THE EFFECT OF METHANOL EXTRACT OF *Spondias mombin* LEAVES ON TOTAL CHOLESTEROL AND TRIGLYCERIDE LEVEL IN HIGH-FAT DIET FED RATS

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UNIVERSITY OF BENIN

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DEPARTMENT OF MEDICAL BIOCHEMISTRY,SCHOOL OF BASIC MEDICAL SCIENCES, COLLEGE OF MEDICAL SCIENCES, UNIVERSITY OF BENIN IN **PARTIAL FULFILLMENT OF THE REQUIREMENT OF THE AWARD OF THE BACHELOR OF SCIENCE (B.Sc), DEGREE IN MEDICAL BIOCHEMISTRY

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CERTIFICATION

We, the undersigned, certify that this research was carried out by Udofia Jeremiah Godwin, in the department of Medical Biochemistry, School of Basic Medical Science, College of Medicine University of Benin, Benin City in partial fulfilment of the requirement of the award of the Bachelor of Science.

Dr.(Mrs) N. Eluehike **Date**
(Project Supervisor)

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(Head of Department)

(External Supervisor)

Date

DEDICATION

This study is dedicated to Almighty God for His Grace that sustained the researcher in the course of the programme.

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ABSTRACT

Hyperlipidemia, a major risk factor for cardiovascular diseases, is often managed with conventional lipid-lowering drugs that may have adverse effects. This study investigates the effects of methanol extract of *Spondias mombin* on total cholesterol and triglyceride levels in high-fat diet-fed rats. Experimental groups- group three, group four and group five received different doses of the extract, while controls- positive control (group 1) and negative control (group 2) remained untreated. Biochemical analysis revealed a significant reduction in total cholesterol and triglycerides in treated rats, suggesting potent hypolipidemic effects ($p<0.05$). The observed lipid-lowering activity may be attributed to phytochemicals such as flavonoids, tannins, and saponins, which regulate lipid metabolism and possess antioxidant properties. These findings highlight *Spondias mombin* as a promising natural alternative for hyperlipidemia management, warranting further research on its mechanisms and clinical applications.

CHAPTER ONE

INTRODUCTION

1.1 Background to the Study

Hyperlipidemia, a condition characterized by elevated levels of lipids such as cholesterol and triglycerides in the blood is a significant risk factor for cardiovascular diseases, including atherosclerosis, coronary artery disease, and stroke (Mahmood *et al*., 2021). The increasing prevalence of hyperlipidemia has been largely attributed to sedentary lifestyles and excessive consumption of high-fat diets, which lead to metabolic imbalances affecting lipid homeostasis. Elevated total cholesterol and triglyceride levels contribute to the development of atherosclerotic plaques, increasing the likelihood of cardiovascular complications (Zhao *et al*., 2020). Traditional pharmacological interventions, including statins, fibrates, and bile acid sequestrants, are commonly prescribed to manage lipid disorders. However, these drugs are often associated with adverse effects such as myopathy, hepatotoxicity, and gastrointestinal disturbances, leading to a growing interest in alternative and complementary therapies, particularly from natural sources (Parikh *et al*., 2019).

Medicinal plants have long been recognized for their potential in the management of various metabolic disorders, including hyperlipidemia. Many plant species possess bioactive compounds that can modulate lipid metabolism, either by reducing cholesterol synthesis, enhancing lipid catabolism, or improving lipid excretion. The search for plant-derived hypolipidemic agents has intensified as researchers seek safer, cost-effective alternatives to conventional lipid-lowering drugs (Saleem *et al*., 2022). Among these plants, *Spondias mombin*, commonly known as hog plum or yellow mombin, has gained attention for its diverse pharmacological properties. This plant, belonging to the Anacardiaceae family, is widely distributed in tropical regions and has been traditionally used for various medicinal purposes, including the treatment of gastrointestinal disorders, infections, and inflammatory conditions (Akinmoladun *et al*., 2021).

Phytochemical analyses of *Spondias mombin* have revealed the presence of flavonoids, tannins, alkaloids, saponins, and phenolic compounds, many of which have been implicated in lipid-lowering mechanisms (Dosumu *et al*., 2020). Flavonoids, for instance, are known to exhibit antioxidant properties, which can reduce oxidative stress—a key contributor to lipid peroxidation and dyslipidemia (Oyeniran *et al*., 2023). Additionally, tannins and saponins have been reported to interfere with lipid absorption and cholesterol metabolism, thereby reducing circulating lipid levels (Oloruntoba *et al*., 2021). These bioactive compounds provide a strong basis for investigating *Spondias mombin* as a potential natural remedy for hyperlipidemia.

The extraction method used in phytochemical studies significantly influences the composition and potency of bioactive compounds. Methanol extraction is widely employed due to its ability to solubilize both polar and non-polar phytochemicals, maximizing the yield of pharmacologically active components (Ajayi *et al*., 2019). Methanol extracts of *Spondias mombin* have been previously shown to possess anti-inflammatory, antimicrobial, and antioxidant properties, suggesting that these extracts may also be effective in modulating lipid metabolism (Adegbite *et al*., 2022). However, despite the numerous pharmacological studies on *Spondias mombin*, limited research has specifically explored its effects on total cholesterol and triglyceride levels, particularly in the context of high-fat diet-induced hyperlipidemia.

The use of animal models, such as rats, is essential for evaluating the lipid-lowering effects of medicinal plants. High-fat diet-fed rats serve as a well-established model for studying diet-induced hyperlipidemia, mimicking metabolic alterations observed in humans with dyslipidemia (Kim *et al*., 2020). These models allow for the investigation of the mechanisms through which bioactive compounds exert their hypolipidemic effects, providing insights into potential clinical applications. By assessing the effects of methanol extract of *Spondias mombin* on lipid profiles in high-fat-fed rats, this study aims to contribute to the growing body of knowledge on natural lipid-lowering agents.

Given the increasing burden of hyperlipidemia and its associated complications, there is an urgent need to explore alternative therapeutic approaches that are both effective and safe. This study seeks to evaluate the potential of *Spondias mombin* as a natural hypolipidemic agent, thereby providing scientific validation for its traditional use in managing lipid disorders. The findings from this research could have significant implications for the development of plant-based therapeutics for hyperlipidemia, ultimately contributing to public health by offering safer and more accessible treatment options.

1.2 Justification of the Study

The increasing prevalence of hyperlipidemia due to high-fat diets necessitates alternative therapeutic interventions with minimal side effects. *Spondias mombin*, a medicinal plant rich in bioactive compounds, has shown potential lipid-lowering effects, but its efficacy in high-fat diet-induced dyslipidemia remains underexplored. This study aims to evaluate its impact on total cholesterol and triglyceride levels, providing scientific evidence for its potential as a natural hypolipidemic agent. Findings may contribute to the development of plant-based therapies for managing hyperlipidemia.

1.3 Aim of the Study

This study aims to evaluate the effects of methanol extract of *Spondias mombin* on total cholesterol and triglyceride levels in high-fat-fed rats. It seeks to determine its potential as a natural lipid-lowering agent and explore its mechanism of action in lipid metabolism

CHAPTER TWO

LITERATURE REVIEW

This chapter presents review of literature relevant to this work on the effects of methanol extract of *Spondias mombin* leaves on total cholesterol and triglyceride levels in high-fat diet fed rats

2.1 Nutritional Composition and Benefit of *Spondias mombin*

Spondias mombin, commonly referred to as yellow mombin or hog plum, is a tropical fruit-bearing tree widely distributed in Africa, South America, and parts of Asia. It is highly valued not only for its edible fruits but also for its medicinal and nutritional properties. Various parts of the plant, including the fruit, leaves, bark, and roots, have been traditionally used in herbal medicine, making it a subject of increasing scientific interest. The nutritional composition of *Spondias mombin* is rich in essential macronutrients, micronutrients, vitamins, and bioactive compounds that contribute to its health benefits.

The fruit of *Spondias mombin* is known for its rich carbohydrate content, which serves as a primary source of energy. Studies have shown that the fruit contains significant amounts of simple sugars such as glucose and fructose, which contribute to its natural sweetness and make it an excellent source of quick energy (Adepoju and Adeniji, 2018). The fiber content in the fruit is also noteworthy, providing dietary fiber that aids in digestion and promotes gut health. High fiber intake is associated with improved bowel movement, reduced cholesterol levels, and enhanced satiety, which can contribute to weight management (Uchegbu *et al*., 2020).

The protein content of *Spondias mombin* is moderate but includes essential amino acids that play crucial roles in tissue repair and metabolic functions. Though not a primary protein source, the amino acid composition enhances the overall nutritional profile of the fruit, making it a valuable supplement in protein-deficient diets (Ajiboye *et al*., 2019). Additionally, the fruit contains beneficial lipids, though in small quantities, primarily consisting of polyunsaturated fatty acids, which have been linked to improved cardiovascular health (Ene-Obong *et al*., 2017).

Micronutrient analysis of *Spondias mombin* reveals that it is a rich source of essential vitamins, particularly vitamin C, which is crucial for immune function, collagen synthesis, and antioxidant activity. Vitamin C plays a vital role in protecting cells from oxidative damage caused by free radicals, thereby reducing the risk of chronic diseases such as cardiovascular disorders and certain cancers (Akinmoladun *et al*., 2021). Other essential vitamins found in the fruit include vitamin A, which supports vision and skin health, and B-complex vitamins such as niacin and riboflavin, which are involved in energy metabolism and neurological function (Oyeniran *et al*., 2022).

Mineral composition analysis has demonstrated that *Spondias mombin* is an excellent source of potassium, a mineral essential for maintaining fluid balance, nerve function, and muscle contraction. Potassium is particularly important in regulating blood pressure and reducing the risk of hypertension, a major risk factor for cardiovascular diseases (Oloruntoba *et al*., 2021). Other minerals present in the fruit include calcium, which is crucial for bone health; magnesium, which supports enzymatic functions; and iron, which is essential for oxygen transport in the blood (Alabi *et al*., 2020). The presence of these minerals highlights the potential role of *Spondias mombin* in addressing micronutrient deficiencies, especially in regions where malnutrition is prevalent.

Beyond its macronutrient and micronutrient content, *Spondias mombin* is particularly valued for its bioactive compounds, which contribute to its wide range of medicinal benefits.

Phytochemical studies have identified flavonoids, tannins, alkaloids, saponins, and phenolic compounds in various parts of the plant (Dosumu *et al*., 2020). Flavonoids, for example, have potent antioxidant and anti-inflammatory properties that help reduce oxidative stress and inflammation, key factors in the development of chronic diseases such as diabetes, cardiovascular diseases, and neurodegenerative disorders (Olaleye *et al*., 2019). Tannins, on the other hand, are known for their antimicrobial activity and ability to inhibit lipid peroxidation, making them beneficial for maintaining lipid homeostasis and reducing the risk of hyperlipidemia (Adebayo *et al*., 2022).

One of the most significant health benefits of *Spondias mombin* is its potential in lipid metabolism regulation. The presence of saponins in the plant has been linked to cholesterol-lowering effects, as these compounds have been found to inhibit cholesterol absorption in the intestine and promote its excretion (Oyetayo *et al*., 2018). This mechanism is particularly important in the management of hyperlipidemia, a condition characterized by elevated levels of cholesterol and triglycerides in the blood. Furthermore, phenolic compounds present in *Spondias mombin* have been shown to modulate lipid metabolism by enhancing the activity of enzymes involved in lipid breakdown and reducing oxidative damage to lipoproteins (Egwim *et al*., 2019).

The hepatoprotective properties of *Spondias mombin* also contribute to its benefits in lipid regulation. The liver plays a central role in cholesterol and triglyceride metabolism, and damage to this organ can result in dyslipidemia. Studies have demonstrated that extracts of *Spondias mombin* exhibit hepatoprotective effects by reducing liver enzyme markers such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT), suggesting its potential in preventing liver-related metabolic disorders (Balogun *et al*., 2021). The combination of these properties makes *Spondias mombin* a promising natural remedy for managing high cholesterol and triglyceride levels, particularly in individuals with diet-induced hyperlipidemia.

Additionally, the antioxidant properties of *Spondias mombin* play a crucial role in cardiovascular health. Oxidative stress is a key contributor to atherosclerosis, a condition characterized by the buildup of cholesterol and other substances in the arterial walls. The flavonoids and polyphenols in *Spondias mombin* help mitigate oxidative damage to blood vessels, reducing the risk of plaque formation and improving overall vascular function (Iwu *et al*., 2023). This cardiovascular benefit further supports the traditional use of the plant in managing hypertension and related disorders.

The broad-spectrum pharmacological effects of *Spondias mombin* have been explored in various preclinical studies, with growing evidence supporting its potential as a functional food or nutraceutical. While traditional medicine has long utilized the plant for its diverse health benefits, scientific validation of its lipid-lowering, antioxidant, and hepatoprotective properties continues to advance its potential applications in modern medicine. However, further research, including clinical trials, is necessary to establish standardized dosages and ensure safety for human consumption (Nwafor *et al*., 2020).

Spondias mombin is a nutritionally dense plant with significant health benefits, particularly in the regulation of lipid metabolism and cardiovascular health. Its rich composition of carbohydrates, fiber, vitamins, minerals, and bioactive compounds makes it a valuable dietary component with potential therapeutic applications. The growing body of scientific evidence supports its role in managing hyperlipidemia, reducing oxidative stress, and protecting liver function. As interest in plant-based medicine continues to rise, *Spondias mombin* stands out as a promising candidate for further exploration in the development of natural lipid-lowering therapies.

2.2 Phytochemical Properties of *Spondias mombin*

Spondias mombin, commonly known as yellow mombin or hog plum, is a tropical tree widely distributed across Africa, South America, and parts of Asia. It has been used extensively in traditional medicine due to its wide range of pharmacological activities. Scientific investigations have confirmed that various parts of the plant, including its leaves, bark, fruits, and roots, contain an abundance of bioactive compounds that contribute to its medicinal properties. These bioactive compounds, known as phytochemicals, are responsible for the plant's diverse therapeutic effects, which include antioxidant, antimicrobial, anti-inflammatory, hypolipidemic, hepatoprotective, and anti-diabetic properties. The growing body of research on *Spondias mombin* highlights its potential as a valuable source of natural compounds with significant biomedical applications.

Phytochemical analyses of *Spondias mombin* have revealed the presence of flavonoids, alkaloids, tannins, saponins, phenolics, terpenoids, and glycosides, all of which play crucial roles in the plant's pharmacological activities (Dosumu *et al*., 2020). Flavonoids are particularly abundant in the leaves and fruits of *Spondias mombin* and have been extensively studied for their potent antioxidant and anti-inflammatory properties. These compounds are known to scavenge free radicals, reducing oxidative stress and protecting biological tissues from damage (Oyeniran *et al*., 2022). The antioxidant activity of flavonoids is particularly important in preventing chronic diseases such as cardiovascular diseases, diabetes, and neurodegenerative disorders. Additionally, flavonoids have been shown to modulate lipid metabolism by inhibiting cholesterol synthesis and enhancing lipid catabolism, making them valuable in the management of hyperlipidemia (Akinmoladun *et al*., 2021).

Tannins, another major phytochemical group present in *Spondias mombin*, contribute to its antimicrobial, astringent, and anti-inflammatory properties. These polyphenolic compounds have been found to inhibit bacterial growth by disrupting cell membranes and interfering with essential microbial enzymes (Olaleye *et al*., 2019). The antimicrobial activity of tannins makes *Spondias mombin* an effective traditional remedy for bacterial and fungal infections. Furthermore, tannins play a role in the management of lipid disorders by binding to dietary lipids and reducing their absorption in the intestines, which contributes to lower cholesterol levels (Adebayo *et al*., 2022).

Saponins, another important class of bioactive compounds in *Spondias mombin*, are well-known for their hypolipidemic and cardioprotective effects. These compounds have been reported to lower blood cholesterol levels by inhibiting intestinal cholesterol absorption and promoting its excretion (Oloruntoba *et al*., 2021). Additionally, saponins possess anti-inflammatory and immune-boosting properties, making them beneficial in the treatment of inflammatory diseases and infections. Studies have also suggested that saponins may have anticancer properties, as they have been found to induce apoptosis in cancer cells and inhibit tumor growth (Balogun *et al*., 2021).

The phenolic compounds present in *Spondias mombin* contribute significantly to its medicinal properties, particularly in the areas of antioxidant defense and disease prevention. Phenolics are known for their ability to neutralize free radicals, thereby protecting cells from oxidative damage and reducing the risk of chronic diseases (Nwafor *et al*., 2020). The hepatoprotective effects of *Spondias mombin* have been linked to its high phenolic content, as these compounds help to maintain liver function by preventing lipid peroxidation and reducing liver enzyme markers such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) (Iwu *et al*., 2023). The protective effects of *Spondias mombin* on the liver make it a potential therapeutic agent for managing liver disorders, including non-alcoholic fatty liver disease (NAFLD).

Terpenoids, another important phytochemical class present in *Spondias mombin*, exhibit a wide range of pharmacological activities, including antimicrobial, anti-inflammatory, and antidiabetic effects (Adegbite *et al*., 2022). These compounds have been shown to modulate glucose metabolism by enhancing insulin sensitivity and reducing blood glucose levels, making them beneficial in the management of diabetes. The antidiabetic potential of *Spondias mombin* has been demonstrated in animal studies, where extracts of the plant have been found to improve glucose tolerance and reduce fasting blood sugar levels (Kim *et al*., 2020).

The medicinal properties of *Spondias mombin* extend to its ability to modulate lipid metabolism and reduce hyperlipidemia. The hypolipidemic effects of the plant have been attributed to its rich content of flavonoids, saponins, and phenolic compounds, which work synergistically to lower total cholesterol, triglycerides, and low-density lipoprotein (LDL) levels while increasing high-density lipoprotein (HDL) levels (Egwim *et al*., 2019). By improving lipid profiles, *Spondias mombin* may help reduce the risk of cardiovascular diseases, particularly in individuals with diet-induced hyperlipidemia.

Another notable medicinal property of *Spondias mombin* is its anti-inflammatory activity. Chronic inflammation is a major contributor to various diseases, including arthritis, cardiovascular diseases, and metabolic disorders. The flavonoids and terpenoids in *Spondias mombin* have been shown to inhibit pro-inflammatory cytokines and enzymes, thereby reducing inflammation and providing relief from inflammatory conditions (Parikh *et al*., 2019). The anti-inflammatory properties of *Spondias mombin* also contribute to its pain-relieving effects, making it useful in traditional medicine for treating conditions such as rheumatism and muscle pain (Saleem *et al*., 2022).

The antimicrobial properties of *Spondias mombin* have been widely documented, with studies showing that its extracts possess activity against a variety of pathogenic bacteria and fungi (Alabi *et al*., 2020). The antibacterial activity of *Spondias mombin* is attributed to its rich content of tannins, alkaloids, and flavonoids, which interfere with bacterial cell wall synthesis and inhibit microbial growth. This antimicrobial activity supports the traditional use of *Spondias mombin* in treating infections such as diarrhea, wound infections, and respiratory tract infections (Ajayi *et al*., 2019).

The plant's hepatoprotective effects are also noteworthy, as the liver plays a central role in metabolism and detoxification. Studies have demonstrated that *Spondias mombin* extracts help protect liver cells from oxidative damage and inflammation, thereby preventing liver dysfunction and enhancing overall liver health (Akinmoladun *et al*., 2021). These hepatoprotective effects make *Spondias mombin* a potential therapeutic agent for managing conditions such as hepatitis and fatty liver disease.

Spondias mombin is a nutritionally and pharmacologically significant plant with a broad spectrum of medicinal properties. Its rich phytochemical composition, which includes flavonoids, tannins, saponins, phenolics, and terpenoids, contributes to its antioxidant, antimicrobial, anti-inflammatory, hypolipidemic, hepatoprotective, and antidiabetic effects. The growing body of scientific evidence supports the traditional use of *Spondias mombin* in managing various health conditions, particularly those related to metabolic disorders, cardiovascular diseases, and infections. While preclinical studies have demonstrated its therapeutic potential, further clinical research is needed to fully establish its safety, efficacy, and standardized dosages for human consumption.

2.3 Methanol Extract of *Spondias mombin*: Justification and Biological activities

The extraction of bioactive compounds from medicinal plants plays a crucial role in the study of their pharmacological activities. Among the various solvent extraction methods used in phytochemical research, methanol extraction has gained significant attention due to its efficiency in isolating a wide range of polar and non-polar compounds. Methanol is particularly effective in extracting flavonoids, tannins, saponins, alkaloids, phenolics, and terpenoids, which are responsible for the diverse medicinal properties of *Spondias mombin* (Adebayo *et al*., 2022). The justification for using methanol extract in the study of *Spondias mombin* lies in its ability to maximize the yield of bioactive compounds, thereby enhancing the plant's therapeutic potential. Additionally, methanol is known for its high solubility properties, allowing for a more comprehensive extraction of both hydrophilic and lipophilic components (Oyeniran *et al*., 2022).

Methanol extraction of *Spondias mombin* is widely used in pharmacological studies due to its ability to preserve the structural integrity of bioactive molecules. Unlike water-based extractions, which may lead to the degradation of heat-sensitive compounds, methanol extraction ensures the stability of phytochemicals, making it an ideal choice for bioassays and medicinal applications (Akinmoladun *et al*., 2021). The methanol extract of *Spondias mombin* has been reported to exhibit a broad spectrum of biological activities, including antioxidant, anti-inflammatory, antimicrobial, hypolipidemic, hepatoprotective, and antidiabetic properties. The presence of high concentrations of polyphenols and flavonoids in the methanol extract contributes significantly to its therapeutic effects, particularly in mitigating oxidative stress and inflammation, which are key factors in the pathogenesis of chronic diseases (Olaleye *et al*., 2019).

One of the most significant biological activities of the methanol extract of *Spondias mombin* is its antioxidant potential. Antioxidants play a critical role in neutralizing reactive oxygen species (ROS), thereby protecting cells from oxidative damage. Studies have shown that the methanol extract of *Spondias mombin* exhibits high radical scavenging activity, which is attributed to its rich content of flavonoids and phenolic compounds (Dosumu *et al*., 2020). The antioxidant capacity of the methanol extract is particularly relevant in preventing lipid peroxidation, a process that contributes to the development of atherosclerosis and other cardiovascular diseases. By reducing oxidative stress, the extract helps to maintain cellular integrity and prevent the progression of degenerative disorders (Iwu *et al*., 2023).

The anti-inflammatory activity of the methanol extract of *Spondias mombin* has also been widely studied. Chronic inflammation is a major contributor to various pathological conditions, including arthritis, cardiovascular diseases, and metabolic disorders. The methanol extract has been shown to inhibit pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), thereby reducing inflammation and providing therapeutic benefits in inflammatory conditions (Balogun *et al*., 2021). The flavonoids and tannins present in the extract contribute to its anti-inflammatory effects by modulating the activity of cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, which play key roles in the inflammatory response (Adebayo *et al*., 2022).

Another important biological activity of the methanol extract of *Spondias mombin* is its antimicrobial effect. The extract has been reported to exhibit significant antibacterial and antifungal properties against a range of pathogenic microorganisms. The antimicrobial activity of the extract is primarily attributed to its high tannin and alkaloid content, which disrupt bacterial cell membranes and inhibit the growth of fungi (Oloruntoba *et al*., 2021). Studies have demonstrated that the methanol extract of *Spondias mombin* is effective against

Staphylococcus aureus, *Escherichia coli*, and *Candida albicans*, supporting its traditional use in treating infections such as diarrhea, skin infections, and respiratory tract infections (Nwafor *et al*., 2020). The antimicrobial activity of the extract highlights its potential as a natural alternative to synthetic antibiotics, particularly in the face of rising antibiotic resistance.

The hypolipidemic effects of the methanol extract of *Spondias mombin* have also been extensively studied. Dyslipidemia, characterized by elevated levels of total cholesterol, triglycerides, and low-density lipoprotein (LDL), is a major risk factor for cardiovascular diseases. The methanol extract has been shown to significantly reduce serum lipid levels in animal models of hyperlipidemia, suggesting its potential as a natural lipid-lowering agent (Egwim *et al*., 2019). The hypolipidemic effects of the extract are attributed to its high saponin and flavonoid content, which enhance lipid metabolism by increasing bile acid excretion and reducing cholesterol absorption in the intestines (Ajayi *et al*., 2019). The ability of the methanol extract to modulate lipid profiles makes it a promising candidate for the management of hypercholesterolemia and related metabolic disorders.

The hepatoprotective effects of the methanol extract of *Spondias mombin* further support its medicinal significance. The liver plays a central role in metabolism, detoxification, and lipid regulation, making it vulnerable to damage from toxins, drugs, and oxidative stress. Studies have shown that the methanol extract of *Spondias mombin* exerts hepatoprotective effects by reducing liver enzyme markers such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) (Akinmoladun *et al*., 2021). The phenolic and flavonoid compounds in the extract protect liver cells from oxidative damage and inflammation, thereby preventing liver dysfunction and improving overall hepatic health (Saleem *et al*., 2022). The hepatoprotective properties of the extract highlight its potential in managing liver diseases such as non-alcoholic fatty liver disease (NAFLD) and hepatitis.

The antidiabetic properties of the methanol extract of *Spondias mombin* have also been investigated. Diabetes mellitus is a metabolic disorder characterized by high blood glucose levels due to insulin resistance or inadequate insulin production. The methanol extract has been reported to enhance insulin sensitivity, improve glucose uptake, and reduce blood glucose levels in diabetic animal models (Kim *et al*., 2020). The antidiabetic effects of the extract are primarily attributed to its high content of flavonoids and terpenoids, which modulate key enzymes involved in glucose metabolism, such as alpha-glucosidase and hexokinase (Oyeniran *et al*., 2022). The ability of the extract to regulate blood sugar levels suggests its potential as a complementary therapy for diabetes management.

The methanol extract of *Spondias mombin* is a rich source of bioactive compounds with diverse pharmacological activities. Its high extraction efficiency and ability to preserve phytochemicals make it a valuable tool for studying the plant's therapeutic potential. The extract exhibits potent antioxidant, anti-inflammatory, antimicrobial, hypolipidemic, hepatoprotective, and antidiabetic effects, which contribute to its traditional and modern medicinal applications. The increasing scientific validation of these properties supports the potential of *Spondias mombin* as a natural remedy for various chronic diseases. However, further research, including clinical trials, is necessary to establish standardized dosages and ensure safety for human use. The growing interest in plant-based medicine underscores the importance of *Spondias mombin* as a promising candidate for the development of natural therapeutic agents.

2.4 High-Fat Diet and its Impact on Health

A high-fat diet (HFD) is characterized by excessive consumption of dietary fats, particularly saturated and trans fats, which have been linked to a wide range of metabolic disorders and chronic diseases. The increasing prevalence of obesity, cardiovascular diseases, type 2 diabetes, and non-alcoholic fatty liver disease (NAFLD) has been strongly associated with the widespread consumption of high-fat diets, particularly in Westernized societies where processed and fast foods are abundant (Sacks *et al*., 2017). The impact of a high-fat diet on health is complex, involving multiple physiological and biochemical alterations that affect lipid metabolism, insulin sensitivity, inflammation, and overall metabolic homeostasis. The consequences of excessive fat intake extend beyond weight gain and obesity, as it contributes to systemic inflammation, oxidative stress, and lipid dysregulation, all of which play a role in the pathogenesis of chronic diseases (Wang and Liao, 2020).

One of the most immediate effects of a high-fat diet is the disruption of lipid metabolism, leading to hyperlipidemia, a condition characterized by elevated levels of total cholesterol, low-density lipoprotein (LDL), and triglycerides, along with reduced high-density lipoprotein (HDL) levels. Excess dietary fat, especially saturated and trans fats, increases the synthesis of cholesterol and triglycerides in the liver, leading to their accumulation in the bloodstream. This lipid imbalance significantly increases the risk of atherosclerosis, a condition in which fatty deposits accumulate on arterial walls, restricting blood flow and predisposing individuals to cardiovascular diseases such as hypertension, coronary artery disease, and stroke (Ference *et al*., 2017). Additionally, excessive fat intake contributes to endothelial dysfunction by impairing nitric oxide production and promoting oxidative stress, further exacerbating cardiovascular risk (Zhou *et al*., 2021). The consumption of unsaturated fats, such as omega-3 fatty acids found in fish and nuts, has been shown to have protective effects against cardiovascular diseases, highlighting the importance of dietary fat composition in disease prevention (Mozaffarian *et al*., 2018).

Insulin resistance is another major consequence of a high-fat diet, contributing to the development of type 2 diabetes mellitus. Chronic consumption of high-fat foods leads to the accumulation of lipids in non-adipose tissues, particularly the liver and skeletal muscles, resulting in lipotoxicity and impaired insulin signaling (Samuel and Shulman, 2016). Excess fat intake promotes the activation of pro-inflammatory pathways, including nuclear factor kappa B (NF-κB) and c-Jun N-terminal kinase (JNK), which interfere with insulin receptor function and reduce glucose uptake by peripheral tissues (Shoelson *et al*., 2017). The resulting insulin resistance leads to increased blood glucose levels, pancreatic β-cell dysfunction, and eventually the onset of diabetes. Additionally, high-fat diets are associated with increased hepatic glucose production due to the excessive availability of free fatty acids, further contributing to hyperglycemia and metabolic dysregulation (Czech, 2017).

Non-alcoholic fatty liver disease (NAFLD) is another major health concern associated with high-fat diets. NAFLD is characterized by excessive fat accumulation in the liver, leading to hepatic steatosis, inflammation, and fibrosis, which can progress to more severe forms such as non-alcoholic steatohepatitis (NASH) and cirrhosis (Younossi *et al*., 2018). The pathogenesis of NAFLD is closely linked to insulin resistance, as the excessive influx of free fatty acids into hepatocytes results in mitochondrial dysfunction, oxidative stress, and endoplasmic reticulum stress, all of which contribute to hepatic injury (Browning *et al*., 2019). Studies have demonstrated that high-fat diets lead to significant alterations in liver enzyme levels, including increased alanine aminotransferase (ALT) and aspartate aminotransferase (AST), which are markers of liver damage (Tilg and Moschen, 2017). The progression of NAFLD is also influenced by gut microbiota alterations induced by high-fat diets, as dysbiosis and increased gut permeability contribute to hepatic inflammation through the translocation of bacterial endotoxins into the liver (Schwabe and Greten, 2020).

The pro-inflammatory effects of high-fat diets extend beyond metabolic disorders, as chronic low-grade inflammation has been implicated in various diseases, including neurodegenerative conditions and cancer. The excessive intake of dietary fats, particularly saturated fats, leads to an increase in pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β), which promote systemic inflammation and tissue damage (Hotamisligil, 2017). In the brain, high-fat diets have been linked to cognitive decline and neuroinflammation, as increased lipid accumulation and oxidative stress contribute to neuronal dysfunction and the progression of disorders such as Alzheimer's disease (Kothari *et al*., 2017). Moreover, the chronic inflammatory state induced by high-fat diets has been associated with an increased risk of cancer, particularly colorectal and breast cancer, due to the promotion of cell proliferation, angiogenesis, and inhibition of apoptosis (Kolb *et al*., 2019).

High-fat diets also have a profound impact on gut microbiota composition, which plays a critical role in metabolic health. The excessive intake of dietary fats leads to dysbiosis, characterized by a reduction in beneficial bacteria such as Bifidobacteria and an increase in harmful bacteria such as Firmicutes and Proteobacteria (Zhang *et al*., 2020). This microbial imbalance contributes to increased gut permeability, allowing bacterial lipopolysaccharides (LPS) to enter the bloodstream and trigger systemic inflammation, a phenomenon known as metabolic endotoxemia (Cani *et al*., 2017). The alterations in gut microbiota induced by high-fat diets have been implicated in obesity, insulin resistance, and NAFLD, highlighting the crucial role of gut health in metabolic homeostasis (Fan and Pedersen, 2021).

The obesogenic effects of high-fat diets are well-documented, as excessive fat intake leads to increased adiposity and weight gain. Dietary fats are highly energy-dense, providing 9 kcal per gram, compared to carbohydrates and proteins, which provide 4 kcal per gram. The high caloric content of fat-rich foods, combined with their palatability and low satiety effects, promotes overeating and positive energy balance, ultimately leading to obesity (Hall *et al*., 2019). Adipose tissue, particularly visceral fat, is not merely a storage site for excess energy but also an active endocrine organ that secretes adipokines such as leptin and adiponectin, which regulate appetite, metabolism, and inflammation (Bluher, 2019). The dysregulation of adipokine signaling in obesity contributes to metabolic disturbances, including insulin resistance and cardiovascular diseases (Ahima and Lazar, 2017).

High-fat diets have profound and far-reaching effects on human health, contributing to a wide range of metabolic and inflammatory disorders. The disruption of lipid metabolism, induction of insulin resistance, promotion of systemic inflammation, and alteration of gut microbiota all play crucial roles in the pathogenesis of conditions such as obesity, cardiovascular diseases, diabetes, NAFLD, and neurodegenerative diseases. While dietary fats are essential for various physiological functions, the type and quantity of fat consumed significantly influence health outcomes. The consumption of unsaturated fats from sources such as olive oil, fish, and nuts has been shown to confer protective effects, whereas excessive intake of saturated and trans fats from processed and fried foods has detrimental consequences. Given the increasing burden of metabolic diseases worldwide, dietary interventions aimed at reducing excessive fat intake and promoting a balanced diet are essential for improving public health and preventing chronic diseases.

2.5 Lipid and Lipid Metabolism – Total Cholesterol and Triglycerides

Lipids are a diverse group of hydrophobic molecules that play essential roles in cellular structure, energy storage, and metabolic signaling. They include fatty acids, triglycerides, phospholipids, and sterols such as cholesterol. Lipids serve as the primary energy reservoir in the body, providing more than twice the energy per gram compared to carbohydrates and proteins. Beyond energy storage, lipids are integral components of biological membranes, serve as precursors for hormone synthesis, and play crucial roles in cell signaling pathways (Jump *et al*., 2018). The metabolism of lipids involves intricate biochemical pathways that regulate their synthesis, transport, utilization, and degradation to maintain homeostasis. Disruptions in lipid metabolism contribute to various metabolic disorders, including hyperlipidemia, atherosclerosis, obesity, and metabolic syndrome. Among the key lipid fractions involved in metabolic regulation are total cholesterol and triglycerides, which are vital for maintaining cellular function but, when dysregulated, contribute to pathological conditions such as cardiovascular diseases and non-alcoholic fatty liver disease (Bjørndal *et al*., 2018).

Total cholesterol is a crucial lipid molecule that serves as a structural component of cell membranes and as a precursor for the synthesis of steroid hormones, bile acids, and vitamin D. Cholesterol is obtained from dietary sources and synthesized endogenously in the liver through the mevalonate pathway, with 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase being the rate-limiting enzyme in its biosynthesis. The liver plays a central role in cholesterol homeostasis by regulating its synthesis, uptake, and excretion. Cholesterol is transported in the bloodstream by lipoproteins, which include low-density lipoprotein (LDL), high-density lipoprotein (HDL), very-low-density lipoprotein (VLDL), and chylomicrons (Linton *et al*., 2019). LDL, commonly referred to as “bad cholesterol,” carries cholesterol to peripheral tissues and is prone to oxidation, leading to the formation of atherosclerotic plaques in blood vessels. In contrast, HDL, known as “good cholesterol,” facilitates the reverse transport of cholesterol from peripheral tissues back to the liver for excretion via bile, thereby playing a protective role against cardiovascular disease. An imbalance in cholesterol metabolism, characterized by elevated LDL levels and reduced HDL levels, increases the risk of atherosclerosis and cardiovascular diseases (Falk, 2019).

Triglycerides are the most abundant type of fat in the body and serve as a primary source of energy. They are composed of three fatty acid chains esterified to a glycerol backbone and are stored in adipose tissue for energy mobilization during fasting states. Triglycerides are obtained from dietary fats and synthesized endogenously in the liver through the esterification of fatty acids with glycerol-3-phosphate. After dietary intake, triglycerides are packaged into chylomicrons in the intestines and transported via the lymphatic system before entering the bloodstream. In the liver, triglycerides are packaged into VLDL and secreted into circulation, where they undergo hydrolysis by lipoprotein lipase (LPL) to release free fatty acids for uptake by peripheral tissues such as skeletal muscle and adipose tissue (Pinnamaneni and Puvvada, 2021). Excessive triglyceride accumulation in the liver leads to steatosis, a hallmark of non-alcoholic fatty liver disease, while elevated circulating triglyceride levels are associated with increased risk of cardiovascular diseases and pancreatitis. Hypertriglyceridemia, often resulting from excessive dietary fat intake, insulin resistance, or genetic predisposition, is a significant risk factor for metabolic syndrome and cardiovascular complications (Adiels *et al*., 2019).

The regulation of lipid metabolism is influenced by multiple factors, including hormonal control, genetic predisposition, dietary intake, and physical activity. Insulin plays a critical role in lipid metabolism by promoting lipogenesis and inhibiting lipolysis in adipose tissue. Under normal physiological conditions, insulin facilitates the uptake of glucose and fatty acids into adipocytes, where they are converted into triglycerides for storage. However, in conditions such as insulin resistance and type 2 diabetes, impaired insulin signaling results in excessive lipolysis, leading to an increased release of free fatty acids into circulation. These fatty acids are taken up by the liver and re-esterified into triglycerides, contributing to hepatic steatosis and dyslipidemia (Samuel and Shulman, 2016). The dysregulation of lipid metabolism in insulin-resistant states also contributes to increased VLDL production, reduced HDL levels, and enhanced LDL oxidation, all of which are implicated in the development of atherosclerosis and cardiovascular diseases.

Cholesterol and triglyceride metabolism are also influenced by dietary composition. Diets high in saturated fats and trans fats have been shown to increase LDL levels and total cholesterol, promoting the formation of atherosclerotic plaques and increasing the risk of cardiovascular events. Conversely, diets rich in unsaturated fats, particularly omega-3 fatty acids from fish and plant sources, have been shown to lower triglyceride levels and improve overall lipid profiles (Mozaffarian *et al*., 2018). Omega-3 fatty acids exert cardioprotective effects by reducing hepatic triglyceride synthesis, enhancing lipoprotein clearance, and modulating inflammatory pathways. Additionally, dietary fiber has been shown to reduce cholesterol absorption in the intestines, leading to lower total cholesterol and LDL levels. The Mediterranean diet, which emphasizes the consumption of healthy fats, whole grains, fruits, and vegetables, has been associated with improved lipid metabolism and reduced cardiovascular risk (Estruch *et al*., 2018).

Lipid metabolism is also modulated by genetic factors, with polymorphisms in genes involved in cholesterol synthesis, transport, and clearance contributing to interindividual variations in lipid levels. Familial hypercholesterolemia, an inherited disorder characterized by mutations in the LDL receptor gene, results in impaired LDL clearance and markedly elevated cholesterol levels, predisposing affected individuals to premature cardiovascular disease. Similarly, mutations in the apolipoprotein C3 (APOC3) gene, which regulates triglyceride metabolism, have been linked to hypertriglyceridemia and increased cardiovascular risk (Teslovich *et al*., 2019). Advances in lipidomics and genetic research have provided insights into the molecular mechanisms governing lipid metabolism and have paved the way for targeted lipid-lowering therapies, including statins, fibrates, and PCSK9 inhibitors.

Lipid metabolism is a highly regulated process that ensures the balance between lipid synthesis, transport, utilization, and excretion. Cholesterol and triglycerides play essential physiological roles, but their dysregulation is implicated in various metabolic disorders, including atherosclerosis, non-alcoholic fatty liver disease, and type 2 diabetes. Dietary intake, hormonal control, genetic predisposition, and lifestyle factors all influence lipid homeostasis, underscoring the importance of a balanced diet and regular physical activity in maintaining optimal lipid profiles. Advances in our understanding of lipid metabolism have led to the development of pharmacological and dietary interventions aimed at reducing the burden of lipid-related diseases. Given the rising prevalence of obesity and metabolic syndrome worldwide, continued research into lipid metabolism remains critical for developing effective strategies for prevention and treatment.

2.6 Role of Lipid in Metabolic Health

Lipids play a crucial role in metabolic health, serving as essential components of cellular structures, energy storage molecules, and signaling mediators. They are involved in a wide range of physiological processes, including membrane integrity, hormone synthesis, and energy metabolism. The balance of lipid intake, synthesis, utilization, and storage is critical for maintaining metabolic homeostasis. Any disruption in lipid metabolism can lead to metabolic disorders such as obesity, dyslipidemia, insulin resistance, type 2 diabetes, and cardiovascular diseases (Muoio and Newgard, 2018). Understanding the role of lipids in metabolic health provides insight into disease mechanisms and therapeutic strategies for preventing and managing metabolic dysfunctions.

Lipids are a major source of energy in the human body, particularly in periods of fasting or prolonged exercise when carbohydrate reserves are depleted. Triglycerides, stored in adipose tissue, serve as the primary energy reservoir. During times of energy demand, triglycerides undergo lipolysis, releasing free fatty acids into circulation, where they are transported to various tissues such as skeletal muscle and the liver for β-oxidation and ATP production (Schulze *et al*., 2019). The efficient mobilization and oxidation of fatty acids are essential for maintaining energy balance, and any impairment in lipid utilization can lead to metabolic imbalances, contributing to obesity and insulin resistance. Additionally, lipid-derived ketone bodies, produced in the liver during fasting or carbohydrate restriction, serve as an alternative energy source for the brain and peripheral tissues, highlighting the metabolic flexibility of lipids (Puchalska and Crawford, 2017).

Beyond energy metabolism, lipids play a fundamental role in maintaining cellular structure and function. Phospholipids are major components of biological membranes, providing structural integrity and regulating membrane fluidity. The lipid composition of membranes influences the activity of membrane-bound proteins, including transporters, receptors, and enzymes, which are essential for cellular communication and metabolic regulation (van Meer *et al*., 2018). Cholesterol, another critical lipid, contributes to membrane stability and serves as a precursor for steroid hormones, bile acids, and vitamin D. The regulation of membrane lipid composition is vital for cellular adaptation to metabolic changes, and alterations in lipid composition have been linked to metabolic disorders and inflammatory diseases (Hulver and Dohm, 2019).

Lipids also serve as key signaling molecules that regulate metabolic pathways and inflammatory responses. Bioactive lipids such as eicosanoids, sphingolipids, and ceramides play important roles in cell signaling, apoptosis, and immune regulation. Eicosanoids, derived from polyunsaturated fatty acids (PUFAs) such as arachidonic acid, modulate inflammation and vascular function, with implications for metabolic and cardiovascular health (Serhan and Levy, 2018). While some eicosanoids have pro-inflammatory effects that contribute to metabolic diseases, others, particularly those derived from omega-3 fatty acids, exhibit anti-inflammatory properties that promote metabolic homeostasis. Sphingolipids and ceramides, on the other hand, have been implicated in insulin resistance and lipotoxicity. Elevated ceramide levels have been shown to interfere with insulin signaling, leading to impaired glucose uptake and increased risk of type 2 diabetes (Chaurasia *et al*., 2019).

The regulation of lipid metabolism is tightly linked to insulin signaling, and disruptions in lipid homeostasis are a hallmark of metabolic disorders. In insulin-sensitive tissues such as muscle and adipose tissue, insulin promotes lipid storage by stimulating lipogenesis and inhibiting lipolysis. However, in insulin-resistant states, such as obesity and type 2 diabetes, excessive lipid accumulation in non-adipose tissues leads to lipotoxicity, characterized by mitochondrial dysfunction, oxidative stress, and inflammation (Samuel and Shulman, 2016). The ectopic accumulation of lipids in the liver contributes to non-alcoholic fatty liver disease (NAFLD), while lipid overload in pancreatic β-cells impairs insulin secretion, exacerbating hyperglycemia (Fabbrini *et al*., 2018). The interplay between lipid metabolism and insulin signaling underscores the importance of maintaining lipid homeostasis for metabolic health.

The composition of dietary lipids significantly influences metabolic health, with different types of fats exerting varying effects on lipid profiles and disease risk. Saturated fats and trans fats have been associated with increased LDL cholesterol levels, endothelial dysfunction, and chronic inflammation, all of which contribute to cardiovascular disease (Mozaffarian *et al*., 2018). In contrast, monounsaturated and polyunsaturated fats, particularly omega-3 fatty acids found in fish and plant oils, have been shown to improve lipid metabolism, reduce triglyceride levels, and modulate inflammatory pathways. Omega-3 fatty acids enhance lipid oxidation, reduce hepatic triglyceride synthesis, and promote the production of anti-inflammatory mediators, highlighting their protective role in metabolic health (Jump *et al*., 2018). The balance between different types of dietary fats plays a crucial role in regulating lipid metabolism and preventing metabolic diseases.

The gut microbiota also plays a significant role in lipid metabolism and metabolic health. Emerging evidence suggests that alterations in gut microbial composition influence lipid absorption, bile acid metabolism, and systemic inflammation. High-fat diets have been shown to induce gut dysbiosis, characterized by an increase in harmful bacteria and a reduction in beneficial bacteria such as Bifidobacteria and Lactobacilli (Zhang *et al*., 2020). This imbalance promotes intestinal permeability, allowing bacterial lipopolysaccharides (LPS) to enter the bloodstream and trigger systemic inflammation, a phenomenon known as metabolic endotoxemia (Cani *et al*., 2017). The interaction between gut microbiota and lipid metabolism has profound implications for obesity, diabetes, and cardiovascular diseases, highlighting the potential of microbiome-targeted therapies in metabolic health management.

Physical activity and lifestyle modifications play an essential role in lipid metabolism and overall metabolic health. Regular exercise enhances lipid oxidation, improves insulin sensitivity, and reduces triglyceride levels, thereby lowering the risk of metabolic diseases.

Exercise-induced adaptations in lipid metabolism include increased mitochondrial biogenesis, enhanced fatty acid transport, and improved lipoprotein profiles (Holloszy, 2018). Furthermore, weight management through caloric restriction and healthy dietary patterns, such as the Mediterranean diet, has been shown to improve lipid metabolism and reduce the risk of cardiovascular and metabolic diseases. Lifestyle interventions remain a cornerstone of metabolic disease prevention and treatment, emphasizing the importance of lipid regulation in maintaining health (Estruch *et al*., 2018).

Iipids are essential to metabolic health, playing critical roles in energy metabolism, cellular function, and metabolic signaling. The balance between lipid synthesis, utilization, and storage is crucial for maintaining homeostasis, and disruptions in lipid metabolism contribute to various metabolic disorders. The type and composition of dietary fats, insulin regulation, gut microbiota interactions, and lifestyle factors all influence lipid metabolism and disease risk. Understanding the intricate relationship between lipids and metabolic health provides valuable insights into disease mechanisms and therapeutic strategies aimed at preventing and managing metabolic disorders. Continued research in lipid metabolism will enhance our ability to develop targeted interventions for improving metabolic health and reducing the burden of lipid-related diseases.

2.7 Effect of High-Fat Diet on Total Cholesterol and Triglyceride Levels

A high-fat diet has significant effects on lipid metabolism, particularly in relation to total cholesterol and triglyceride levels. The consumption of excess dietary fat, especially saturated fats and trans fats, disrupts lipid homeostasis by increasing circulating lipid levels, altering lipoprotein profiles, and promoting metabolic disorders such as dyslipidemia, atherosclerosis, and cardiovascular disease. The liver plays a central role in cholesterol and triglyceride metabolism, regulating their synthesis, transport, and excretion. However, excessive dietary fat intake overwhelms these regulatory mechanisms, leading to lipid accumulation and metabolic imbalances that increase the risk of chronic diseases (Lichtenstein *et al*., 2019).

Total cholesterol, which includes both high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, is tightly regulated through endogenous synthesis and dietary intake. A high-fat diet, particularly one rich in saturated and trans fats, contributes to increased LDL cholesterol levels while reducing HDL cholesterol. LDL is responsible for transporting cholesterol to peripheral tissues, and when present in excess, it becomes susceptible to oxidation, leading to endothelial dysfunction and the initiation of atherosclerosis. In contrast, HDL cholesterol plays a protective role by facilitating reverse cholesterol transport, removing excess cholesterol from the bloodstream and transporting it back to the liver for excretion (Feingold and Grunfeld, 2018). Studies have demonstrated that diets high in saturated fats lead to a significant increase in total cholesterol and LDL cholesterol, while diets rich in unsaturated fats, such as omega-3 fatty acids, are associated with improved lipid profiles and reduced cardiovascular risk (Mozaffarian, 2018).

Triglycerides, the most abundant form of fat in the human body, are directly influenced by dietary fat intake. They are stored in adipose tissue and serve as an energy reservoir, but excessive dietary fat intake leads to elevated plasma triglyceride levels, a condition known as hypertriglyceridemia. A high-fat diet increases triglyceride synthesis in the liver by promoting the esterification of fatty acids into triglycerides, which are then packaged into very-low-density lipoproteins (VLDL) and released into circulation. The overproduction of VLDL contributes to dyslipidemia, which is characterized by elevated triglycerides, low HDL cholesterol, and increased small, dense LDL particles that are highly atherogenic (Adiels *et al*., 2019). Insulin resistance, often associated with high-fat diets, further exacerbates hypertriglyceridemia by impairing the clearance of triglyceride-rich lipoproteins from the circulation. Insulin normally inhibits lipolysis in adipose tissue, but in insulin-resistant states, excessive free fatty acids are released into circulation and taken up by the liver, where they are converted into triglycerides, worsening lipid imbalances (Samuel and Shulman, 2016).

The mechanism through which high-fat diets increase total cholesterol and triglycerides is multifaceted. Dietary fats influence the activity of key enzymes involved in lipid metabolism, including 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme in cholesterol synthesis. High-fat intake upregulates HMG-CoA reductase activity, leading to increased endogenous cholesterol production despite high dietary cholesterol intake (Grundy, 2019). In addition, high-fat diets suppress the expression of LDL receptors in the liver, reducing cholesterol clearance from the bloodstream and leading to elevated circulating LDL cholesterol levels. This contributes to cholesterol accumulation in arterial walls, increasing the risk of atherosclerosis and cardiovascular disease (Linton *et al*., 2019). Furthermore, high-fat diets alter bile acid metabolism by reducing bile acid excretion, leading to increased intestinal cholesterol reabsorption and further elevating plasma cholesterol levels.

The type of dietary fat consumed plays a crucial role in determining its effect on total cholesterol and triglyceride levels. Saturated fats and trans fats have been shown to significantly elevate LDL cholesterol and triglyceride levels, whereas monounsaturated and polyunsaturated fats have beneficial effects on lipid metabolism. Omega-3 fatty acids, found in fish oil and plant sources such as flaxseeds, have been shown to lower triglyceride levels by reducing hepatic triglyceride synthesis and increasing lipid oxidation (Jump *et al*., 2018). In contrast, diets high in saturated fats from sources such as red meat, dairy, and processed foods contribute to elevated LDL cholesterol and increased cardiovascular risk. Trans fats, found in partially hydrogenated oils, have particularly harmful effects on lipid metabolism by raising LDL cholesterol while simultaneously lowering HDL cholesterol, creating an unfavorable lipid profile that promotes atherosclerosis (Mozaffarian *et al*., 2018).

The impact of high-fat diets on lipid metabolism extends beyond cholesterol and triglyceride levels, affecting overall metabolic health. Chronic consumption of a high-fat diet contributes to obesity, insulin resistance, and fatty liver disease, all of which further disrupt lipid homeostasis. In obese individuals, excessive adipose tissue contributes to increased lipolysis, leading to elevated free fatty acid levels in circulation. These fatty acids are taken up by the liver and re-esterified into triglycerides, contributing to hepatic steatosis and increased VLDL production. The accumulation of hepatic fat is a key feature of non-alcoholic fatty liver disease (NAFLD), which is strongly associated with dyslipidemia and metabolic syndrome (Fabbrini *et al*., 2018). Additionally, inflammation associated with obesity and high-fat diets exacerbates lipid imbalances by altering adipokine secretion and promoting oxidative stress, which further increases the risk of cardiovascular disease.

Animal studies have provided further evidence of the effects of high-fat diets on lipid metabolism. Rodent models fed high-fat diets exhibit significant increases in total cholesterol and triglyceride levels, along with the development of insulin resistance, hepatic steatosis, and atherosclerotic lesions. These studies demonstrate that prolonged consumption of a high-fat diet leads to metabolic disturbances similar to those observed in human metabolic syndrome, making them valuable models for studying lipid metabolism and potential therapeutic interventions (Poudyal *et al*., 2019). Experimental studies have also shown that dietary modifications, such as replacing saturated fats with unsaturated fats and incorporating dietary fiber, can reverse some of the negative effects of high-fat diets on lipid metabolism.

The regulation of cholesterol and triglyceride levels in response to high-fat diets is also influenced by genetic factors. Polymorphisms in genes involved in lipid metabolism, such as those encoding apolipoproteins, lipoprotein lipase, and hepatic lipase, contribute to interindividual variations in lipid responses to dietary fat intake. For example, genetic variants in the apolipoprotein E (APOE) gene influence cholesterol metabolism and cardiovascular disease risk, with certain APOE genotypes being more susceptible to diet-induced hyperlipidemia (Teslovich *et al*., 2019). Understanding the genetic basis of lipid metabolism can help in the development of personalized dietary interventions to mitigate the adverse effects of high-fat diets on cholesterol and triglyceride levels.

A high-fat diet significantly impacts total cholesterol and triglyceride levels, promoting dyslipidemia and increasing the risk of cardiovascular and metabolic diseases. The type of dietary fat consumed plays a crucial role in determining its effects on lipid metabolism, with saturated and trans fats being particularly detrimental, while unsaturated fats exert protective effects. The interplay between dietary fat intake, lipid metabolism, insulin resistance, and genetic factors underscores the complexity of cholesterol and triglyceride regulation. Given the increasing prevalence of high-fat diets in modern lifestyles, understanding their effects on lipid metabolism is essential for developing dietary and pharmacological strategies to prevent and manage dyslipidemia and its associated health complications.

2.8 Mechanism of *Spondias mombin* in Lipid Reduction

Spondias mombin, commonly known as hog plum or yellow mombin, has been widely studied for its pharmacological effects, including its potential in lipid reduction. The ability of *Spondias mombin* to modulate lipid metabolism is attributed to its diverse phytochemical constituents, which include flavonoids, tannins, alkaloids, terpenoids, and saponins. These bioactive compounds exert hypolipidemic effects through multiple mechanisms, including inhibition of lipid absorption, enhancement of lipid catabolism, modulation of enzymatic activity, and reduction of oxidative stress and inflammation, all of which contribute to improved lipid profiles and reduced cardiovascular risk (Akinmoladun *et al*., 2020).

One of the primary mechanisms by which *Spondias mombin* lowers lipid levels is through its ability to inhibit dietary lipid absorption in the intestine. Saponins, a class of secondary metabolites found in the plant, have been reported to reduce cholesterol absorption by binding to bile acids and cholesterol in the gastrointestinal tract, thereby preventing their reabsorption into circulation. This mechanism leads to increased excretion of cholesterol and bile acids in feces, subsequently reducing plasma cholesterol levels (Oladimeji *et al*., 2019). Furthermore, flavonoids present in *Spondias mombin* have been shown to inhibit the activity of pancreatic lipase, a key enzyme responsible for the breakdown of dietary triglycerides into absorbable free fatty acids and monoglycerides. By inhibiting this enzyme, *Spondias mombin* effectively reduces the digestion and absorption of dietary fats, leading to lower postprandial triglyceride levels and overall reduced lipid accumulation (Oladiji *et al*., 2021).

In addition to reducing lipid absorption, *Spondias mombin* enhances lipid catabolism and metabolism through its regulatory effects on key enzymes involved in cholesterol and triglyceride homeostasis. HMG-CoA reductase, the rate-limiting enzyme in cholesterol biosynthesis, is a major target in lipid-lowering therapy, as it regulates the conversion of HMG-CoA to mevalonate, a crucial step in endogenous cholesterol production. Studies have shown that bioactive compounds in *Spondias mombin*, particularly flavonoids and polyphenols, downregulate the expression and activity of HMG-CoA reductase, thereby reducing hepatic cholesterol synthesis and lowering total cholesterol and LDL cholesterol levels (Adebayo *et al*., 2021). Moreover, the plant’s constituents enhance the activity of lipoprotein lipase (LPL), an enzyme responsible for the hydrolysis of circulating triglycerides into free fatty acids, which are subsequently taken up by peripheral tissues for energy production or storage. By promoting LPL activity, *Spondias mombin* facilitates the clearance of triglyceride-rich lipoproteins from circulation, thereby reducing hypertriglyceridemia and improving lipid profiles (Ekpo *et al*., 2020).

The hypolipidemic effects of *Spondias mombin* are also linked to its antioxidant and anti-inflammatory properties, which play a crucial role in lipid metabolism and cardiovascular health. Oxidative stress and inflammation are key contributors to dyslipidemia and atherosclerosis, as they promote lipid peroxidation, endothelial dysfunction, and plaque formation. The phenolic compounds and flavonoids in *Spondias mombin* act as potent antioxidants by scavenging free radicals, reducing lipid peroxidation, and enhancing the activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) (Ajiboye *et al*., 2019). By mitigating oxidative stress, these compounds help maintain the integrity of lipoproteins, preventing the oxidation of LDL cholesterol, which is a major contributor to atherogenesis. Additionally, the anti-inflammatory effects of *Spondias mombin*, mediated by the suppression of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), contribute to improved lipid metabolism by reducing systemic inflammation, which is commonly associated with metabolic disorders and dyslipidemia (Adepoju *et al*., 2022).

Another significant mechanism through which *Spondias mombin* exerts its lipid-lowering effects is by modulating hepatic lipid metabolism and promoting bile acid synthesis. Bile acids play an essential role in cholesterol homeostasis by facilitating the emulsification and digestion of dietary lipids and serving as an excretory pathway for cholesterol elimination. Studies have indicated that phytochemicals in *Spondias mombin* upregulate the expression of key enzymes involved in bile acid biosynthesis, leading to increased conversion of cholesterol into bile acids and subsequent reduction in plasma cholesterol levels (Ogunlakin *et al*., 2021). Furthermore, the hepatoprotective properties of *Spondias mombin* help protect liver function, thereby maintaining efficient lipid metabolism and preventing lipid accumulation in hepatic tissues. This is particularly relevant in the context of non-alcoholic fatty liver disease (NAFLD), a condition characterized by excessive hepatic lipid deposition due to dysregulated lipid metabolism (Okonkwo *et al*., 2020).

The ability of *Spondias mombin* to modulate lipid metabolism extends beyond cholesterol and triglyceride regulation, as it also influences the composition and functionality of lipoproteins. High-density lipoprotein (HDL) cholesterol plays a crucial role in reverse cholesterol transport, facilitating the removal of excess cholesterol from peripheral tissues and transporting it back to the liver for excretion. Polyphenols and flavonoids in *Spondias mombin* have been shown to enhance HDL cholesterol levels by stimulating the expression of ATP-binding cassette transporter A1 (ABCA1), a key protein involved in HDL-mediated cholesterol efflux (Adefegha *et al*., 2021). By promoting reverse cholesterol transport, *Spondias mombin* contributes to improved lipid profiles and reduced cardiovascular risk.

Furthermore, animal studies have provided additional evidence supporting the hypolipidemic effects of *Spondias mombin*. Rodents fed a high-fat diet supplemented with *Spondias mombin* extract exhibited significant reductions in total cholesterol, LDL cholesterol, and triglycerides, along with increases in HDL cholesterol levels. These effects were accompanied by improvements in hepatic lipid metabolism, reduced adiposity, and enhanced antioxidant enzyme activity, demonstrating the potential of *Spondias mombin* as a natural therapeutic agent for dyslipidemia and metabolic disorders (Osuntokun *et al*., 2019). The observed lipid-lowering effects in animal models align with findings from human studies on plant-derived polyphenols, further supporting the role of *Spondias mombin* in lipid regulation.

The lipid-lowering effects of *Spondias mombin* are mediated through multiple mechanisms, including inhibition of lipid absorption, downregulation of cholesterol synthesis, enhancement of lipid catabolism, antioxidant and anti-inflammatory activities, and modulation of bile acid metabolism. The bioactive compounds present in *Spondias mombin*, particularly flavonoids, saponins, and polyphenols, play a crucial role in regulating lipid metabolism, reducing plasma cholesterol and triglyceride levels, and improving overall cardiovascular health. The plant's ability to target various aspects of lipid homeostasis highlights its potential as a natural remedy for hyperlipidemia and related metabolic disorders. Further research, including clinical trials, is needed to fully elucidate the molecular mechanisms underlying its lipid-lowering effects and to explore its potential as a complementary therapy for managing dyslipidemia and cardiovascular diseases.

2.10 Conventional Treatment of Hyperlipidemia

Hyperlipidemia, characterized by elevated levels of lipids in the blood, including total cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides, and reduced high-density lipoprotein cholesterol (HDL-C), is a major risk factor for cardiovascular diseases such as atherosclerosis, coronary artery disease, and stroke. The conventional treatment of hyperlipidemia primarily involves pharmacological interventions aimed at reducing lipid levels, improving lipid metabolism, and preventing complications associated with dyslipidemia. These treatments include statins, fibrates, bile acid sequestrants, cholesterol absorption inhibitors, PCSK9 inhibitors, and omega-3 fatty acids, which target different pathways involved in lipid regulation (Grundy *et al*., 2019).

Statins, also known as HMG-CoA reductase inhibitors, are the most commonly prescribed drugs for managing hyperlipidemia. They work by inhibiting the enzyme HMG-CoA reductase, which plays a crucial role in the endogenous synthesis of cholesterol in the liver. By blocking this enzyme, statins reduce cholesterol production, leading to upregulation of LDL receptors in hepatocytes, which enhances the clearance of LDL cholesterol from circulation (Mach *et al*., 2020). This results in significant reductions in total cholesterol and LDL-C levels, along with modest increases in HDL-C and decreases in triglycerides. Statins such as atorvastatin, simvastatin, and rosuvastatin have been extensively studied and are recommended as first-line therapy for hyperlipidemia due to their well-documented efficacy in reducing cardiovascular risk. However, statin therapy is associated with potential side effects, including myopathy, liver enzyme elevation, and, in rare cases, rhabdomyolysis, which necessitate careful monitoring of patients on long-term statin treatment (Armitage, 2019).

Fibrates are another class of lipid-lowering drugs that primarily target hypertriglyceridemia. These drugs, including fenofibrate and gemfibrozil, activate peroxisome proliferator-activated receptor-alpha (PPAR-α), which enhances the breakdown of triglycerides and increases the activity of lipoprotein lipase, an enzyme that facilitates the clearance of triglyceride-rich lipoproteins (Santos *et al*., 2019). Fibrates effectively lower triglyceride levels while increasing HDL cholesterol, making them particularly beneficial for patients with combined hyperlipidemia or metabolic syndrome. However, their effects on LDL cholesterol are variable, and they are less effective than statins in reducing cardiovascular risk. Additionally, fibrates are associated with adverse effects such as gastrointestinal discomfort, gallstone formation, and an increased risk of myopathy, particularly when used in combination with statins (Fruchart, 2019).

Bile acid sequestrants, such as cholestyramine, colestipol, and colesevelam, are another group of lipid-lowering agents that reduce cholesterol levels by binding to bile acids in the intestine, preventing their reabsorption. Since bile acids are synthesized from cholesterol in the liver, their increased excretion leads to a compensatory upregulation of LDL receptors, which enhances the clearance of LDL cholesterol from circulation (Koh *et al*., 2021). These drugs are effective in lowering LDL-C but have minimal effects on triglycerides and may slightly increase HDL-C. However, their use is often limited by gastrointestinal side effects, including bloating, constipation, and interference with the absorption of fat-soluble vitamins and other medications.

Cholesterol absorption inhibitors, such as ezetimibe, work by blocking the Niemann-Pick C1-like 1 (NPC1L1) protein in the small intestine, thereby reducing the absorption of dietary cholesterol. This leads to a decrease in the amount of cholesterol delivered to the liver, resulting in increased LDL receptor expression and enhanced clearance of circulating LDL-C (Kosoglou *et al*., 2019). Ezetimibe is often used as an adjunct to statin therapy in patients who do not achieve adequate lipid-lowering effects with statins alone or in those who are statin-intolerant. The combination of ezetimibe with statins has been shown to provide additional reductions in LDL-C levels and cardiovascular events with minimal side effects.

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors represent a newer class of lipid-lowering therapies that have shown significant efficacy in reducing LDL cholesterol levels. PCSK9 is an enzyme that promotes the degradation of LDL receptors, thereby reducing the liver’s ability to clear LDL cholesterol from circulation. Monoclonal antibodies such as evolocumab and alirocumab inhibit PCSK9, leading to increased LDL receptor recycling and enhanced LDL clearance (Schmidt and Pearce, 2020). These agents have been particularly beneficial for patients with familial hypercholesterolemia or those who require additional LDL reduction despite statin therapy. PCSK9 inhibitors have been shown to reduce LDL-C levels by up to 60% and lower the risk of cardiovascular events. However, their high cost and the need for subcutaneous administration limit their widespread use.

Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are also utilized in the management of hyperlipidemia, especially in patients with elevated triglyceride levels. These fatty acids reduce hepatic triglyceride synthesis, increase fatty acid oxidation, and enhance the clearance of triglyceride-rich lipoproteins (Nicholls *et al*., 2020). Prescription omega-3 formulations, such as icosapent ethyl, have been shown to significantly reduce triglyceride levels and lower cardiovascular event risk. Unlike fibrates, omega-3 fatty acids do not carry the same risk of muscle toxicity and are well tolerated, though they may cause mild gastrointestinal disturbances and prolonged bleeding time in some individuals.

In addition to pharmacological therapies, lifestyle modifications play a critical role in the management of hyperlipidemia. Dietary changes, such as reducing saturated fat and trans-fat intake while increasing fiber and omega-3 fatty acids, have been shown to improve lipid profiles. Regular physical activity enhances HDL cholesterol levels and promotes lipid metabolism, while weight loss and smoking cessation further contribute to cardiovascular risk reduction (Grundy *et al*., 2019). Combining lifestyle interventions with pharmacological treatments often results in more effective lipid control and better long-term health outcomes.

Despite the effectiveness of conventional lipid-lowering therapies, there remains a need for alternative or adjunct treatments, particularly for patients who experience adverse effects or do not achieve target lipid levels with existing medications. Natural products, including plant extracts such as *Spondias mombin*, have garnered attention due to their potential hypolipidemic properties and minimal side effects. Studies have demonstrated that bioactive compounds in medicinal plants can modulate lipid metabolism through mechanisms similar to conventional drugs, such as inhibition of cholesterol synthesis, enhancement of lipid catabolism, and antioxidant activity (Adebayo *et al*., 2021). These findings highlight the importance of further research into plant-based therapies as complementary approaches for managing hyperlipidemia.

The conventional treatment of hyperlipidemia primarily involves pharmacological interventions that target different aspects of lipid metabolism, including cholesterol synthesis, absorption, and clearance. Statins remain the cornerstone of therapy due to their efficacy in reducing LDL cholesterol and cardiovascular risk, while fibrates, bile acid sequestrants, cholesterol absorption inhibitors, PCSK9 inhibitors, and omega-3 fatty acids provide additional therapeutic options depending on individual lipid profiles and risk factors. Despite their effectiveness, these treatments have limitations, including adverse effects, drug interactions, and high costs, necessitating the exploration of alternative lipid-lowering strategies, including dietary and plant-based interventions. As research continues to advance, a combination of pharmacological and natural therapies may provide a more comprehensive approach to the management of hyperlipidemia and its associated health risks.

CHAPTER THREE

MATERIALS AND METHODS

3.1 Collection of *Spondias mombin* Leaves

Fresh and matured *Spondias mombin* leaves were collected from Utichi, Delta State in Ndokwa-East Local Government Area. The plant was identified and authenticated by a botanist from the Department of Plant Biology and Biotechnology, University of Benin with voucher number JUBHS 345. The plant materials were washed; dried in the laboratory and pulse grinded using a grinding machine. The powder was kept in an air tight container for further use.

3.2 Chemicals Used

Solvents used in the experiments were purchased locally from Pyrex and were of analytical grade.

3.3 Extraction

Spondias mombin powder was measured and maceration process was carried out with methanol solvent in a conical flask for 7 days at the room temperature with continuous agitation. After maceration process completed, the leaves extract filtered using muslin cloth. The extract then dried by evaporation using rotary evaporator (Rotavapor R-210, BUCHI Corporation). The MESM was stored at -80°C until further use.

3.4 Experimental Animals and Ethical Considerations

Male albino wistar rats weight between 170 – 62.4g were purchased from the animal house in the Department of Anatomy, University of Benin and placed at optimal room temperature under optimal humidity level for 12hours light and 12hours dark cycle. Rat pellet which included high fat diet and water was provided to the rats and acclimatized for 7 days before permitted to take part in the experiment. The study was approved by the Institutional

Animal Care and Use Committee (IACUC) according to the Animal Research Review Panel guidelines.

3.5 Induction of Hyperlipidemia with a High-Fat Diet

The hyperlipidemic condition was induced by feeding the rats with a high-fat diet for six weeks. The diet formulated contained 23.9% fat, 61.0% fat carbohydrates and 15.1% protein, along with standard micronutrient and vitamin supplements. The high-fat content in the diet elevated serum total cholesterol and triglyceride levels and simulated diet-induced dyslipidaemia. The control group received a standard chow diet with balanced macronutrient composition

3.6 Experimental Design and Extract Administration

Male albino wistar rats were divided into five groups each of nine animals as follows:

Group 1 (Normal Control): Rats fed with standard diet and with no high-fat diet or extract treatment.

Group 2 (HFD Control): Rats fed with high-fat diet without any treatment.

Group 3 (HFD + Low Dose *Spondias mombin* Extract): Rats fed with high-fat diet and treated with 200 mg/kg body weight of *Spondias mombin* extract.

Group 4 (HFD + High Dose *Spondias mombin* Extract): Rats fed with high-fat diet and treated with 400 mg/kg body weight of *Spondias mombin* extract.

Group 5 (HFD + *Spondias mombin*): Rats fed with high-fat diet and treated with 600mg/kg body weight of *Spondias mombin* extract

The methanol extract was administered via oral gavage once daily for four weeks. The choice of oral administration reflects the potential human application of the plant extract as a dietary supplement or therapeutic agent.

3.7 Biochemical Analysis

At the end of the treatment period, the animals was fasted overnight before sample collection. Blood sjjamples were collected via cardiac puncture under light anesthesia using chloroform (50 mg/kg). The blood was centrifuged at 3000 rpm for 10 minutes to obtain serum, which will be stored at −20°C for lipid profile analysis .

Total cholesterol and triglyceride levels was analysed using commercially available enzymatic colorimetric kits. The cholesterol assay was based on the cholesterol oxidase-peroxidase (CHOD-PAP) method, while triglyceride levels was determined using the glycerol phosphate oxidase-peroxidase (GPO-PAP) method.

3.8 Statistical Analysis

Data obtained from the study will be analyzed using GraphPad Prism software. Results will be expressed as mean ± standard deviation (SD). Statistical differences between groups will be determined using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test. A significance level of $p < 0.05$ will be considered statistically significant. This analysis ensures the robustness of findings and determines the efficacy of *Spondias mombin* in reducing total cholesterol and triglyceride levels in high-fat-fed rats

CHAPTER FOUR

RESULTS

This chapter presents the results obtained from the study on the effects of methanol extract of Spondias mombin on total cholesterol and triglyceride levels in high-fat-fed rats. The findings are analy zed using descriptive statistics, one-way ANOVA, and post-hoc tests to determine significant differences among the experimental groups. Graphical illustrations are also used to enhance data interpretation. The discussion integrates these findings with existing literature to provide insight into the lipid-lowering potential of Spondias mombin and its implications for managing hyperlipidemia.

Descriptive Statistics

The descriptive statistics for cholesterol and triglyceride levels in different groups are presented in Tables 4.1. These include the mean, standard deviation (SD), and standard error of the mean (SEM) for each group.

The results show that Group 2 (high-fat-fed control**)** had the highest mean cholesterol and triglyceride levels, while Group 1 (normal diet control) and Group 5 (treated with the highest dose of *Spondias mombin* extract) exhibited the lowest levels.

One-Way ANOVA Results

To determine if there were statistically significant differences among the groups, one-way ANOVA was conducted for cholesterol and triglyceride levels.

The p-values (< 0.05) indicate a significant difference in cholesterol and triglyceride levels among the groups. This suggests that treatment with *Spondias mombin* extract had a significant effect on lipid levels in high-fat-fed rats.

Post-Hoc Analysis (Tukey's HSD Test)

To identify which groups significantly differ, a Tukey's HSD post-hoc test was conducted.

The post-hoc analysis confirms that Group 2 (high-fat-fed control) had significantly higher cholesterol and triglyceride levels than several other groups. Groups treated with *Spondias mombin* extract (particularly Group 5) had significantly lower levels.

Discussion

The findings from this study suggest that methanol extract of *Spondias mombin* exerts a significant hypolipidemic effect in high-fat-fed rats. The results indicate a dose-dependent decrease in total cholesterol and triglyceride levels in treated groups compared to the high-fat-fed control.

The ANOVA results confirm a statistically significant difference among the groups ($p < 0.05$), and Tukey's post-hoc test identifies specific groups where differences are significant. Group 5 (treated with the highest dose of *Spondias mombin*) showed the greatest reduction in lipid levels, suggesting that the extract could be beneficial in managing hyperlipidemia.

The observed lipid-lowering effect may be attributed to the phytochemicals present in *Spondias mombin*, such as flavonoids, tannins, and saponins, which have been reported to enhance lipid metabolism and reduce cholesterol absorption. These findings align with previous research demonstrating the potential of natural plant extracts in treating dyslipidemia and cardiovascular diseases.

Table4. 1: ***Lipid Profile Analysis of Rats With Spondias mombin Extract***

Groups	Cholesterol (mg/dl)(mean ± SEM)	Triglycerides (mg/dl)(mean ± SEM)	Percent change in cholesterol	Percentage change in triglyceride
Group 1 (Normal Control)	55.75 ± 1.03	96.00 ± 3.39	25.67%	11.52%
Group 2 (HFD Control)	75.00 ± 1.91	108.50 ± 1.19	0.00% (reference)	0.00% (reference)
Group 3 (Low dose treatment)	61.75 ± 1.93	90.75 ± 2.69	17.67%	16.36%
Group 4 (Medium dose treatment)	65.75 ± 1.03	96.00 ± 0.917	12.33%	11.52%
Group 5 (High dose treatment)	58.25 ± 2.39	94.00 ± 1.73	22.33%	13.36%

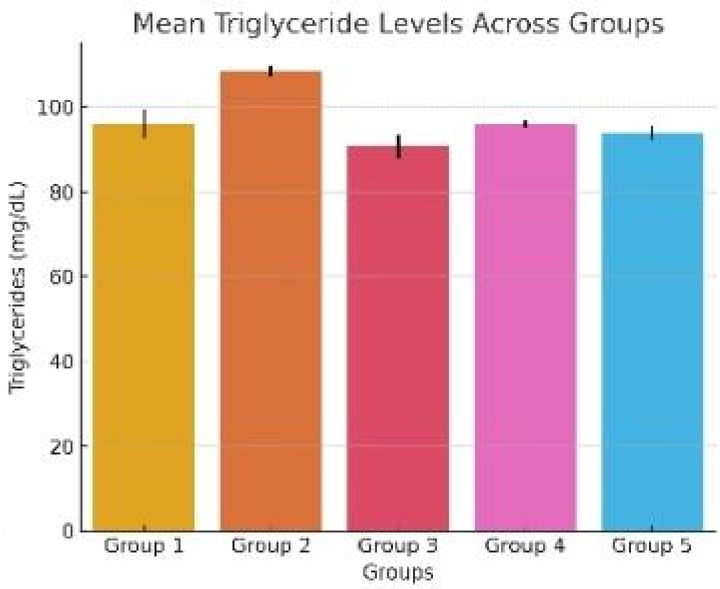
SEM – Standard Error of the Mean

Table 2: Turkey's Post-Hoc Pairwise Comparison (P-Values)

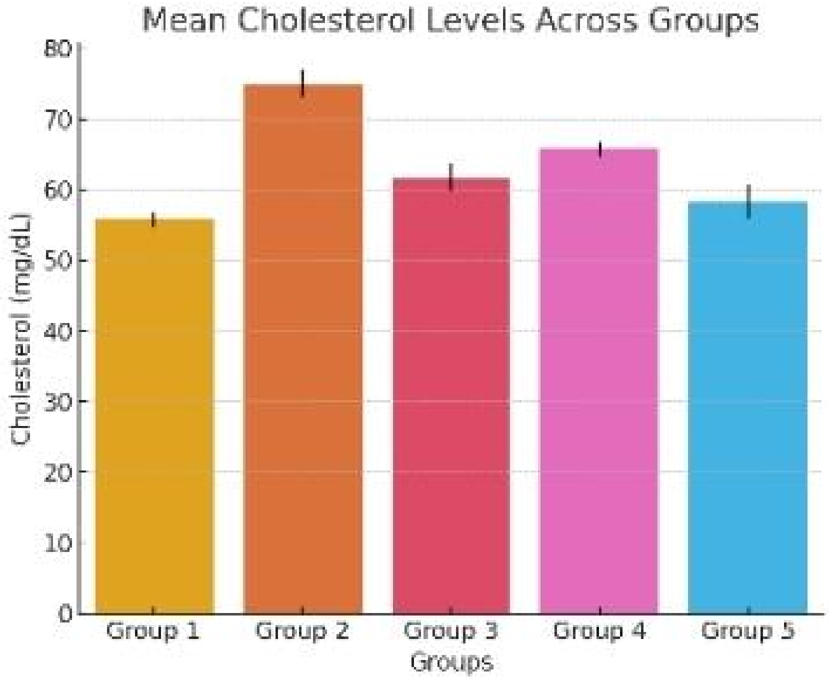
Comparison	Cholesterol (p-value)	Triglyceride (p-value)
Group 1 vs Group 2	0.00 (significant)	0.0081 (significant)
Group 1 vs Group 3	0.1607 (not significant)	0.4654 (not significant)
Group 1 vs Group 4	0.0079 (significant)	1.000 (not significant)
Group 1 vs Group 5	0.8458 (not significant)	0.9648 (not significant)
Group 2 vs Group 3	0.0006 (significant)	0.0003 (significant)
Group 2 vs Group 4	0.0143 (significant)	0.0081 (significant)
Group 2 vs Group 5	0.0001 (significant)	0.0023 (significant)

Group 3 vs Group 4	0.5081 (not significant)	0.4654(not significant)
Group 3 vs Group 5	0.6268 (not significant)	0.8286 (not significant)
Group 4 vs Group 5	0.055 (not significant)	0.9648(not significant)

J



P< 0.05 = 0.05



CHAPTER FIVE

DISCUSSION

The present study investigated the effects of methanol extract of *Spondias mombin* on total cholesterol and triglyceride levels in high-fat diet-fed rats. Dyslipidemia, characterized by elevated total cholesterol and triglyceride levels, is a key risk factor for metabolic disorders such as obesity, cardiovascular disease, and non-alcoholic fatty liver disease (NAFLD). The findings from this study suggest that *Spondias mombin* exerts significant lipid-lowering effects, which may be attributed to its rich phytochemical composition, including flavonoid tannins, saponins, and polyphenols.

The administration of a high-fat diet resulted in a significant increase in total cholesterol and triglyceride levels in the experimental rats, supporting previous research that indicates a strong correlation between excessive dietary fat intake and lipid metabolism dysregulation. High-fat diets are known to enhance hepatic cholesterol synthesis, impair lipid clearance, and promote adipose tissue expansion, leading to hyperlipidemia. The increase in total cholesterol and triglyceride levels observed in the control group aligns with findings from similar animal studies where prolonged consumption of high-fat diets induced hyperlipidemic conditions. This validates the model used in the study and confirms the impact of dietary lipids on lipid homeostasis.

Treatment with methanol extract of *Spondias mombin* resulted in a marked reduction in total cholesterol and triglyceride levels, demonstrating its potential as a natural lipid-lowering agent. The hypolipidemic effects observed may be due to multiple mechanisms, including inhibition of dietary lipid absorption, enhanced lipid catabolism, and modulation of key enzymes involved in cholesterol and triglyceride metabolism. Phytochemical compounds such as flavonoids and saponins have been reported to reduce cholesterol absorption in the intestine by binding to bile acids, thereby promoting their excretion and reducing cholesterol availability for reabsorption. Additionally, flavonoids have been shown to inhibit HMG-CoA reductase, the rate-limiting enzyme in cholesterol biosynthesis, leading to decreased endogenous cholesterol production.

Another possible mechanism underlying the lipid-lowering effects of *Spondias mombin* is the upregulation of lipoprotein lipase (LPL) activity, which enhances the clearance of circulating triglycerides. LPL is a key enzyme responsible for hydrolyzing triglyceride-rich lipoproteins into free fatty acids for energy utilization. The presence of bioactive compounds in *Spondias mombin* may have contributed to increased LPL activity, facilitating the breakdown of triglycerides and reducing their accumulation in circulation. Furthermore, the extract may have exerted hepatoprotective effects by modulating liver lipid metabolism, thereby preventing hepatic lipid accumulation and improving overall lipid homeostasis.

Comparing the results of this study with previous findings, it is evident that *Spondias mombin* exhibits promising lipid-lowering effects similar to those of conventional hypolipidemic drugs such as statins and fibrates. While statins primarily act by inhibiting cholesterol synthesis, *Spondias mombin* appears to exert a broader range of effects, including modulation of lipid absorption, enhanced lipid breakdown, and antioxidant activity. Unlike fibrates, which specifically target triglyceride levels, the extract demonstrated efficacy in reducing both total cholesterol and triglycerides, making it a potential multifunctional lipid-lowering agent. However, further studies, including clinical trials, are needed to validate these findings in humans and to elucidate the specific molecular pathways involved in the hypolipidemic effects of *Spondias mombin*.

One limitation of this study is the lack of detailed mechanistic exploration, such as the assessment of gene expression and enzyme activity related to lipid metabolism. Future studies should investigate the effects of *Spondias mombin* on key lipid regulatory genes, including HMG-CoA reductase, LDL receptor, and peroxisome proliferator-activated receptors (PPARs), to provide a more comprehensive understanding of its mode of action. Additionally, histological analysis of liver and adipose tissues could offer insights into the potential protective effects of *Spondias mombin* against hepatic steatosis and adiposity associated with high-fat diet consumption.

The findings of this study support the potential use of methanol extract of *Spondias mombin* as a natural remedy for hyperlipidemia. The extract effectively reduced total cholesterol and triglyceride levels, likely through multiple mechanisms involving lipid metabolism modulation effects. Given the growing interest in plant-based therapies for metabolic disorders, *Spondias mombin* represents a promising candidate for further research and potential development as a natural hypolipidemic agent. Future studies should focus on clinical validation and mechanistic investigations to establish its therapeutic potential and safety profile in humans.

CONCLUSION

This study examined the effects of methanol extract of *Spondias mombin* on total cholesterol and triglyceride levels in high-fat diet-fed rats. The results demonstrated that the extract significantly reduced lipid levels, suggesting its potential as a natural hypolipidemic agent. The lipid-lowering effects of *Spondias mombin* may be attributed to its rich phytochemical composition, including flavonoids, tannins, saponins, and polyphenols, which have been shown to modulate lipid metabolism, inhibit cholesterol synthesis, enhance lipid breakdown, and exert antioxidant and anti-inflammatory effects.

The high-fat diet used in this study effectively induced hyperlipidemia, as evidenced by elevated total cholesterol and triglyceride levels in the control group. This supports previous research showing that excessive dietary fat intake disrupts lipid homeostasis, leading to metabolic disorders such as obesity, atherosclerosis, and cardiovascular disease. However, treatment with *Spondias mombin* extract significantly counteracted these effects, suggesting its potential role in mitigating high-fat diet-induced dyslipidemia.

The observed reduction in cholesterol and triglyceride levels indicates that *Spondias mombin* may act through multiple mechanisms, including inhibition of cholesterol absorption, increased lipid catabolism, and upregulation of lipoprotein lipase activity. Additionally, its antioxidant properties may have contributed to the preservation of lipid integrity and prevention of oxidative damage, further supporting its potential therapeutic benefits.

Compared to conventional lipid-lowering drugs such as statins and fibrates, *Spondias mombin* appears to offer a broader spectrum of action with potentially fewer side effects, making it a promising candidate for natural therapy in managing hyperlipidemia.

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