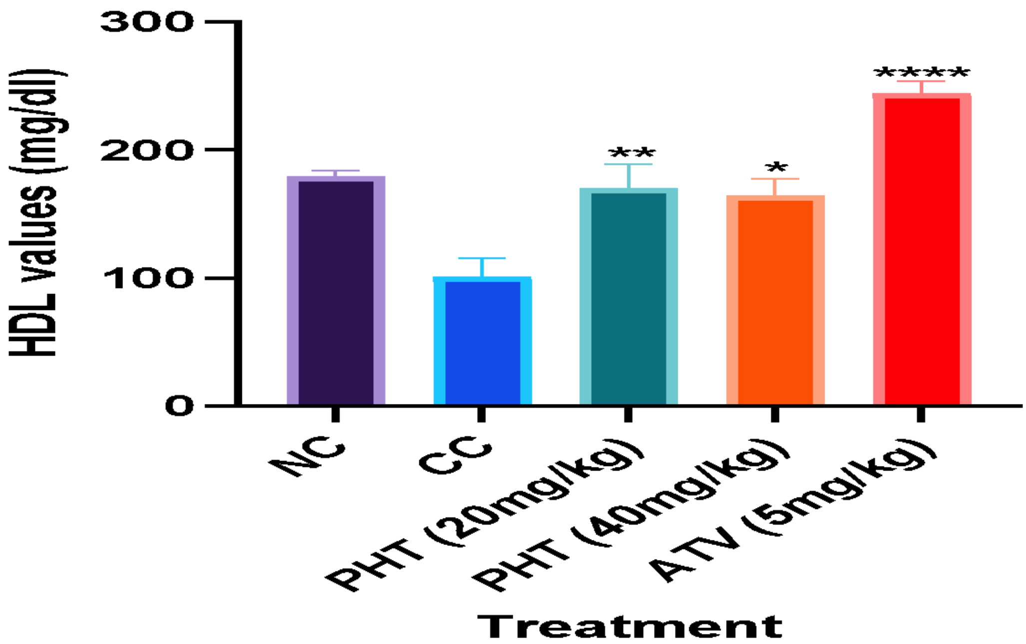

Figure 4: The effect of polyherbal tea on high density lipoprotein levels in cholesterol induced hyperlipidemia and atherosclerosis in Wistar rats.

The aqueous extract of polyherbal tea (20mg/kg and 40mg/kg) and Artovastatin (5mg/kg) increased high density lipoprotein levels in cholesterol induced hyperlipidemia and atherosclerosis when compared to Cholesterol Control ($p<0.05$; $p\leq0.001$). NC: Normal Control, CC: Cholesterol Control, PHT: Polyherbal Tea, ATV: Artovastatin. The data is represented as ±S.E.M, n=5.

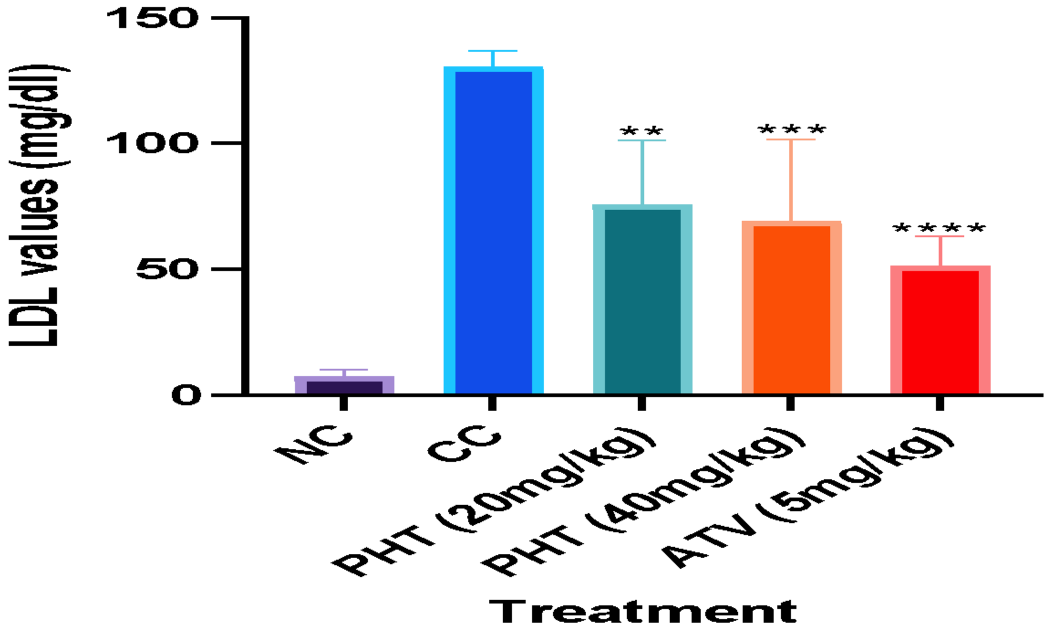

Figure 5: The effect of polyherbal tea on low density lipoprotein levels in cholesterol induced hyperlipidemia and atherosclerosis in Wistar rats.

The aqueous extract of polyherbal tea (20mg/kg and 40mg/kg) and Artovastatin (5mg/kg) reduced low density lipoprotein levels in cholesterol induced hyperlipidemia and atherosclerosis when compared to Cholesterol Control ($p<0.05$; $p\leq0.001$). NC: Normal Control, CC: Cholesterol Control, PHT: Polyherbal Tea, ATV: Artovastatin. The data is represented as ±S.E.M, n=5.

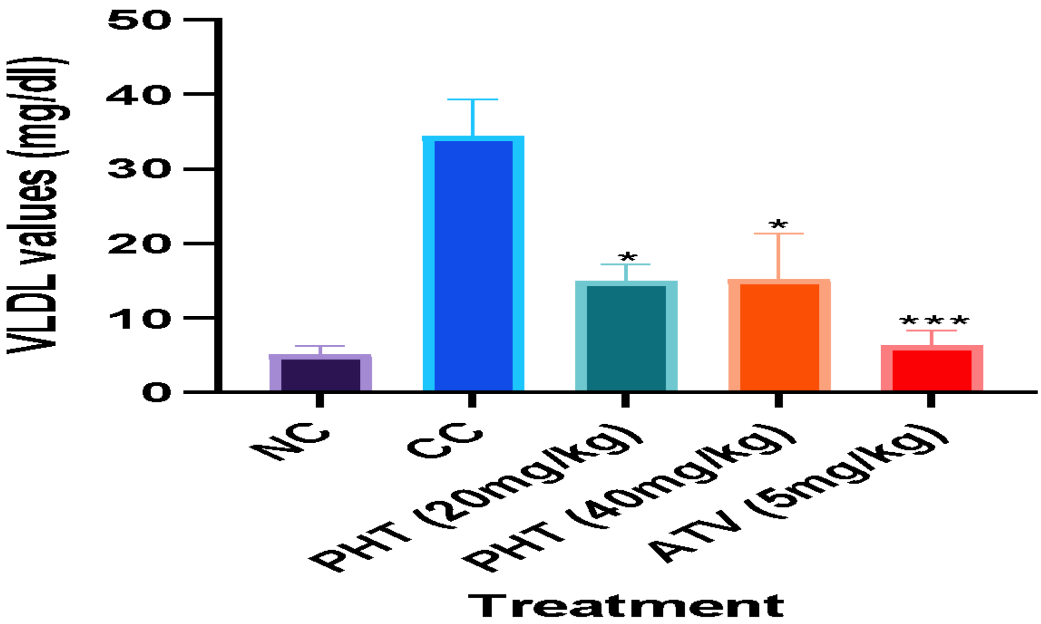

Figure 6: The effect of polyherbal tea on very low density lipoprotein levels in cholesterol induced hyperlipidemia and atherosclerosis in Wistar rats.

The aqueous extract of polyherbal tea (20mg/kg and 40mg/kg) and Artovastatin (5mg/kg) reduced very low density lipoprotein levels in cholesterol induced hyperlipidemia and atherosclerosis when compared to Cholesterol Control ($p<0.05$; $p\leq0.001$). NC: Normal Control, CC: Cholesterol Control, PHT: Polyherbal Tea, ATV: Artovastatin. The data is represented as ±S.E.M, n=5.

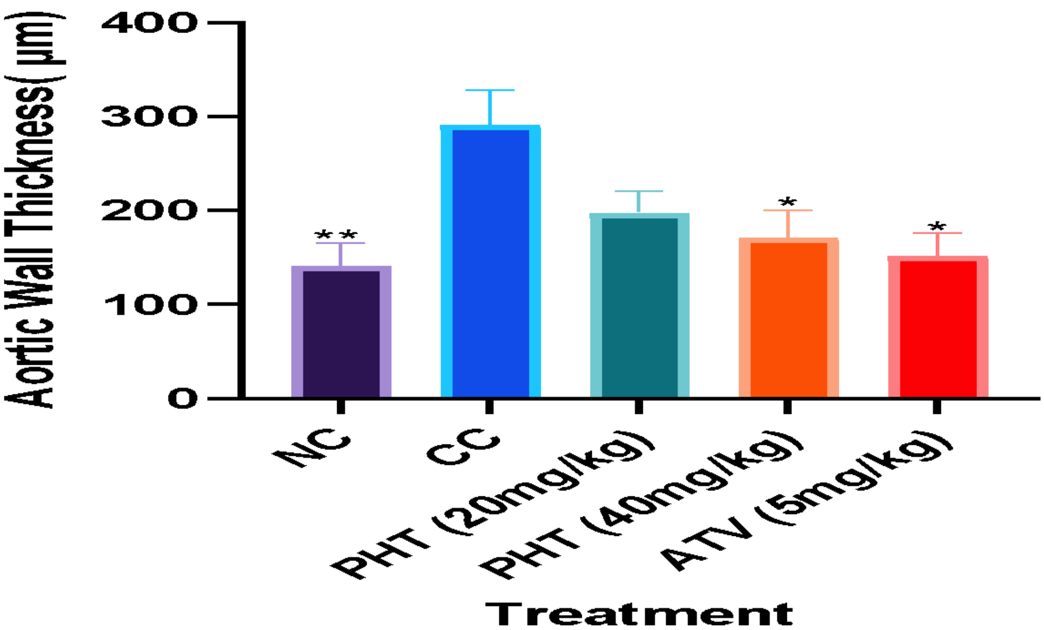

Figure 7: The effect of polyherbal tea on aortic wall thickness in cholesterol induced hyperlipidemia and atherosclerosis in Wistar rats.

The aqueous extract of polyherbal tea (20mg/kg and 40mg/kg) and Artovastatin (5mg/kg) reduced aortic wall thickness in cholesterol induced hyperlipidemia and atherosclerosis when compared to Cholesterol Control ($p<0.05$; $p\leq0.001$). NC: Normal Control, CC: Cholesterol Control, PHT: Polyherbal Tea, ATV: Artovastatin. The data is represented as ±S.E.M, n=5.

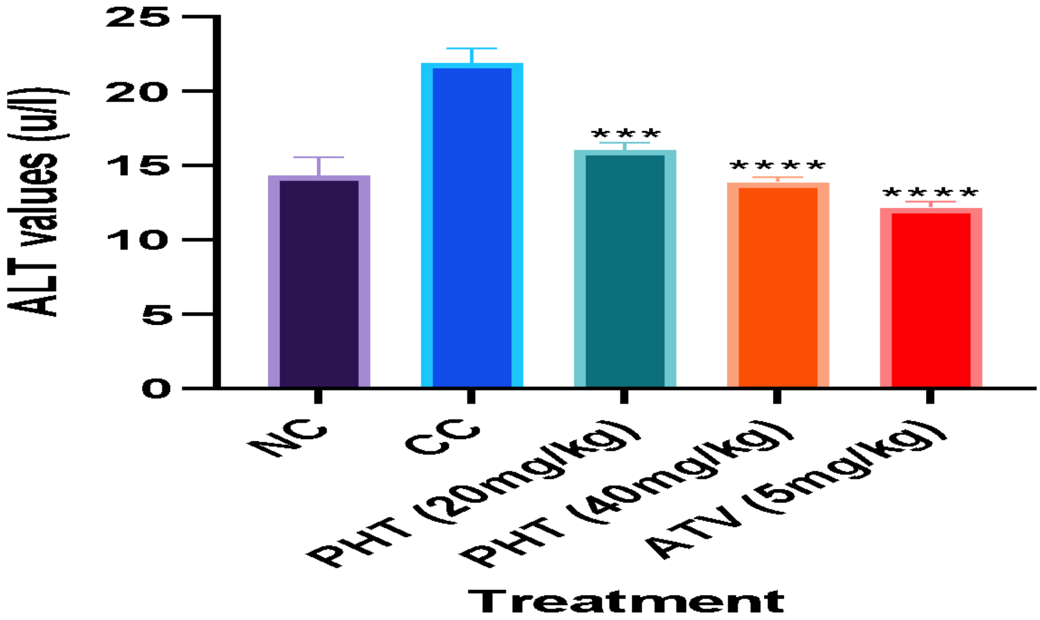

Figure 8. The effect of polyherbal tea on alanine transaminase levels in cholesterol induced hyperlipidemia and atherosclerosis in Wistar rats.

The aqueous extract of polyherbal tea (20mg/kg and 40mg/kg) and Artovastatin (5mg/kg) reduced alanine transaminase levels in cholesterol induced hyperlipidemia and atherosclerosis when compared to Cholesterol Control ($p<0.05$; $p\leq0.001$). NC: Normal Control, CC: Cholesterol Control, PHT: Polyherbal Tea, ATV: Artovastatin. The data is represented as ±S.E.M, n=5.

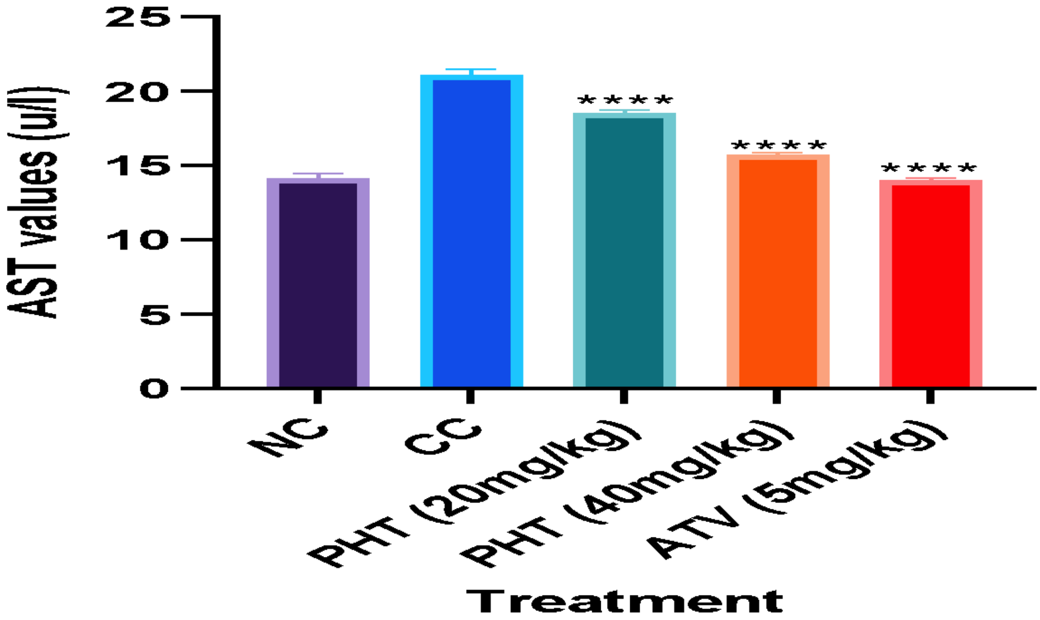

Figure 9. The effect of polyherbal tea on aspartate aminotransferase levels in cholesterol induced hyperlipidemia and atherosclerosis in Wistar rats.

The aqueous extract of polyherbal tea (20mg/kg and 40mg/kg) and Artovastatin (5mg/kg) reduced aspartate aminotransferase levels in cholesterol induced hyperlipidemia and atherosclerosis when compared to Cholesterol Control ($p<0.05$; $p\leq0.001$). NC: Normal Control, CC: Cholesterol Control, PHT: Polyherbal Tea, ATV: Artovastatin. The data is represented as ±S.E.M, n=5.

The effect of 28 days daily oral administration of polyherbal formulated tea (*Ageratum conyzoides, Anthocleistadjalonensis, Zingiber officinale, Allium sativum, and Thespesia garckeana*) on histopathological parameters

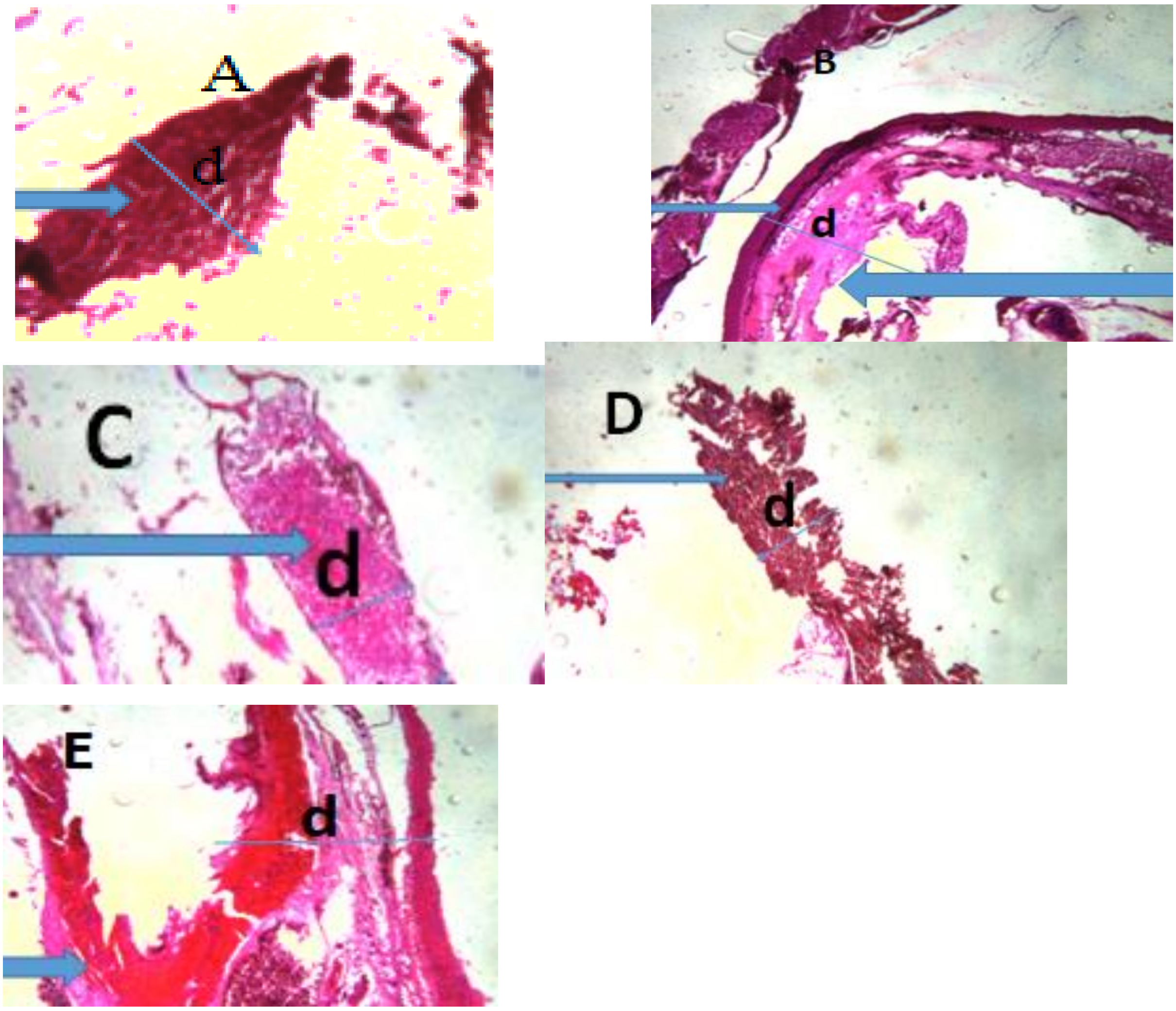

Plate A – The section of the aorta displays an aortic wall (indicated by the thin arrow) and shows no signs of atheroma. The characteristics observed are consistent with those of a normal aorta (normal control).

Plate B – The section of the aorta displays an aortic wall (indicated by the thin arrow) and an overlying atheroma (indicated by the thick arrow). The observed features are consistent with a diagnosis of atherosclerosis (cholesterol control).

Plate C – The section of the aorta displays an aortic wall (indicated by the thin arrow) and shows no signs of atheroma. The observed features are consistent with a normal aorta (PHT 20 mg/kg).

Plate D – The section of the aorta shows an aortic wall (indicated by the thin arrow) with no evidence of atheroma. These features suggest a diagnosis of atherosclerosis (PHT 40 mg/kg).

Plate E – The section of the aorta displays an aortic wall (indicated by the thin arrow) and shows no evidence of atheroma. The observed features are consistent with a normal aorta (ATV 5 mg/kg). d: diameter of the aortic wall.

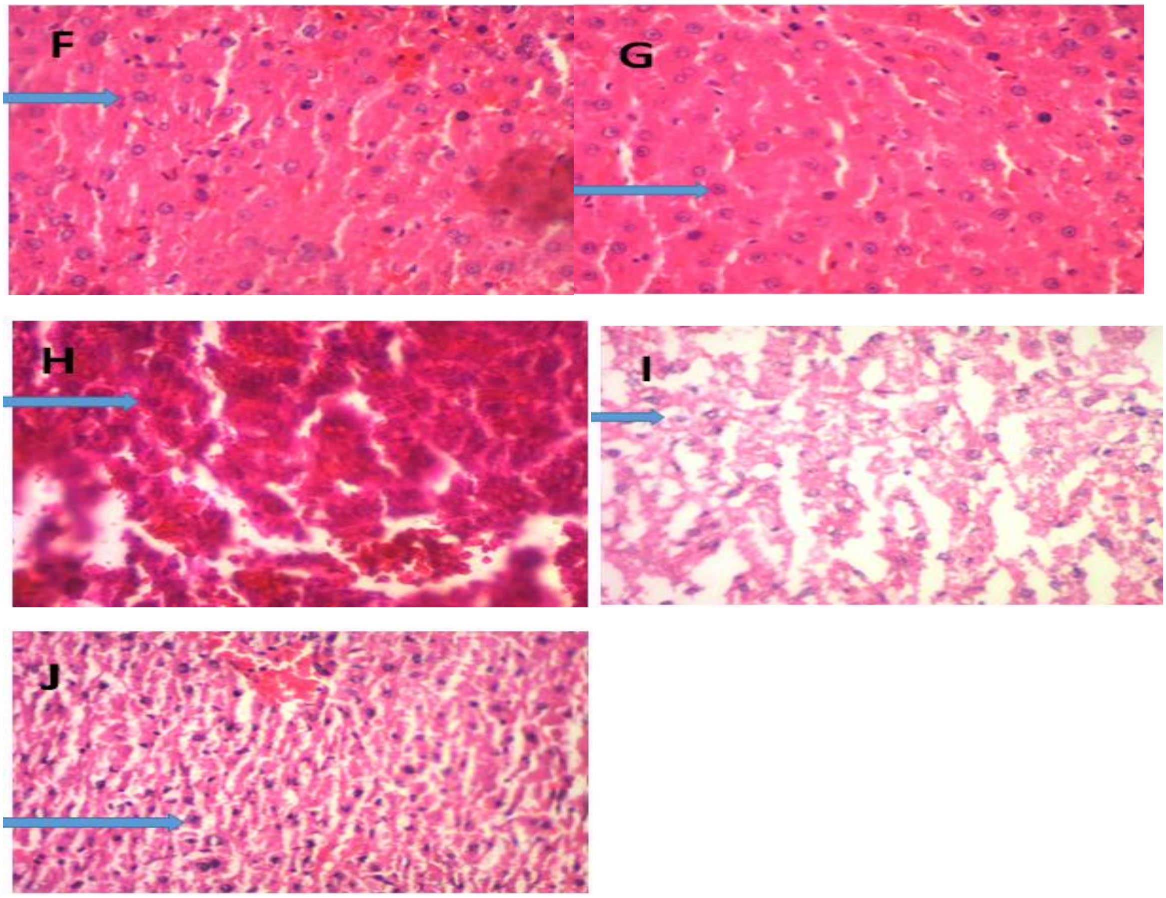

Plate F – A section of the liver reveals hepatocytes (indicated by an arrow), characterised by eosinophilic cytoplasm surrounding centrally positioned normochromic nuclei with indistinct nucleoli. The observed features are consistent with those of normal hepatocytes, serving as the normal control.

Plate G – A section of the liver reveals hepatocytes (indicated by an arrow) characterised by eosinophilic cytoplasm surrounding a centrally positioned normochromic nucleus with indistinct nucleoli. The observed features are consistent with those of normal hepatocytes (cholesterol control).

Plate H – A section of the liver displays hepatocytes (indicated by an arrow) characterised by eosinophilic cytoplasm that surrounds a centrally positioned normochromic nucleus with indistinct nucleoli. The cytoplasm encircles the centrally located nucleus. These features suggest the presence of steatosis (PHT 20 mg/kg).

Plate I – A section of the liver shows hepatocytes (arrow) with eosinophilic cytoplasm containing microvacuoles (ballooning degeneration); the cytoplasm surrounds a centrally placed nucleus. The observed features are consistent with those of normal hepatocytes (PHT 40 mg/kg).

Plate J – presents a section of the liver displaying hepatocytes (indicated by an arrow) characterised by eosinophilic cytoplasm that contains microvacuoles, suggestive of ballooning degeneration; the cytoplasm encircles centrally positioned nuclei. The observed features are indicative of steatosis (ATV 5 mg/kg).

CHAPTER FIVE

DISCUSSION AND CONCLUSION

5.1 DISCUSSION

This study evaluated the effects of a polyherbal tea formulation containing *Ageratum conyzoides, Anthocleista djalonensis, Zingiber officinale, Allium sativum, and Thespesia garckeana* on hyperlipidemia and atherosclerosis in Wistar rats. In this study, the polyherbal tea administered at 20 mg/kg and 40 mg/kg significantly prevented weight gain when compared with the cholesterol control ($p < 0.05$) (see Figure 1). Likewise, the standard medication, atorvastatin at 5 mg/kg, reduced body weight gain in cholesterol-induced rats. Weight gain in cholesterol-fed rats is often associated with increased adiposity and lipid accumulation (Hosseini and Hosseinzadeh, 2015). The prevention of excessive weight gain by the polyherbal tea therefore suggests that the formulation possesses antihyperlipidemic properties. The noted anti-obesity effect can be ascribed to various plants in the formulation. *Zingiber officinale* (ginger) and *Allium sativum* (garlic) possess phytochemicals, including gingerols and organosulfur compounds, which mitigate weight gain by regulating lipid metabolism and suppressing adipogenesis (Shaik Mohamed Sayed et al., 2023). Adeyemi et al. (2019) assert that plant-based formulations abundant in flavonoids, saponins, and polyphenols, such as *Anthocleista djalonensis, Zingiber officinale,* and *Allium sativum,* can diminish lipid absorption in the intestine and enhance fat metabolism by elevating bile acid secretion and fatty acid oxidation. These reports correspond with the body-weight findings of this study.

The cholesterol control group showed elevated organ-to-body weight ratios (liver, kidney, spleen, and heart) compared to the normal control group. This signifies organ hypertrophy resulting from cholesterol excess and lipid accumulation (Khan et al., 2014). Administration of the polyherbal tea at dosages of 20 mg/kg and 40 mg/kg significantly reduced the organ-to-body weight ratio ($p < 0.05$), with the higher dosage (40 mg/kg) exhibiting a more pronounced effect (see Table 1). This result indicates that the polyherbal formulation effectively safeguarded vital organs from cholesterol-induced hypertrophy and dysfunction. The result was comparable to atorvastatin, confirming its protective action. Shubhada et al. (2020) assert that polyherbal extracts, including *Ageratum conyzoides, Zingiber officinale,* and *Allium sativum,* possess antioxidant and hypolipidemic properties that can mitigate organ hypertrophy in hyperlipidemic rats.

The biochemical analysis indicated that polyherbal tea significantly reduced total cholesterol ($p < 0.05$; see Figure 2) and triglycerides ($p < 0.05$; see Figure 3) in comparison to the cholesterol control. Elevated cholesterol and triglyceride levels are associated with the development of atherosclerotic plaques (Nordestgaard et al., 2020), and their reduction indicates that the tea possesses lipid-lowering properties. Moreover, the tea increased HDL levels (see Figure 4), which is advantageous as HDL facilitates the transport of cholesterol away from tissues and arteries (Ndrepepa, 2021). Simultaneously, the tea significantly reduced ($p < 0.05$) LDL (see Figure 5) and VLDL (see Figure 6), both of which are detrimental lipoproteins that facilitate atherosclerosis (Ference et al., 2017). These findings indicate that polyherbal tea can enhance lipid balance and diminish cardiovascular risk. The cholesterol control group exhibited increased aortic wall thickness; however, administration of polyherbal tea at both dosages diminished this thickness (see Figure 7). The result indicates that the tea could safeguard the vascular system by inhibiting plaque accumulation and arterial thickening. Akintunde et al. (2022) assert that polyphenol-rich herbal remedies, including *Zingiber officinale, Allium sativum,* and *Thespesia garckeana,* mitigate endothelial dysfunction and decelerate vascular remodelling, corroborating the findings of this study. In the cholesterol control group, the liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were elevated, indicating hepatocellular injury resulting from cholesterol overload and oxidative stress (Batty et al., 2022). The administration of polyherbal tea at dosages of 20 mg/kg and 40 mg/kg significantly reduced ALT and AST levels ($p < 0.05$; see Figures 8 and 9) in comparison to the cholesterol control, suggesting hepatoprotective effects. This suggests that the tea not only improves lipid metabolism but also prevents liver injury. Beyang et al. (2024) reported similar findings, indicating that herbal extracts rich in flavonoids and alkaloids, such as *Zingiber officinale,* and *Anthocleista djalonensis*, stabilise liver enzymes in hyperlipidemic rats.

The histological results supported the biochemical findings. The aortic sections of rats in the cholesterol control group showed features of atherosclerosis, such as thickened walls and atheroma (see Plate B), while the normal control group had normal aortic walls with no sign of atheroma (see Plate A). The polyherbal tea at 20 mg/kg and 40 mg/kg showed no evidence of atheroma (see Plates C and D), which is similar to the standard drug atorvastatin (see Plate E). Likewise, the liver sections of the cholesterol control showed fatty changes (see Plate G), while treatment with polyherbal tea (see Plates H and I) showed improvement in liver architecture with fewer signs of steatosis compared to the control group. The findings validate that the polyherbal tea possesses hepatoprotective and anti-atherosclerotic properties. Comparable histological recovery, characterised by a reduction in fatty infiltration and enhancement of hepatocyte morphology, has been documented in studies utilising extracts from plants such as *Zingiber officinale* and *Allium sativum* (Shubhada et al., 2020). The advantageous effects of the polyherbal tea identified in this study can be ascribed to the phytochemicals contained in the herbal formulation. Compounds like flavonoids, polyphenols, saponins, and alkaloids, prevalent in plants such as *Zingiber officinale, Allium sativum, Anthocleista djalonensis, Thespesia garckeana,* and *Ageratum conyzoides,* are recognised for their significant antioxidant, hypolipidemic, and anti-inflammatory effects. These mechanisms explain the improvement in lipid profile, reduction in aortic wall thickening, and stabilization of liver enzymes.

5.2 CONCLUSION

The polyherbal tea formulation, consisting of *Ageratum conyzoides, Anthocleista djalonensis, Zingiber officinale, Allium sativum*, and *Thespesia garckeana*, may exhibit antihyperlipidemic, anti-atherosclerotic, and hepatoprotective properties.

REFERENCES

Adedapo, A. A., Jimoh, F. O., and Afolayan, A. J. (2015). Assessment of the medicinal potentials of *Ziziphus mucronata*leaves. *African Journal of Pharmacy and Pharmacology,***9**(23): 648–656.

Adeyemi, O. A., Olajide, J. K., Adeyemo, O. O., and Olamide, O. O. (2019). Effect of a polyherbal formula (made from *Alstonia boonei* and *Picralima nitida*) on lipid profile and atherogenic indices in high-fat diet-fed Wistar rats. *Journal of Integrative Medicine*, **17**(2): 115–123.

Akintunde, A. A., Adebola, O. E., and Balogun, M. O. (2022). Association of dietary polyphenols with cardiovascular outcomes: A systematic review and meta-analysis. *Journal of Clinical Medicine,* **11**(18):5364.

Akinmoladun, A. C., Okewale, A. O., and Akpan, M. O. (2020). Anti-hyperlipidemic and anti-atherogenic effects of a Nigerian polyherbal remedy on Wistar rats. *International Journal of Phytomedicine,* **12**(4): 456–465.

Anyanwu, G. O., Onyeneke, C. E., and Rauf, K. (2015). Medicinal plants of the genus *Anthocleista*—A review of their ethnobotany, phytochemistry and pharmacology. *Journal of Ethnopharmacology,* **175**:648–667.

Arnett, D. K., Blumenthal, R. S., Albert, M. A., Buroker, A. B., Goldberger, Z. D., Hahn, E. J., et al. (2019). 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease. *Circulation,* **140**(11):e596–e646.

Asgharpour, M. J., Ahmadi, F., and Alimohammadi, M. (2021). Efficacy of oral administration of *Allium sativum* powder: Effects on lipid profile and renal protection in hemodialysis patients. *International Journal of Clinical Practice,* **75**(12):e14822.

Ataei, T., Tabaei, A., and Khodadadi, A. (2022). Berberine and its derivatives: A patent review on their therapeutic potential against metabolic syndrome. *Expert Opinion on Therapeutic Patents,* **32**(1): 1–15.

Averbukh, L. D., Chen, P., and Jones, H. M. (2022). Statin-induced liver injury patterns: A clinical review. *Journal of Clinical and Translational Hepatology,* **10**: 1–12.

Azantsa, B. G., Mbiantcha, M., Ateufack, G., Dimo, T., and Dongmo, A. B. (2022). Polyherbal formulation of *Allium sativum* and *Persea americana* seed extracts: Lipid-lowering and antioxidant effects in high-fat/high-sucrose diet-fed rats. *BMC Complementary Medicine and Therapies,* **22**(1): 65.

Aziza S., Hussein S.A., Abdel-Magid A.D., Abu-ghallaza A.M. (2015). Biochemical study on the effect of alpha-lipoic acid on lipid metabolism of rats fed high fat diet. Benha Veterinary Medical Journal **28**(1): 109-119.

Banach, M., Kopeć, G., and Rysz, J. (2017). The reality of statin adherence: A review of the literature and practical recommendations. *Archives of Medical Science,* **13**(5):987–996.

Barkas, F., Tsiattopoulou, A., Kasimis, M., Sarafidis, P. A., and Elisaf, M. S. (2023). Plant sterols and plant stanols in cholesterol management: An update. *Nutrients,* **15**(4):895.

Batty, M., Malhotra, A., and Ferraro, D. (2022). The role of oxidative stress in atherosclerosis: From initiation to therapeutic target. *Cells,* **11**(23):3843.

Beyang, M., Ngangmou, N. T., Mache, G. A., Ejoh, R. A., Dobgima, J. F., Tatsadjieu, N. L., and Mbofung, C. M. F. (2024). Effect of *Garcinia kola* consumption on lipid profile and body weight of rats fed with high-fat diet. *Asian Food Science Journal,* **23**(6): 30–43.

Berberich, A. J., and Hegele, R. A. (2019). The complex molecular genetics of familial hypercholesterolemia. *Endocrine Reviews,* **40**(4):1184–1205.

Borén, J., Chapman, M. J., Krauss, R. M., Packard, C. J., et al. (2020). Low-density lipoproteins cause atherosclerotic cardiovascular disease: Pathophysiological, genetic, and therapeutic insights—EAS consensus statement. *European Heart Journal,* **41**(24):2313–2330.

Cai, Y., Yang, Q., Yu, Y., Yang, F., Bai, R., and Fan, X. (2023). Efficacy and underlying mechanisms of berberine against lipid metabolic diseases: A review. *Frontiers in Pharmacology,* **14**:1283784.

Chahal, R., Kaur, M., Bhardwaj, U., Kaur, P., Kaur, A., and Bhardwaj, A. (2021). *Ageratum conyzoides* L. and its secondary metabolites in the management of different clinical conditions: A review. *Journal of Applied Pharmaceutical Science,* **11**(05):159–171.

Chester, A., Patel, J., and Shah, B. (2021). From Fleming to Endo: The discovery of statins. *Proceedings of the Japan Academy, Series B,* **97**(5):484–498.

Cole, T. G., and Jeyaraj, P. (2015). High-density lipoprotein cholesterol (HDL-C) measurement methods. *Methods in Molecular Biology,***1245**: 229–237.

Cui, Y., Wang, Z., and Chen, S. (2020). Green tea extracts and catechins in the management of dyslipidemia: A meta-analysis of randomized controlled trials. *Clinical Nutrition,* **39**(8):2631–2641.

Daiber, A., Steven, S., Weber, A., and Oelze, M. (2020). Revisiting pharmacology of oxidative stress and endothelial dysfunction: Therapeutic opportunities. *Free Radical Biology and Medicine,* **152**: 44–59.

Dhanik, J., Arya, N., and Nand, V. (2017). A review on *Zingiber officinale*. *Journal of Pharmacognosy and Phytochemistry,* **6(**3):174–184.

Ebrahimzadeh, A., Hadi, A., and Pourmasoumi, M. (2022). The effect of ginger supplementation on metabolic profiles in patients with type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials. *Clinical Nutrition,* **41**(4):877–887.

Eqbal, A., Khan, M. I., and Ahmad, I. (2022). Cholesterol-lowering mechanisms of bioactive terpenes: A review. *Journal of Agricultural and Food Chemistry,* **70**(34):10189–10204.

Ference, B. A., Ginsberg, H. N., Graham, I., Ray, K. K., Packard, C. J., Bruckert, E., et al. (2017). Low-density lipoproteins cause atherosclerotic cardiovascular disease. *European Heart Journal,* **38**(32):2459–2472.

Goldberg, I. J., Eckel, R. H., and McPherson, R. (2020). Triglycerides and heart disease: Still a hypothesis? *Arteriosclerosis, Thrombosis, and Vascular Biology,* **40**(5):973–975.

Gonfa, N., Birhane, T., and Teklay, G. (2023). Anti-inflammatory effects of plant compounds in the prevention of atherosclerosis: A review. *Nutrients,* **15**(16):3564.

Grundy, S. M., Stone, N. J., Bailey, A. L., Beam, C., Birtcher, K. K., Blumenthal, R. S., et al. (2018). 2018 AHA/ACC guideline on the management of blood cholesterol. *Journal of the American College of Cardiology,* **73**(24):e285–e350.

Grundy, S. M., Stone, N. J., and Greenland, P. (2019). Non-statin therapies for cardiovascular risk reduction: A scientific statement from the American Heart Association. *Circulation,* **139**(25): e1082–e1143.

Han, S., Kim, H. G., and Choi, M. S. (2016). Effects of phytosterols on cholesterol and triglyceride metabolism in rats. *Journal of Nutritional Biochemistry,* **28**: 10–17.

Hassan, S. M., et al. (2020). Acute and Subchronic Toxicity Studies of Combretum collinum Methanol Root Extract in Albino Rats. *International Journal of Biosciences, Cardiology and Research Reports*, **29**(10): 9-28.

Hosseini, E., and Hosseinzadeh, H. (2015). Review on the effects of saffron on obesity and lipid metabolism. *Journal of Applied Pharmaceutical Science*, **5**(9): 1-8.

Ibrahim, M., Shehu, M. B., and Usman, B. A. (2025). Exploring the role of curcumin in mitigating oxidative stress to alleviate lipid metabolism disorders. *Frontiers in Pharmacology,* **16**: 1517174.

Iloabuchi, G. C., Uwaoma, R., and Okeke, P. E. (2024). Effects of *Azanza garckeana* fruit pulp on metabolic syndrome in Wistar rats fed on high-fructose diet. *University Journal of Medical Research,* **2024**(1): 1–10.

Kafunda, M., Kaaya, E. E., Lema, K. G., and Mpila, S. N. (2017). Review of the ethnobotanical uses, phytochemicals and pharmacological activities of *Azanza garckeana* (F. Hoffmann) Exell and Hillc. *Journal of Ethnopharmacology,* **198**:345–351.

Kato-Noguchi, H., Olayiwola, O. A., and Sunohara, Y. (2024). Defense molecules of the invasive plant species *Ageratum conyzoides* L. *Molecules,* **29**(19):4673.

Kaur, A., Batish, D. R., Kaur, S., Chauhan, B. S., and Kohli, R. K. (2023). Ecology, biology, environmental impacts, and management of an agro-environmental weed *Ageratum conyzoides*. *Plants,* **12**(11):2153.

Khan, V. A., Sharma, V., Khan, S. A., and Khan, Z. A. (2014). Organ-to-body weight ratio and its application in studies of safety pharmacology. *Journal of Toxicology and Applied Pharmacology*, **1**(2): 1–5.

Khera, A. V., Emdin, C. A., Smith, L. P., Assimes, T. L., Hassanzadeh, M., Samani, N. J., and Kathiresan, S. (2017). Genetic analysis of the relationship between Lp(a) concentration and coronary disease. *New England Journal of Medicine*, **377**(6):513–522.

Kiyama, R., Hirata, T., and Akagi, T. (2021). Evaluation of ginger compounds on cholesterol metabolism using HepG2 cells. *Food Science and Nutrition,* **9**(8):4474–4481.

Kouakou, P. S., Tano, K., Kone, S., and Bamba, M. (2023). Chemical characterization and biological abilities of *Anthocleista djalonensis* collected from two locations of Ivory Coast. *eFood: Food, Agriculture and Environment,* **5**(4): e2602.

Kushwaha, S., Singh, D. V., and Gupta, A. K. (2016). High-fat diet induced hyperlipidemia in Wistar rats: A model for screening anti-hyperlipidemic drugs. *International Journal of Basic and Clinical Pharmacology,* **5**(5): 1859–1864.

Liu, Y., Liu, C., Kou, X., Wang, Y., Yu, Y., Zhen, N., Jiang, J., Zhaxi, P., and Xue, Z. (2022). Synergistic hypolipidemic effects and mechanisms of phytochemicals: A review. *Foods,* **11**(18): 2774.

Libby, P., Buring, J. E., Badimon, L., Hansson, G. K., Deanfield, J., Bittencourt, M. S., Lüscher, T. F., and Mock, M. B. (2019). Atherosclerosis. *Nature Reviews Disease Primers,* **5:**56.

Libby, P. (2021). The changing landscape of atherosclerosis. *Nature,* **592**(7855): 524–533.

Mach, François; Baigent, Colin; Catapano, Alberico L.; Koskinas, Konstantinos C.; Casula, Manuela; Badimon, Lina; Chapman, M. John; De Backer, Guy G.; Delgado, Victoria; Ference, Brian A.; Graham, Ian M.; Halliday, Alison; Landmesser, Ulf; Mihaylova, Borislava; Pedersen, Terje R.; Riccardi, Gabriele; Richter, Dimitrios J.; Sabatine, Marc S.; Taskinen, Marja-Riitta; Tokgozoglu, Lale; Wiklund, Olov; and the ESC Scientific Document Group (2020). 2019

ESC/EAS guidelines for the management of dyslipidaemias. *European Heart Journal,* **41**(1):111–188.

Mao, Q. Q., Xu, X. Y., Cao, S. Y., Gan, R. Y., Corke, H., Beta, T., and Li, H. B. (2019). Bioactive compounds and bioactivities of ginger (*Zingiber officinale*). *Critical Reviews in Food Science and Nutrition,* **59**(1): 1–29.

Martin, S. S., Blaha, M. J., Elshazly, M. B., Toth, P. P., Kwiterovich, P. O., Blumenthal, R. S., and Jones, S. R. (2013). Comparison of a novel method vs the Friedewald equation for estimating low-density lipoprotein cholesterol levels from the standard lipid profile. *Journal of the American Medical Association*, **310**(19):2061–2068.

Mgalula, M. E., Hanyani, E., and Nyaruwata, C. (2024). An ethnobotanical survey of wild edible fruit species in Miombo woodlands: *Thespesia garckeana* occurrence and local uses. *PLOS ONE,* **19**(2): e0298031.

Mohammed, J., Jiya, N., and Oladimeji, T. (2019). Hepatoprotective effect of Ziziphus mauritiana fruit extract against paracetamol-induced liver damage in rats. *Journal of Intercultural Ethnopharmacology*, **8**(1):1–8.

Ndrepepa, G. (2021). High-density lipoprotein cholesterol and cardiovascular disease: roles and clinical implications. *Clinica Chimica Acta*, **514**: 148-161.

Newman, C. B., Preiss, D., Jarcho, J. A., and Handelsman, M. J. (2019). Statin safety and associated adverse events: A scientific statement from the American Heart Association. *Arteriosclerosis, Thrombosis, and Vascular Biology,* **39**(2):e38–e81.

Nordestgaard, B. G., Chapman, M. J., Humphries, S. E., von Eckardstein, H., Stock, J. K., Masana, L., Sijbrands, E. J., Parhofer, K. G., Reiner, Ž., Gylling, H., Gielen, S., Harzer, K., Kees, H., Hovingh, G. K., Lareu, F. V., Voutilainen, S., Knuuti, J., Jänne, J., Pedersen, K. L., and Boman, K. (2013). Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population. *European Heart Journal,* **34**(45):3478–3490.

Nordestgaard, B. G., Varbo, A., Langsted, A., Kamstrup, P. R., Tybjærg-Hansen, A., and Langsted, A. (2020). Triglycerides and cardiovascular disease: a narrative review. *European Heart Journal,* **41**(29):2736–2746.

Nutraceutical Review. (2022). Nutraceutical potentials of *Azanza garckeana* (snot apple)—A review. *International Journal of Food Science and Nutrition,* **73**(6):724–734.

Obia, O., Okeke, P. E., and Uwaoma, R. (2024). The effect of hydro-methanolic seed extract of *Azanza garckeana* (Goron Tula) on lipid profile and oxidative stress markers of male Wistar rats. *International Journal of Medical, Engineering and Pharmaceutical Research*, **8**(5):83–89.

Pourmasoumi, M., Nikpayam, O., and Abolhasani, S. (2018). Effect of ginger supplementation on lipid profile: A systematic review and meta-analysis of randomized clinical trials. *Phytotherapy Research,* **32**(9):1790–1798.

Putri, N. A., Rachmawati, D., Aulifa, D. L., and Subarnas, A. (2021). Wound healing effectivity of the ethanolic extracts of *Ageratum conyzoides* L. leaf (white and purple), *Centella asiatica*, and astaxanthin gel preparation. *International Journal of Applied Pharmaceutics,* **13**(5):84–88.

Raal, F. J., and Santos, R. D. (2023). Familial hypercholesterolemia: Pathophysiology, diagnosis, and management. *Endocrine Reviews,* **44**(4):582–601.

Rafiu, B. O., Olowokudejo, J. D., and Okoro, B. N. (2025). Ethnobotanical uses of plants in Nigeria: An analysis of records (1964–2024). *PLOS ONE,* **20**(1):e0315340.

Rosenson, R. S., Hegele, R. A., and Koenig, W. (2020). Role of HDL in atherosclerosis and cardiovascular disease. *Nature Reviews Cardiology,* **17**(1):22–36.

Salih, A. K., Ali, N. A., and Hamid, P. G. (2023). Effect of ginger (*Zingiber officinale*) intake on human serum lipid profile: Systematic review and meta-analysis. *Phytotherapy Research,* **37**(10):4153–4169.

Sandesara, P. B., Marshall, A. C., Toth, P. P., Virani, S., Shah, S. J., Aday, A. W., Martin, S. S., and Bhatt, D. L. (2019). Forgotten lipids: Triglycerides, remnant cholesterol, and atherosclerotic cardiovascular disease. *Endocrine Reviews,* **40**(2):537–557.

Shaik Mohamed Sayed, S., Sudhakar, K., Govindarajulu, P., Thangaraj, S., Ganesan, K., and Baskar, P. (2023). Anti-obesity effects of natural compounds: A focus on gingerols, curcuminoids, and their synergistic mechanisms. *European Journal of Pharmacology*, **940**: 175494.

Shalini S., Kumar R.R., Birendra S. (2014-2015). Comparative antihyperlipidemic activity of methanolic extract of Terminalia arjuna bark and its phytosome. *International Journal of PharmTech Research* **7**(3):540-549.

Shubhada, M., Jeyaraj, A., and Cole, P. P. (2020). Histopathological effects of a polyherbal mixture on liver and kidney of high-fat diet fed rats. *International Journal of Pharma and Bio Sciences,* **11**(2):1–10.

Shukla, R., Soni, S., and Agrawal, A. (2020). Effects of phytochemicals from plant-based functional foods on hyperlipidemia and their underpinning mechanisms. *Critical Reviews in Food Science and Nutrition,* **60**(19): 3290-3305.

Sleiman, C., O'Connor, P., and Kelly, E. (2024). Garlic (*Allium sativum*) and hypertension: Efficacy, mechanism of action, and clinical evidence. *Nutrients,* **16**(17):2895.

Sniderman, A. D., Thanassoulis, G., O'Meara, E., and Toth, P. P. (2019). The relationship between elevated plasma triglycerides and cardiovascular risk. *Current Cardiology Reports*, **21**(9):97.

Suvarna, S. K. (2019). The importance of standardization in routine hematoxylin and eosin staining. *Biotechnic and Histochemistry*, **94**(1): 1–11.

Taskinen, M.-R., and Borén, J. (2015). New insights into the pathophysiology of diabetic dyslipidemia. *Atherosclerosis,* **239**(2):483–495.

Toth, P. P., Potter, W. E., and Johnson, E. L. (2019). Atorvastatin in the prevention of cardiovascular disease. *Expert Review of Cardiovascular Therapy,* **17**(5):329–340.

Toth, P. P., Banach, M., Farnier, M., Tomlinson, B., Foody, J., and Catapano, A. L. (2022). Triglyceride-rich lipoproteins, remnant cholesterol, and atherosclerotic cardiovascular disease risk in statin-treated patients. *Atherosclerosis,* **349**:148–158.

Turner, R. M., Marikar, J., Olsson, P., and Johnson, E. (2019). Statin-related myotoxicity: A comprehensive review of mechanisms and management. *Journal of Clinical Medicine,* **8**(1):22.

Uwaya, D. O. and Effiong, O. N. (2024). Quantification of phytochemical constituents and non-enzymatic antioxidants of polyherbal formulated tea on antitussive, expectorant and analgesic activity in rodents. *Research in Biotechnology and Environmental Sciences*, **3**(1): 9-17.

Vetrivadivelan K., Venkateswaran K.V., Selvasubramanian S., Selvasubramanian P.S.L.(2012). Antihyperlipidemic effect of Tinospora cordifolia extract in streptozotocin induced diabetic rats. *International Journal of Pharmaceutical Sciences and Research* **3**(5):1423-1429.

Ward, H., Phillips, S., and Taylor, C. (2019). Statin therapy and cognitive decline: A population-based cohort study. *Atherosclerosis,* **289**:137–143.

Weerawatanakorn, M., Ekorus, J. J., and Ratti, S. (2024). Exploring phytochemical mechanisms in the prevention of hypercholesterolemia: Recent advances. *Journal of Agricultural and Food Chemistry,* **72**(15):6825–6840.

Yusuf, A. A., Adeleke, R. A., and Ajani, O. O. (2023). Attenuating effects of *Azanza garckeana* fractions on diabetes-induced dyslipidaemia, hepatopathy, and nephropathy in rats. *American Journal of Translational Research,* **15**(10):1–18.

Zhao, X., Cheng, T., Xia, H., Yang, Y., and Wang, S. (2024). Effects of garlic on glucose parameters and lipid profiles in adults: An updated systematic review and meta-analysis of randomized controlled trials. *Phytotherapy Research,* **38**(5):2234–2249.