MOLECULAR DOCKING OF *Solanum aethiopicum* FRUITS EXTRACT AGAINST HUMAN HMG-CoA REDUCTASE AND PANCREATIC TAG LIPASE FOR OBESITY MANAGEMENT

BY

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CERTIFICATION

This is to certify that this research titled "**Molecular Docking of *Solanum aethiopicum* Fruits Extract against Human HMG CoA reductase and Pancreatic TAG lipase for obesity management".** was carried out by **AJAYI-OBE, Kehinde Catherine,** with matriculation number **21/15BSB002**, and submitted to the Department of Biological Sciences (Biochemistry), Faculty of Computing and Applied Sciences, in partial fulfillment of the requirements for the award of Bachelor of Science (B.Sc.) Degree in Biochemistry.

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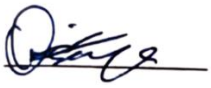

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DEDICATION

This project write-up is dedicated to my wonderful parents, Mr. and Mrs. Ajayi-obe.

ACKNOWLEDGEMENT

My gratitude goes to Almighty God, who has been my Helper and Sustainer in all areas. Glory be to His Holy name.

My appreciation also goes to my dedicated and patient supervisor, Dr. S.T. Farohunbi, who is also the Head of the Department of Biochemistry, for his excellent supervision and relevant efforts towards the achievement of my project. Thank you so much, sir. Special appreciation to all the hardworking and sacrificing lecturers in the department, Mrs. Faith Olaitan, Mr. Peter Ayodele, Mr. Lukman Bello, Mr. Oladapo Bamidele, Mrs. Oluwadamilola Ezekiel, and Mrs Amaka Lawrence, who had such a profound impact on me, inspiring me to become a better person, I also appreciate Mrs. Roseline Ajiboye and Ms. Princess for their support in the laboratory. I greatly appreciate all your contributions.

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Abstract

Obesity remains one of the major global health challenges, often managed with drugs such as Orlistat and Statins. While effective, these synthetic agents are limited by adverse effects that compromise long−term compliance. This study explored the inhibitory potential of *Solanum aethiopicum* fruit-selected phytochemicals against two key enzymes in lipid metabolism, human 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMG-CoA reductase) and pancreatic TAG lipase. Eighteen (18) phytochemical constituents were profiled from the fruit extract, using high-performance liquid chromatography (HPLC), among which eight (8) structurally based identified compounds were subjected to molecular docking with AutoDock Vina. Standard inhibitors, rosuvastatin for HMG-CoA, and β-lactone for pancreatic TAG lipase, served as references. Binding interactions were analyzed to identify key stabilizing residues. The results showed that the binding potential of chlorogenic acid (−7.1 kcal/mol), followed by delphinidin (−7.0 kcal/mol), quercetin (−7.0 kcal/mol), kaempferol (−7.0 kcal/mol), and myricetin (−7.0 kcal/mol), showed stronger binding affinities toward human HMG-CoA reductase compared with rosuvastatin (−6.5 kcal/mol). Delphinidin (−7.2 kcal/mol), quercetin (−7.2 kcal/mol), and kaempferol (−7.2 kcal/mol) demonstrated higher affinities for pancreatic TAG lipase relative to the standard inhibitor β-lactone (−6.4 kcal/mol). Molecular interaction profiling revealed hydrogen bonding and hydrophobic stabilization with catalytic residues, including TYR479, ASN529, and ARG568 in HMG-CoA reductase, and GLN146, THR54, and SER73 in TAG lipase. These findings suggest quercetin and delphinidin as promising dual inhibitors with the potential to modulate lipid absorption and cholesterol biosynthesis simultaneously. Their strong affinities support their possible development into functional food-derived agents for obesity management. Further experimental validation through in vitro and in vivo studies is warranted to confirm their therapeutic potential.

Keywords: *Solanum aethiopicum*; obesity; human HMG-CoA reductase; pancreatic TAG lipase; binding affinity; molecular docking.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background of the Study

Lipid metabolism disorders and obesity have become major global health challenges, significantly contributing to the rise in chronic illnesses such as cardiovascular disease, type 2 diabetes, and metabolic syndrome (Han & Lean, 2016). Obesity is a major global health burden, affecting over 1 billion people worldwide as of 2025, with prevalence steadily increasing in both developed and developing nations (World Health Organization, 2025). It is characterized by abnormal or excessive fat accumulation (Bray *et al*., 2017). It is strongly associated with comorbidities such as cardiovascular diseases, type 2 diabetes, insulin resistance, hypertension, and non-alcoholic fatty liver disease (Ng *et al.*, 2014; WHO, 2024). According to the World Health Organization (2025), cardiovascular diseases remain the leading cause of death globally, accounting for an estimated 17.9 million deaths annually. These complications are largely driven by disruptions in lipid metabolism, particularly elevated triglycerides, low-density lipoprotein (LDL), and imbalances in cholesterol and fatty acid levels (Ademosun *et al.,* 2024).

Current pharmacological treatments for obesity, such as orlistat, target lipid metabolism by inhibiting pancreatic lipase**,** thereby reducing fat absorption. Orlistat exhibits negligible systemic absorption due to its high molecular weight (~495.7 g/mol) and bulky, lipophilic structure, violating both Lipinski's and Veber's criteria (Liu et al., 2024). This results in limited systemic exposure and minimal toxicity, with its ADMET profile largely defined by local action and a low risk of drug-drug interactions (Zhou et al., 2023). Rosuvastatin, a hydrophilic statin that lowers cholesterol by inhibiting HMG-CoA reductase, better aligns with drug-likeness parameters, exhibiting moderate bioavailability (~20%), low lipophilicity, and high polarity, typical of BCS Class 3 drugs. Although poorly water-soluble, its bioavailability is enhanced through innovative formulations, such as fast-dissolving films. Genetic variations affecting transporters influence their absorption and metabolism, shaping their ADMET profile (Ashraf et al., 2023).

However, despite their efficacy, these synthetic agents are often discontinued due to unpleasant gastrointestinal side effects, including oily stools, flatulence, and diarrhea, which limit patient compliance and long-term use (Sims *et al.*, 2020). This has intensified the search for safer, affordable, and more effective therapeutic alternatives (Najmi *et al.*, 2021). Natural products, particularly medicinal plants, are increasingly recognized for their multi-targeted effects, including antioxidant, anti-inflammatory, and lipid-lowering properties (Panda *et* al., 2023; El-Saadony *et al.,* 2025).

The 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase is the rate-limiting step in cholesterol biosynthesis. Inhibition of human HMG-CoA reductase lowers endogenous cholesterol production and reduces the risk of cardiovascular complications (Zhao *et al*., 2025). Another key enzyme, pancreatic lipase, is a critical therapeutic target due to its role in hydrolyzing dietary triglycerides into absorbable units. Its inhibition reduces intestinal fat absorption and supports weight management (Birari & Bhutani, 2007; Shaik *et al.*, 2023). Recent reviews highlight a renewed interest in plant-derived inhibitors of these enzymes as safer alternatives to synthetic drugs, although mechanistic evidence remains limited and requires further investigation (Subramaniyan, 2025).

1.2 Statement of the Research Problem

The global burden of obesity and its associated metabolic disorders, such as cardiovascular diseases, insulin resistance, and non-alcoholic fatty liver disease, has reached critical levels. According to WHO (2024), more than 890 million adults are currently obese, and projections suggest this number will continue to rise sharply without effective intervention strategies. These disorders are largely driven by disrupted lipid metabolism, particularly elevated levels of LDL-cholesterol and triglycerides (Kearns *et al.*, 2016).

Current treatment options, such as orlistat, are effective but are often discontinued due to their unpleasant side effects (Sims *et al.,* 2020). Furthermore, limited access to conventional drugs in low-resource settings highlights the need for alternative, affordable interventions.

Despite the widespread use of medicinal plants in African traditional medicine, very few have been rigorously studied for their mechanisms of action in lipid metabolism (El-Saadony *et al.*, 2025).

Solanum aethiopicum, though rich in bioactive compounds, remains poorly understood in terms of its potential as a pancreatic lipase inhibitor and lipid-lowering agent (Nwanna *et al*., 2019). Addressing this gap may lead to the development of plant-based anti-obesity therapies with fewer side effects and greater cultural acceptance.

1.3 Overall Objective of the study

The overall objective of the study was to conduct molecular docking of *Solanum aethiopicum* fruit extract against human HMG-CoA reductase and pancreatic TAG lipase for the management of obesity.

1.4 Specific Objectives of the Study

The specific objectives were;

i. to determine the proximate composition of *Solanum aethiopicum* fruits;
ii. to identify the phytochemical compounds of *Solanum aethiopicum* fruits using HPLC;
iii. to evaluate the binding interactions of identified compounds with human HMG-CoA reductase through molecular docking and;
iv. to evaluate the binding interactions of identified compounds with pancreatic lipase through molecular docking.

1.5 Justification of the Study

Solanum aethiopicum is an edible plant traditionally consumed in Africa, but it is often underutilized for its medicinal potential. Obesity and lipid disorders remain major global health concerns, and there is a need for safe, affordable, and locally available alternatives for their management. Analyzing the nutritional composition, phytochemical profile, and molecular interactions of *S. aethiopicum* provides insights into its possible role in obesity control.

This approach supports the development of functional foods and nutraceuticals, promotes the use of indigenous resources, and contributes to sustainable healthcare strategies.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 *Solanum species* and their distribution

The genus *Solanum* belongs to the family Solanaceae. It is regarded as one of the largest and most diverse genera of flowering plants, comprising over 1,400 species distributed across tropical and subtropical regions worldwide (Knapp *et al*., 2019). Members of this genus include important food crops, medicinal plants, and ornamentals, such as potato (*Solanum tuberosum),* tomato (*Solanum lycopersicum*), eggplant (*Solanum melongena*), and several indigenous African vegetables. Their global distribution spans Africa, Asia, South America, and parts of Europe, reflecting their ecological adaptability and cultural significance.

In Africa, Solanum species are widely cultivated and consumed as leafy vegetables and fruits. They play a crucial role in household nutrition, particularly among low-income populations, where they serve as affordable sources of vitamins, minerals, and dietary fiber (Chinedu *et al.,* 2011). In addition, many species are valued in ethnomedicine for the management of ailments such as hypertension, infections, and metabolic disorders.

Among these, *Solanum aethiopicum* (commonly known as the African eggplant or garden egg) is one of the most extensively cultivated indigenous vegetables in West and Central Africa. It is grown mainly in Nigeria, Ghana, Cameroon, and Uganda, where it is consumed both as a fresh fruit and in cooked preparations (Adeniji *et al*., 2021). Closely related species such as *Solanum torvum* and *Solanum lycopersicum* are also important in African diets and traditional medicine. The African eggplant is particularly recognized for its high phenolic and flavonoid content, which contributes to its antioxidant, anti-inflammatory, and potential lipid-lowering properties (Agoreyo *et al.,* 2012).

Overall, the distribution and ethnobotanical use of *Solanum* species highlight their significance not only as staple vegetables but also as potential sources of bioactive compounds with

pharmacological relevance. This provides a strong basis for investigating their roles in the management of obesity and lipid metabolism disorders.

The ecological adaptability and rich ethnobotanical uses of *Solanum aethiopicum*, underscored by recent evaluations of its anti-inflammatory, antioxidant (Lela *et al., 2023),* and anti-obesity properties (Choi et al., 2024; Iheagwam et al., 2024), justify its selection as a central focus in exploring enzyme-targeted anti-obesity research.

2.2 Nutritional and Phytochemical Composition of *Solanum aethiopicum*

Solanum aethiopicum (African eggplant) is widely recognized for its dual role as both a dietary vegetable and a medicinal plant. Its nutritional profile highlights its importance as a functional food, while its phytochemical richness supports its use in ethnomedicine for managing chronic diseases, including obesity and cardiovascular disorders.

Nutritionally, S. aethiopicum fruits are rich in carbohydrates, dietary fiber, and moderate amounts of protein and fat. They also provide essential micronutrients such as calcium, potassium, iron, phosphorus, and magnesium, alongside vitamins including ascorbic acid (vitamin C), vitamin A precursors (carotenoids), and B-complex vitamins (Adeniji *et al.*, 2021). The high fiber content of the fruit contributes to delayed gastric emptying, satiety, and improved glycemic control, making it particularly relevant in weight management strategies.

Phytochemically, S. aethiopicum contains a wide range of bioactive secondary metabolites, including flavonoids, alkaloids, phenolic acids, tannins, saponins, and glycoalkaloids (Agoreyo *et al.,* 2012). These compounds have been linked to diverse biological activities, including antioxidant, anti-inflammatory, antihyperlipidemic, and antimicrobial effects (Femi *et al.*, 2023). Particularly relevant flavonoids, such as quercetin, kaempferol, and rhamnetin, have been reported to inhibit pancreatic lipase and modulate lipid metabolism (Yam*,* 2021; Zheng *et al.*, 2023).

Furthermore, the glycoalkaloids solasodine and solasonine, commonly found in *Solanum* species, are noted for their cholesterol-lowering and cytoprotective properties (Chinedu *et al*., 2011). The phenolic constituents of S. aethiopicum also act as antioxidants by scavenging free radicals and reducing oxidative stress, which is often elevated in obesity and metabolic syndrome.

Taken together, the nutritional and phytochemical composition of S. aethiopicum underscores its potential not only as a food crop but also as a source of pharmacologically active compounds.

These properties justify its investigation as a natural therapeutic candidate for the management of obesity through mechanisms involving human HMG-CoA reductase and pancreatic TAG lipase inhibition.

Given its high fiber, micronutrient, and phenolic content, with antioxidant and hypolipidemic activity confirmed in animal models, characterizing the phytochemical profile of S. aethiopicum aligns directly with identifying compounds capable of inhibiting obesity-related enzymes, such as human HMG-CoA reductase and pancreatic TAG lipase (Salatou *et al*., 2025; Ponticelli *et al*., 2024).

2.3 Overview of Obesity and Lipid Metabolism Disorders

Obesity is a chronic metabolic disorder characterized by excessive accumulation of adipose tissue, predisposing individuals to several non-communicable diseases such as type 2 diabetes mellitus, cardiovascular diseases, and hypertension (Bray *et al.*, 2021). It results primarily from an imbalance between energy intake and expenditure, influenced by poor dietary habits, sedentary lifestyles, and genetic predispositions.

The pathophysiology of obesity is closely linked to lipid metabolism disorders, including hypertriglyceridemia, elevated low-density lipoproteins (LDL), and reduced high-density lipoproteins (HDL) (Kaur & Muthuraman, 2020). Dysregulation of lipid metabolism promotes fat accumulation, insulin resistance, and cardiovascular risk. Consequently, targeting lipid-digesting and cholesterol-synthesizing enzymes such as 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase and pancreatic TAG lipase has become a promising therapeutic approach in managing obesity (Patel *et al.*, 2012). The growing prevalence of obesity and its tight linkage with lipid metabolism disorders justify the urgent exploration of safe, plant-based alternatives for prevention and management (World Health Organization, 2024).

2.4 Human HMG-CoA Reductase: Physiological Role and Therapeutic Target

Human HMG-CoA reductase is the rate-limiting enzyme in the mevalonate pathway, catalyzing the conversion of HMG-CoA to mevalonate, a crucial precursor for cholesterol and other isoprenoids (Zhao *et al.*, 2025). Cholesterol is essential for maintaining cell membrane structure, synthesizing bile acids, and producing steroid hormones. However, excessive cholesterol biosynthesis contributes to hypercholesterolemia and atherosclerosis, both of which are strongly associated with obesity and cardiovascular disease (Goldstein & Brown, 2015).

Clinically, statins (e.g., atorvastatin, simvastatin, rosuvastatin) are widely used as human HMG-CoA reductase inhibitors. They competitively block the enzyme's active site, reducing hepatic cholesterol production and upregulating LDL receptors to enhance clearance of circulating LDL (Bellosta *et al.*, 2020). Despite their effectiveness, long-term statin use may cause myopathy, liver enzyme elevation, and metabolic disturbances, motivating research into natural alternatives.

Plant-derived phytochemicals such as flavonoids, phenolic acids, and saponins have demonstrated inhibitory activity against human HMG-CoA reductase. For example, quercetin and chlorogenic acid downregulate cholesterol biosynthesis by binding to the enzyme's catalytic domain (Kim *et al*., 2022). Thus, natural compounds may provide safer and multifunctional lipid-lowering effects compared to statins.

The therapeutic significance of human HMG-CoA reductase and the need for natural modulators justify its evaluation alongside pancreatic lipase in this research (Patel *et al.*, 2012; Salatou *et al*., 2025).

2.4.1 Mechanism of Action of Human HMG-CoA Reductase

Human HMG-CoA reductase catalyzes the conversion of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) to mevalonate through a two-step reduction process using NADPH. In the first step, NADPH donates a hydride to reduce the thioester bond of HMG-CoA, generating a mevaldyl-CoA intermediate. This intermediate undergoes rearrangement to a thiohemiacetal. In the second step, another NADPH molecule donates a hydride to reduce the thiohemiacetal to mevalonate, while

coenzyme A is released. The resulting mevalonate enters the cholesterol synthesis pathway, contributing to sterol production. (Istvan & Deisenhofer, 2001).

2.5 Pancreatic Lipase: Physiological Role and Therapeutic Target

Pancreatic lipase is a key enzyme secreted by the pancreas that hydrolyzes dietary triglycerides into monoglycerides and free fatty acids, which are subsequently absorbed in the small intestine. This enzymatic activity is central to lipid digestion and energy provision (Birari & Bhutani, 2007). Excessive pancreatic lipase activity promotes increased dietary fat absorption, contributing to fat accumulation and weight gain. Therefore, inhibition of pancreatic lipase reduces intestinal fat absorption, lowers caloric intake, and facilitates weight management (Qu *et al.*, 2020).

Currently, synthetic inhibitors such as orlistat are clinically used to block pancreatic lipase. Orlistat acts by covalently binding to the catalytic serine (Ser 152) of the enzyme, thereby irreversibly inactivating it. However, its use is limited by adverse gastrointestinal effects, including steatorrhea, flatulence, and abdominal discomfort (Heck *et al*., 2000). These limitations have intensified interest in plant-derived lipase inhibitors as safer alternatives (TNK, 2021).

Targeting pancreatic lipase through natural inhibitors represents a rational therapeutic approach for obesity, justifying its inclusion as a major focus of this study (Birari & Bhutani, 2007; Femi *et al*., 2025).

2.5.1 Mechanism of Action of Pancreatic Lipase

Pancreatic lipase catalyzes the breakdown of triglycerides via a catalytic triad composed of Ser152, Asp176, and His263. His263 abstracts a proton from Ser152, thereby activating it to serve as a nucleophile that attacks the carbonyl carbon of the triglyceride. This creates a transient tetrahedral intermediate, which collapses to form an acyl-enzyme complex and release the first fatty acid (Qu *et al*., 2020). A water molecule, activated by His263, then attacks the acyl-enzyme complex, resulting in a second ester bond cleavage that liberates the second fatty acid and leaves behind a monoglyceride. Finally, these products are released from the enzyme into the small intestine, where they are absorbed. (Birari & Bhutani, 2007).

Plate 1: Image of *Solanum aethiopicum*

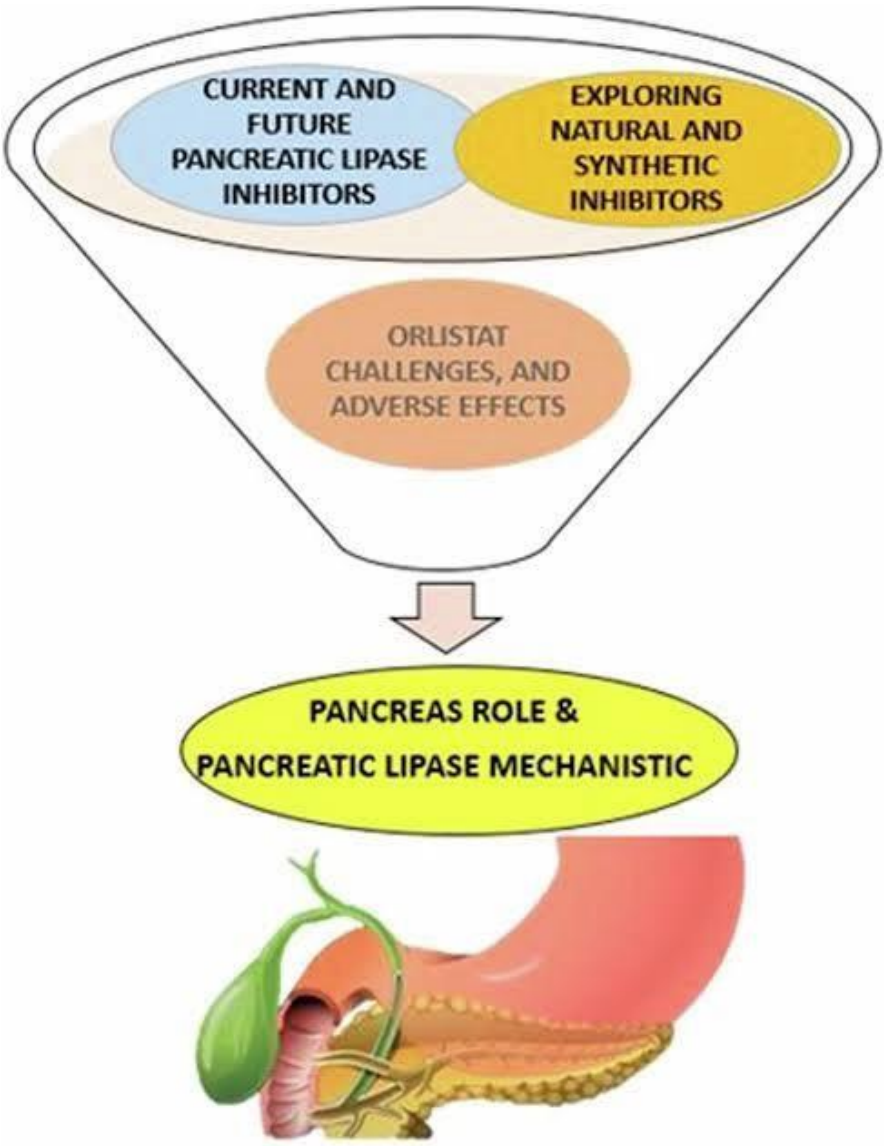

Figure 2: Role of pancreatic lipase inhibition in obesity treatment. Source:

Subramaniyan & Umul (2025).

Table 1: Mechanistic and Therapeutic Comparison Between Orlistat and Plant-derived Phenolic Lipase Inhibitors

Feature	Orlistat	Plant-derived phenolic inhibitors
Mechanism of Action	Irreversible inhibition of pancreatic lipase	Reversible competitive/noncompetitive
Binding Interaction	Covalent binding to serine residues of the lipase active site	Hydrogen bonding, van der Waal
Side Effect	Gastrointestinal discomfort, oily stools	Minimal, often antioxidant benefit
Additional Action	Primarily lipase inhibition	Antioxidant, anti-inflammatory

Source: (Nwanna *et al.,* 2019; El-Seedi *et al.,* 2022)

2.6 Phenolic Compounds and Flavonoids in Human HMG-CoA Reductase and Pancreatic TAG Lipase Inhibition

Phenolic compounds are among the most studied phytochemicals for obesity management. Flavonoids such as quercetin, kaempferol, rhamnetin, and delphinidin inhibit both pancreatic TAG lipase and human HMG-CoA reductase (Yam, 2021).

1. Quercetin exhibits strong anti-lipase activity (IC_{50} 20–30 μM) and also down-regulates cholesterol biosynthesis by binding to HMG-CoA reductase (Kumar *et al.*, 2017).
2. Delphinidin, an anthocyanin, not only inhibits lipase but also prevents adipocyte differentiation and lipid accumulation (Guan *et al.,* 2021).
3. Kaempferol and Rhamnetin, flavonols present in *Solanum* species, demonstrate moderate lipase and reductase inhibition with synergistic antioxidant effects (Femi *et al.,* 2023).

These compounds act through non-covalent interactions such as hydrogen bonding, π-π stacking, and hydrophobic interactions with catalytic residues. In pancreatic TAG lipase, they bind near the catalytic triad, comprising Ser152, Asp176, and His263, while in human HMG-CoA reductase, they block the binding site of human HMG-CoA, thereby reducing mevalonate synthesis (Wang *et al.,* 2025). Highlighting the inhibitory mechanisms of flavonoids and phenolics justifies their exploration in this study, since *Solanum* species (including *Solanum aethiopicum*) are rich in these compounds. Understanding their dual inhibition of pancreatic TAG lipase and human HMG-CoA reductase strengthens the rationale for testing *Solanum species* extract as a potential multi-target anti-obesity agent.

2.7 Molecular Docking and In-Silico Approaches

Molecular docking serves as a vital preclinical tool for understanding interactions between phytochemicals and target enzymes. Compounds such as quercetin and chlorogenic acid have demonstrated favorable binding energies and interaction profiles with pancreatic lipase in silico.

For example, Adelusi *et al.* (2022) reported strong hydrogen bonding and hydrophobic interactions between several plant-derived phenolics and the active site residues of pancreatic lipase, validating

their potential as natural inhibitors. Reviewing molecular docking studies is essential for this research because it provides mechanistic insight into how Solanum-derived phytochemicals may interact with human HMG-CoA reductase and pancreatic TAG lipase. It also supports the integration of computational and experimental approaches, ensuring that the study is grounded in both theoretical predictions and practical validation.

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Plant Material

Fresh *Solanum aethiopicum* fruits were harvested within University of Ilorin premises, Ilorin, Kwara state, Nigeria. The samples were authenticated at the Herbarium of the Department of Plant Biology, Faculty of Life Sciences, University of Ilorin, Kwara State, Nigeria, for proper identification (UILH|004|1250|2025) and authentication.

3.1.2 Chemicals and Reagents

Analytical grade solvents and reagents were used for the analyses. These included hydroethanol, methanol, and acetonitrile. Equipment used included a rotary evaporator, Oven, vortex mixer, grinder, analytical balance, Shimadzu Nexera MX HPLC system, AutoDock vina, Discovery Studio Visualizer, CASTp server, UV detector, and Diode Array Detector.

3.2 Methods

3.2.1 Proximate Analysis of *Solanum aethiopicum*

The proximate composition of *Solanum aethiopicum* fruits was determined using standard Association of Official Analytical Chemists (AOAC, 2023) methods. The parameters analyzed included moisture content, ash content, crude protein, crude lipid, crude fibre, and carbohydrate content. All analyses were performed in triplicate, and the results were expressed as mean ± standard deviation (SD).

3.2.2 Preparation of the Extract

Fruits of *Solanum aethiopicum* were collected, dried in an oven at 65 °C, and ground into a fine powder using a mechanical grinder. Extraction was performed using a hydroethanolic solvent system (70% ethanol:30% distilled water) via cold maceration for 48 hours with intermittent

shaking to enhance extraction efficiency. The extract was filtered through Whatman No. 1 filter paper and concentrated under reduced pressure using a rotary evaporator at 40°C. The crude extract was stored at 4°C for further analysis.

3.3 High-Performance Liquid Chromatography (HPLC) Profiling

High-performance Liquid Chromatography (HPLC) is a method used to separate mixtures of complex samples. HPLC is an active process in which materials are pumped at high pressure through a separation column, which contains a stationary phase, usually chemically functional beads that separate the compound mixtures. Samples are introduced through the injector and carried via the mobile phase across the stationary phase to effect the separation.

3.3.1 Extraction of Phytochemicals for HPLC Analysis

A total of 10 g of the dried powdered *Solanum aethiopicum* fruit was weighed into an amber extraction bottle. Two solvent systems, methanol and acetonitrile, were used independently to maximize the extraction of phytochemicals. To each 10 g sample, 20 mL of solvent (acetonitrile or methanol) was added. The mixture was rigorously shaken for 30 minutes using a vortex mixer. After shaking, the mixture was allowed to settle, and the organic layer (upper phase) was separated and collected into a 25 mL standard flask. The extract was made up to the mark with the same solvent and filtered using Whatman No. 1 filter paper. The filtrate was stored in an amber vial and used for High-Performance Liquid Chromatography (HPLC) analysis.

Procedure

The HPLC analysis was performed using a Shimadzu Nexera MX system. The separation was carried out on a µBondapak C18 column with a length of 100 mm and an internal diameter of 4.6 mm, packed with particles of 7 µm in size. The mobile phase consisted of a methanol and water mixture, and the flow rate was set at 0.08 mL/min (N)**,** 5 mL/min (A), and 1 mL/min as the general flow condition. A sample injection volume of 5 µL was used for each run. Detection was achieved using a UV detector set at 254 nm, complemented by a Diode Array Detector (DAD) for enhanced spectral analysis. The system operated under a pump pressure of 15 MPa to maintain consistent flow and separation efficiency.

3.3.2 Standard Preparation and Calibration

Standard solutions of known phytochemicals such as quercetin, caffeic acid, kaempferol, pelargonidin, myricetin, delphinidin, rhamnetin, and chlorogenic acid were first injected into the HPLC. The chromatogram of each standard was used to identify and establish peak retention times and areas. These standards were used to set up the detection window for subsequent analysis of the sample extract.

3.3.3 Sample Analysis and Quantification

A standard solution of the analyte was first injected into the HPLC system to generate a reference chromatogram**.** The resulting peak's retention time and area were used to set the detection window and confirm analyte identity. Then an aliquot of the extracted test sample was injected under the same chromatographic conditions to obtain its chromatogram. The peak area of the sample was compared to that of the standard, and using the known concentration of the standard, the concentration of the analyte in the sample was calculated using the following formula:

Concentration of Sample (ppm) = (Peak Area of Sample X Standard Concentration) / Peak Area of Standard

This method ensured accurate determination of each phytochemical concentration in parts per million (ppm). The data obtained were presented as retention time, peak area, height, and calculated concentrations. Peaks corresponding to known bioactive compounds were highlighted and their pharmacological relevance discussed in Chapter Four.

3.4. Retrieval and Preparation of Ligand Structures

3.4.1 Ligand preparation

The three-dimensional (3D) structures of the identified phytochemicals were retrieved from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) in Structure Data File (SDF) format. The structures were converted to Protein Data Bank (PDB) format using Open Babel software. Energy minimization was performed using the MMFF94 force field to optimize the molecular

conformations. The minimized structures were then converted to PDBQT format using AutoDock Tools, preparing them for molecular docking studies. The crystal structure of the target proteins (PDB ID: 1HWJ and 2PPL) was downloaded from the Protein Data Bank (PDB). Water molecules, ligands, and other heteroatoms were removed using Discovery Studio Visualizer. The active binding site of the target protein was either determined based on co-crystallized ligand coordinates (1HWJ) or predicted using the CASTp server (2PPL). The grid box dimensions were defined to include the entire active site.

3.4.2 Preparation of Target Proteins for Docking

The crystal structures of the target proteins, 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase, PDB ID: 1HWJ) and pancreatic triacylglycerol lipase (TAG lipase, PDB ID: 2PPL) were obtained from the Protein Data Bank (https://www.rcsb.org/) before docking; all water molecules, co-crystallized ligands, and heteroatoms were removed using Discovery Studio Visualizer to prevent interference with ligand binding. Polar hydrogens were added, and Gasteiger charges were assigned using AutoDock Tools.

For human HMG-CoA reductase (1HWJ), the active binding site was defined based on the coordinates of the co-crystallized ligand. For pancreatic TAG lipase (2PPL), the active binding site was predicted using the Computed Atlas of Surface Topography of Proteins (CASTp) server, which identifies potential binding pockets and cavities within protein structures.

3.4.3 Molecular Docking

Docking was performed using AutoDock Vina under default parameters. Each ligand was docked in triplicate into the active site of the target protein. Binding affinities (kcal/mol) were recorded, and protein ligand interactions, including hydrogen bonds, hydrophobic contacts, and π–π stacking, were analyzed using Discovery Studio Visualizer, with special attention to the catalytic residue.

3.5 Inclusion of Standard Drugs for Comparative Analysis

To contextualize the binding affinities and interactions of the phytochemicals, two standard drugs were included in the docking studies:

- **Beta-lactone**, a known pancreatic TAG lipase inhibitor, served as a reference compound for evaluating the inhibitory potential of the phytochemicals against TAG lipase.
- **Rosuvastatin**, a well-established human HMG-CoA reductase inhibitor (statin), was used as a benchmark for assessing the binding efficacy of the phytochemicals toward human HMG-CoA reductase.

3.6 Statistical Analysis

All experimental data were expressed as mean ± SD of triplicate determinations. Statistical comparisons were performed using one-way ANOVA followed by Tukey's multiple range test in SPSS (Version 20.0, Chicago, IL, USA). Significance was set at $p < 0.05$.

CHAPTER FOUR

4.0 RESULTS

4.1.1 Proximate Composition of *Solanum aethiopicum* Fruits

Table 2 presents the proximate composition of *Solanum aethiopicum* fruits, showing that the crude protein content was 8.53 ± 0.62%, a moderate level that could contribute meaningfully to dietary protein intake and serve as a supplementary protein source in vegetarian diets or in regions with limited animal protein availability. The lipid content, measured at 9.22 ± 0.07%, indicates the presence of essential fatty acids and fat-soluble vitamins important for membrane integrity and metabolic functions, with the relatively higher lipid concentration potentially enhancing the nutritive and therapeutic value of the fruits. The moisture content of 9.21 ± 0.31% is comparatively low, a characteristic that favors longer storage stability and shelf life by reducing microbial proliferation and enzymatic degradation. The total ash content, 7.60 ± 0.02%, reflects mineral richness and suggests the presence of essential elements such as calcium, magnesium, potassium, and trace minerals that are required for metabolic and enzymatic processes, thereby increasing its potential as a functional food ingredient. A notably high crude fibre content of 32.39 ± 0.94% highlights its possible role in digestive health by enhancing gut motility and supporting beneficial microbiota. Carbohydrates made up the highest fraction at 33.09 ± 0.17%, positioning *S. aethiopicum* as an important energy source that can provide substantial caloric contribution in traditional diets and may further support energy metabolism when considered for medicinal or therapeutic applications.

4.1.2 The HPLC Analysis of *Solanum aethiopicum* Fruits Extract

The HPLC analysis of *Solanum aethiopicum* fruit extract revealed the presence of eighteen bioactive phytochemicals, identified by comparing retention times and peak areas with known standards, as shown in Figure 2. These compounds include phenolic acids (such as chlorogenic acid and caffeic acid), flavonoids (like quercetin and kaempferol), and anthocyanins (like delphinidin), all known for their pharmacological importance.

4.1.3 Binding Affinity of Selected Phytochemicals Against Human HMG-COA Reductase and Pancreatic TAG Lipase

The binding affinities of selected phytochemicals from *Solanum aethiopicum* fruits toward two target enzymes, pancreatic triacylglycerol (TAG) lipase and human HMG-CoA reductase, were evaluated using molecular docking and are identified in Tables 5 and 6.

4.1.4 Molecular Docking of the Standard Drugs and the Selected Phytochemicals against Human HMG-COA Reductase and Pancreatic TAG Lipase

Molecular docking analysis of compounds with human HMG-CoA Reductase (1HWJ) and pancreatic TAG Lipase (2PPL) revealed favorable binding interactions within the enzyme active sites, as illustrated in Figure 4–13. In human HMG-CoA Reductase (1HWJ), the standard rosuvastatin (446157) displayed a snug fit, forming hydrogen bonds with TYR479 and ASN567, along with a halogen bond with GLU719 and hydrophobic contacts with residues such as ALA564 and VAL720, suggesting high affinity. The surface representations demonstrated snug accommodation of the ligands into the binding cavities, while 3D interaction views highlighted stabilizing hydrogen bonds and hydrophobic contacts. Delphinidin (128853) exhibited strong binding with electrostatic complementarity and hydrogen bonds involving VAL720, ALA564, TYR479, and ASN529, in addition to π-alkyl interactions with ARG568. Similarly, Pelargonidin (440832) engaged in hydrogen bonding with TYR479 and ASN529, along with π-π stacking and πsigma interactions, indicating robust stability. Caffeic acid (689043) demonstrated hydrogen bonds with TYR479 and ASN567, supported by π-sigma and π-π stacking interactions, while Chlorogenic acid (1794427) formed hydrogen bonds with ASN567 and ASN529 and a carbon–hydrogen bond with ARG571, highlighting a strong binding orientation. In Quercetin (5280343), hydrogen bonds with TYR479, ARG568, and VAL720 were complemented by hydrophobic contacts with ALA564 and TYR479, whereas Kaempferol (5280863) showed hydrogen bonding with ASN567, ASN529, and ALA564, along with π-alkyl interactions with TYR479. Myricetin (5281672) was stabilized by hydrogen bonds with TYR479 and ASN529, carbon–hydrogen bonding with ARG568, and additional hydrophobic interactions, while Rhamnetin (5281691)

exhibited hydrogen bonds with TYR479, ASN529, and ARG571, albeit with a donor–donor clash, alongside π-π stacking and hydrophobic contacts.

In Pancreatic TAG Lipase (2PPL), the standard Beta-lactone (647006) exhibited hydrogen bonding with GLN146, a π-donor hydrogen bond with GLU23, a π-anion interaction with GLU50, and a π-alkyl contact with PRO49. While Delphindin (128853) was anchored by hydrogen bonds with THR54, SER73, and GLN146, supported by π-alkyl interactions with LEU72 and PRO49, despite an unfavorable contact with GLU23. Pelargonidin (440832) engaged in hydrogen bonding with LEU70 and weaker carbon–hydrogen bonds with LEU72 and ARG55, complemented by π-alkyl interaction with LEU71. while caffeic acid (689043) showed hydrogen bonds with PRO49, GLN146, and ASP24, and hydrophobic stabilization with LEU72, though with an unfavorable acceptor–acceptor clash at GLN149. In Chlorogenic acid (1794427)**,** hydrogen bonds with SER73, THR54, and GLN146, a carbon–hydrogen bond with GLY53, and π-anion and π-alkyl interactions reinforced stable binding, with only a minor unfavorable donor–donor clash with THR54. For Kaempferol (5280343), hydrogen bonds with GLU23 and LEU71 were supported by hydrophobic and π-anion interactions, whereas Quercetin (5280863) combined hydrogen bonds with GLU23 and GLU50 with hydrophobic contacts involving PRO49, LEU71, and LEU72. Similarly, Myricetin (5281672) formed hydrogen bonds with THR54, GLN146, and SER73, supported by π-anion and hydrophobic interactions, despite an unfavorable acceptor–acceptor clash. Rhamnetin (5281691) demonstrated dual mode binding through hydrophobic interactions with LEU71, LEU72, and PRO49, along with hydrogen bonds with LEU71, THR54, and GLU23.

4.1.5 Protein-Ligand Interaction Analysis

The interaction patterns of the phytochemicals with both enzymes were further examined. Tables 5 and 6 present the interaction profiles of the selected compounds, highlighting hydrogen bond networks, hydrophobic contacts, and other notable interactions, with emphasis on residues commonly associated with strong binding affinity. Additionally, Table 3 identifies the key residues participating in hydrogen bonding and hydrophobic interactions.

4.1.6 Comparison with Standard Drugs

Binding scores and interaction types of selected phytochemicals were compared with standard drugs used against each enzyme. Table 4 summarizes the comparative profile.

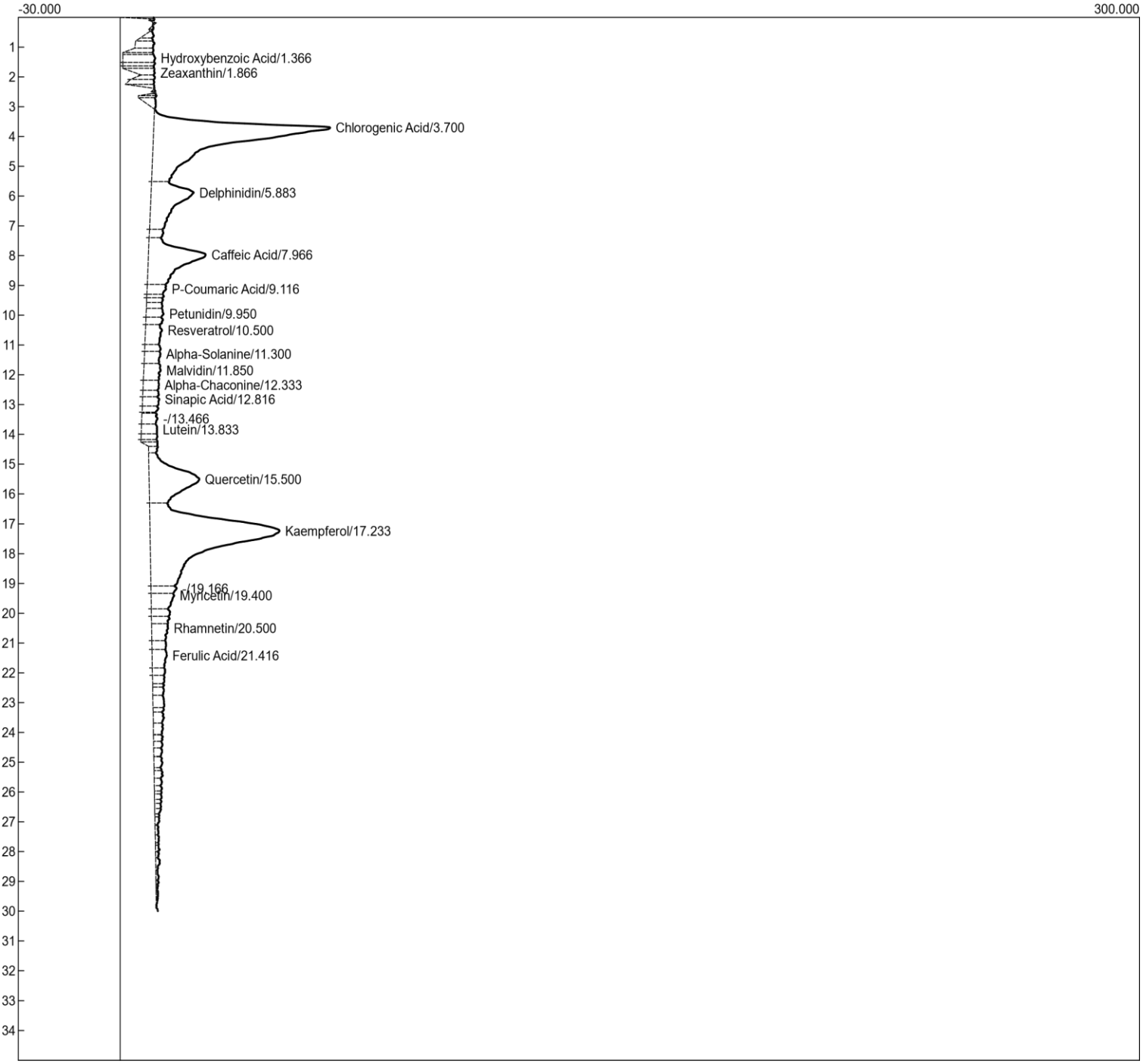

Figure 3: HPLC Chromatogram of Phytochemical Constituents in *Solanum aethiopicum* Fruits Extract

Table 2: Proximate Composition of *Solanum aethiopicum* Fruit

Parameter	Crude Protein Content	Crude lipid Content	Moisture Content	Total Ash Content	Crude fibre Content	Carbohydrate Content
Values (%)	8.53 ± 0.62	9.22 ± 0.07	9.21 ± 0.31	7.60 ± 0.02	32.39 ± 0.94	33.09 ± 0.17

Values are means of three samples ± standard deviation.

Table 3: Important Residues Involved in Binding of High-Affinity Phytochemicals

Protein	Ligands	Residue Involved	Interaction Type
Human HMG-CoA Reductase(1HWJ)	Delphinidin (128853), Rhamnetin (5281691), Pelargonidin (440832), Quercetin (5280343)	TYR479, ASN529, ALA564, ARG568, VAL720, ASN567, SER565, ARG571 GLU23, GLU50 PRO49, LEU71, LEU72, GLN146, THR54, SER73 VAL270, GLU719	Hydrogen bond, hydrophobic, electrostatic, polar reaction
Pancreatic TAG Lipase (2PPL)	Pelargonidin (440832), Quercetin (5280343), Delphinidin (128853)	TYR479, ARG568, ALA564, ASN529, ASN567, VAL720, ARG571, ASP24, ARG55, GLY53	Hydrogen bond, hydrophobic, Vander Waals

Table 4: Comparison of Binding Affinity of Selected Phytochemicals, *Solanum aethiopicum* Fruit Extract with Standard Drugs.

Compound	CID	TAG Lipase (2PPL)	HMG-CoA Reductase	vs. Rosuvastatin	vs. β-Lactone
Rosuvastatin (Standard drug)	446157	—	-6.5	—	—
β-Lactone (Standard drug)	6476006	-6.4	—	—	—
Chlorogenic acid	1794427	−7.1	-7.1	Stronger for HMG-CoA by −0.6	Stronger for both
Delphinidin	128853	-7.2	-7.0	Stronger for both	Stronger for both
Quercetin	5280343	-7.2	-7.0	Stronger for both	Stronger for both
Kaempferol	5280863	-7.2	-7.0	Stronger for both	Stronger for both
Myricetin	5281672	-7.0	-7.0	Stronger for HMG-CoA by −0.5	Stronger for both
Pelargonidin	440832	-6.9	-6.5	Stronger for HMG-CoA	Equal for rosuvastatin
Caffeic acid	689043	-6.1	-5.8	Weaker for both	Weaker for both
Rhamnetin	5281691	-7.1	-6.8	Stronger for both	Stronger for both

Table 5: Binding Affinity and Interaction Profiles of Selected Phytochemicals from *Solanum aethiopicum* Fruit Extract with Human HMG-CoA (PDB ID; 1HWJ)

Compound ID (CID)	Binding Score (kcal/mol)	Hydrogen Bonds (No. & Key Residues)	Hydrophobic Bonds (No. & Key Residues)	Other Interaction(No. & Residues)
Delphinidin (128853)	-7.0	4 (GLN146 (1.89), SER73 (2.46), THR54 (2.12), LEU71 (3.59))	3 (PRO49 (2) (4.58, 5.21), LEU72 (4.24))	3 (GLU23 (4.50),GLU50 (2)(3.94, 3.27))
Pelargonidin (440832)	-6.5	3 (LEU70 (2.92), ARG55 (3.53 A), LEU72 (3.29))	3 (LEU72 (2)(4.91, 4.94), LEU71 (5.09))	
Caffeic acid (689043)	-5.8	3 (GLN146 (2.13), PRO49 (2.01), ASP24 (2.12))	1 (LEU72 (4.60))	
Chlorogenic acid (1794427)	-7.1	3 (SER73 (1.79), GLN146 (2.01), THR54 (2.33), GLY 53 (3.66))	1(PRO49 (5.17))	1 (GLU50 (3.61))
Quercetin (5280343)	-7	2 (GLU23(2.70), LEU71 (3.55))	3 (PRO49 (2) (4.84, 5.36), LEU72 (4.19)	3 (GLU23(4.53), GLU50(4.20, 3.34))
Kaempferol (5280863)	-7	2(GLU23 (1.82), GLU50 (2.11))	5 (LEU71 (3.86), PRO49 (4.91), LEU72(2) (5.48, 5.18))	
Myricetin (5281672)	-7	3(SER73 (2.12), GLN146 (2.06), THR54 (2.27))	3(PR049(2) (4.67,5.21), LEU72 (4.20))	3(GLU23(4.54), GLU50 (2) (4.07, 3.25))
Rhamnetin (5281691)	-6.8	5 (GLN146 (2) (2.83 A, 2.00), GLN149 (2.37), ASP24 (2.40), GLU50 (2.39))	3(PR049(2) (4.85, 5.35), LEU72 (4.20))	3(GLU23(4.52), GLU50 (2) (4.21, 3.36))
Rosuvastatin (446157) (Standard drug)	-6.5	3(THR54 (1.81), GLU23 (2.06) LEUZI (3.59))	3 (LEU25 (5.46), PRO49 (5.30), LEU72 (5.40))	2 (GLN146 (3.67 A), GLU23 (3.24A))
Beta-lactone (6476006) (Standard drug)	-5.9	3(GLN146 2) 2 (2.08, 2.59), GLU23 (3.10))	2(PR049 (2) (4.65, 5.33))	1(GLU50 (4.00)

Table 6: Binding Affinity and Interaction Profiles of Selected Phytochemicals from *Solanum aethiopicum* Fruit Extract with Pancreatic TAG Lipase (PDB ID; 2PPL)

Compound ID (CID)	Binding Score (kcal/mol)	Hydrogen Bonds (No. & Key Residues)	Hydrophobic Bonds (No. & Key Residues)	Other Interaction (No. & Residues)
Delphinidin (128853)	-7.2	5 (TYR479 (2.64), ASN529 (2.44), ALA564 (2.85), VAL720 (2.43), ARG568 (3.59))	4 (ALA564 (3.80), TYR479 (3.62), ARG568 (2) (4.37, 5.21))	
Pelargonidin (440832)	-6.9	2 (TYR479 (2.64), ASN529 (2.37))	4 (ALA564 (3.75), TYR479 (3.62), ARG568 (2) (4.38, 5.17))	
Caffeic acid (689043)	-6.1	3 (ASN567 (2) (2.46, 2.23), TYR479(2.17)	2 (ALA564 (3.52), TYR479 (3.70))	
Chlorogenic acid (1794427)	-7.1	3 (ASNS29 (2.36 A), ASN567 (2.08 A), ARG571 (3.39 A))	4 (ALA564 (3.75), TYR479 (3.62), ARG568 (2), (4.58, 4.97))	
Quercetin (5280343)	-7.2	3 (TYR479 (2.90), VAL720 (2.77), ARG568(2) (3.17, 3.58))	5 (TYR479 (2) (4.03, 3.82), ALA564 (2) (4.31, 4.05), ARG568 (2) (3.93))	
Kaempferol (5280863)	-7.2	5 (ASN567 (2) (2.01, 2.40), ALA564 (2) (2.84,3.55), ASN529 (2.13))	4 (ALA564 (3.76), TYR479 (3.62), ARG568(2) (4.60, 5.17))	
Myricetin (5281672)	-7	3 (TYR479 (2.75), ASN52S (2.54), ARG568 (3.05))	4 (ALA564 (3.76), TYR479 (3.60), ARG568(2) (4.60, 5.09))	
Rhamnetin (5281691)	-7.1	5(TYR479(2.77), ARG571 (2.35), ASN529 (2.23), ARG568 (2), (3.08 3.67))	7 (TYR479 (2) (3.72 A,3.54), ALA564 (2) (4.08, 4.84), ARG568 (2) (4.79, 4.47), VAL720 (5.12))	
Rosuvastatin (446157) (Standard drug)	-7.1	4 (TYR479 (2.86), ASN567 (1.97), SER565 (3.26), VAL270 (3.19))	5 (ALA564 (4.92), ARG568 (4.73), TYR479 (5.05), ARG568 (4.11), VAL720 (5.14)	1 (GLU719(3.49))
Beta-lactone (6476006) (Standard drug)	-6.4	3 (ASN529(2) (2.21, 3.58), TYR479(3.67))		

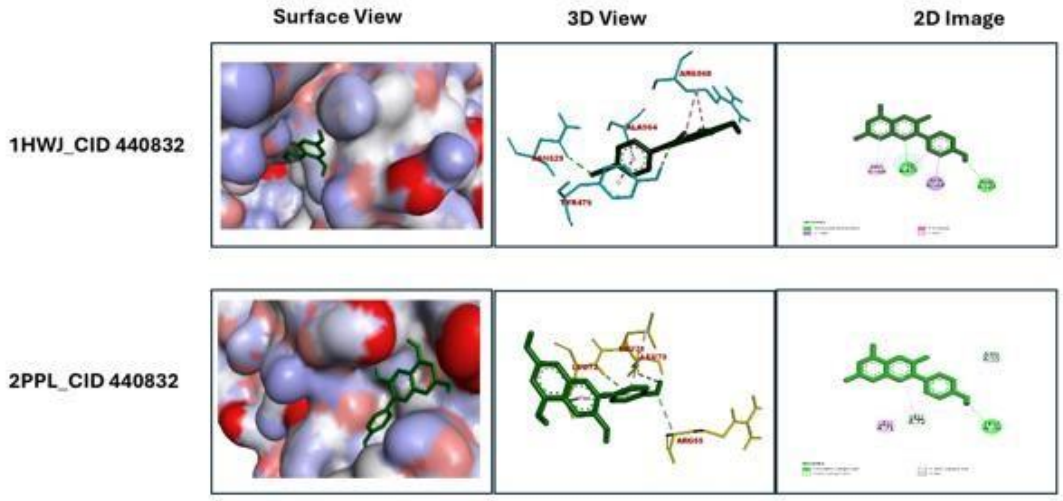

Figure 4: 2D, 3D, and Surface Binding View of Pelargonidin with Human HMG-CoA reductase (1HWJ) & Pancreatic TAG Lipase (2PPL)

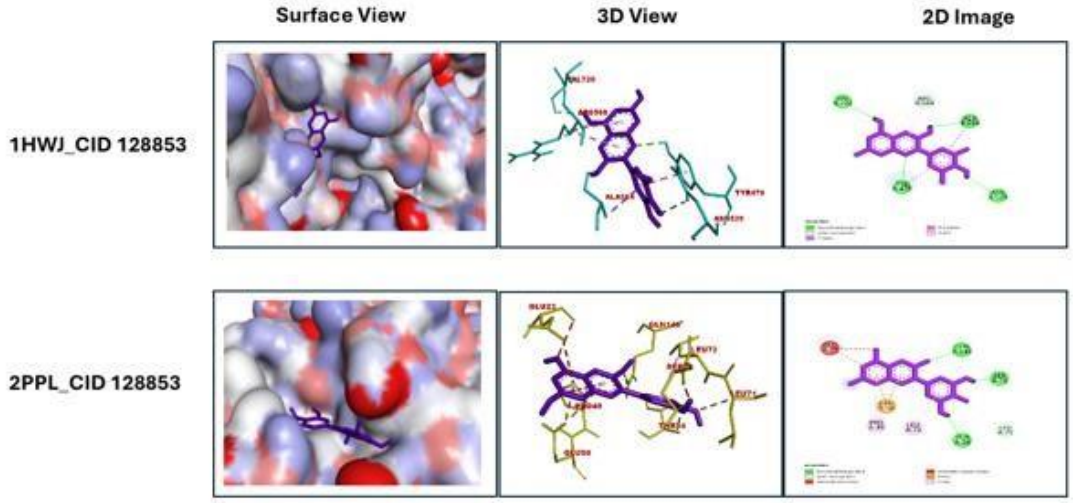

Figure 5: 2D, 3D, and Surface Binding View of Delphinidin Human HMG-CoA reductase (1HWJ) & Pancreatic TAG Lipase (2PPL)

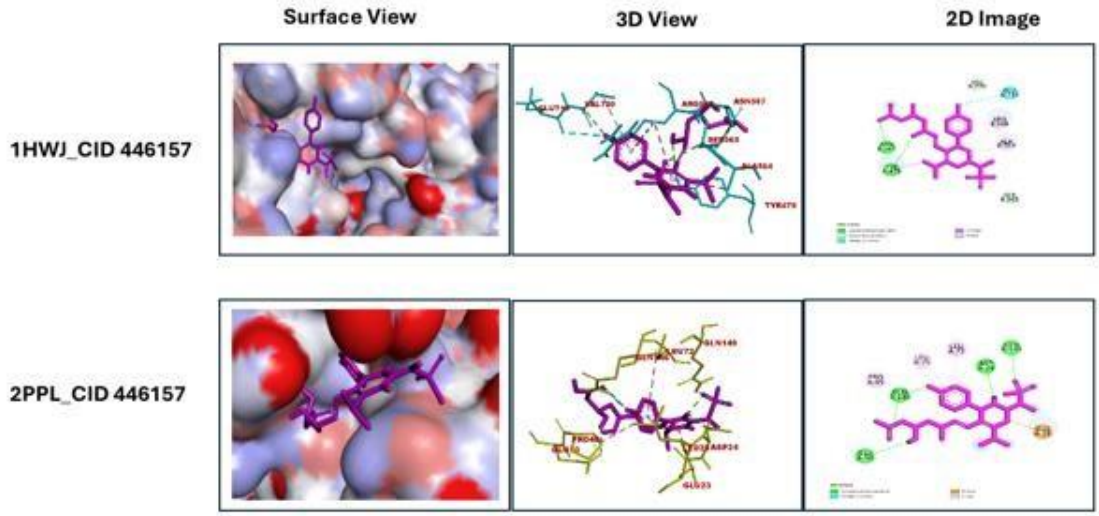

Figure 6: 2D, 3D, and Surface Binding View of Rosuvastatin Human HMG-CoA reductase (1HWJ) & Pancreatic TAG Lipase (2PPL)

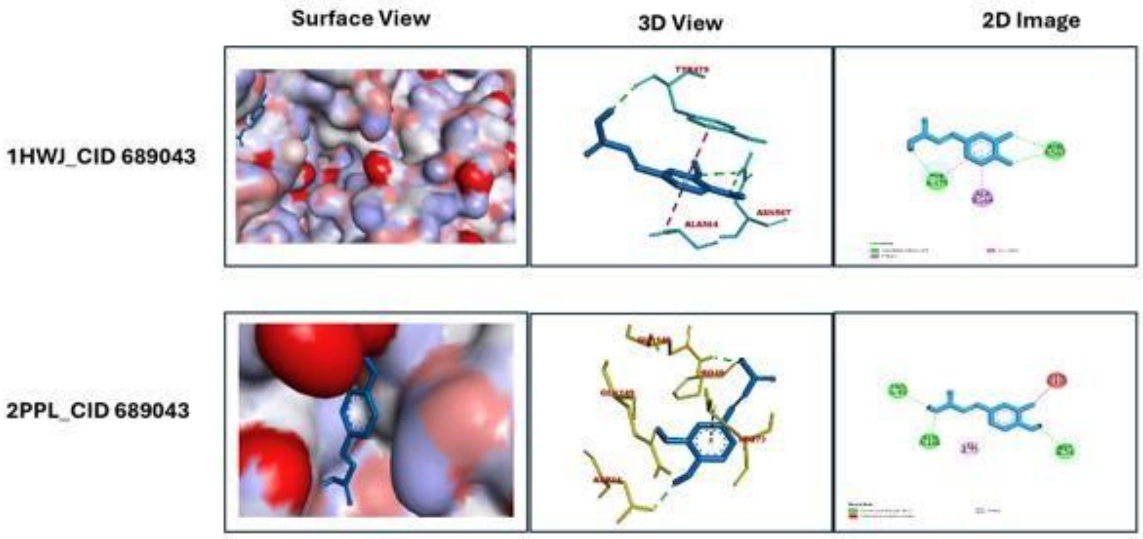

Figure 7: 2D, 3D, and Surface Binding View of Caffeic acid Human HMG-CoA reductase (1HWJ) & Pancreatic TAG Lipase (2PPL)

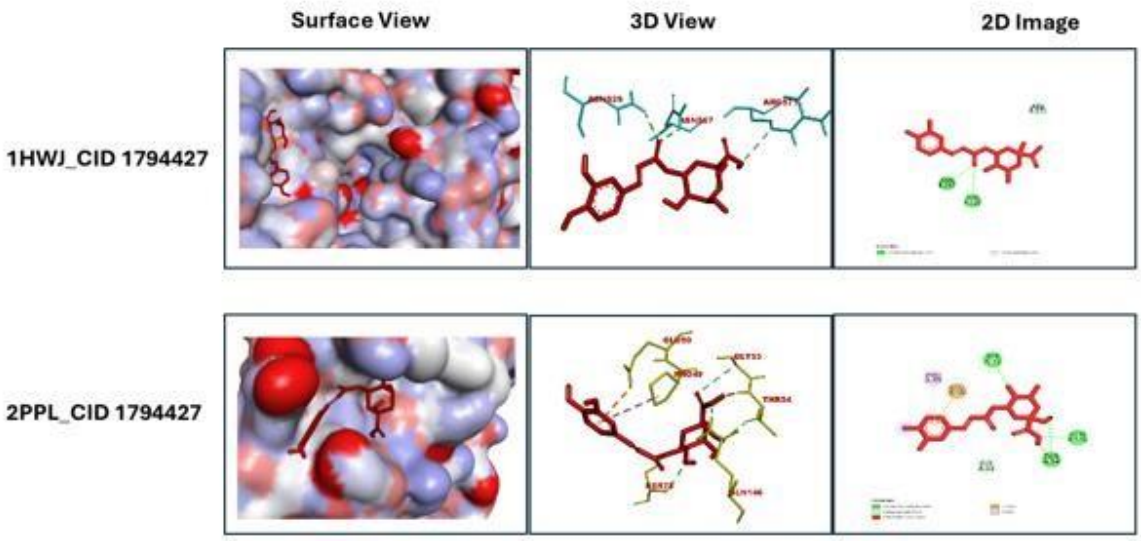

Figure 8: 2D, 3D, and Surface Binding View of Chlorogenic acid Human HMG-CoA reductase (1HWJ) & Pancreatic TAG Lipase (2PPL)

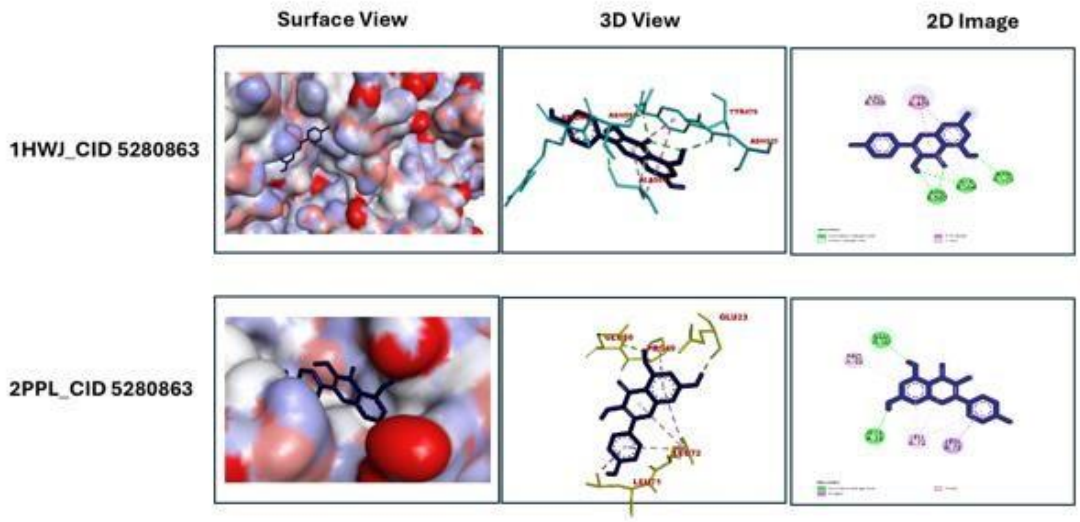

Figure 9: 2D, 3D, and Surface Binding View of kaempferol Human HMG-CoA reductase (1HWJ) & Pancreatic TAG Lipase (2PPL)

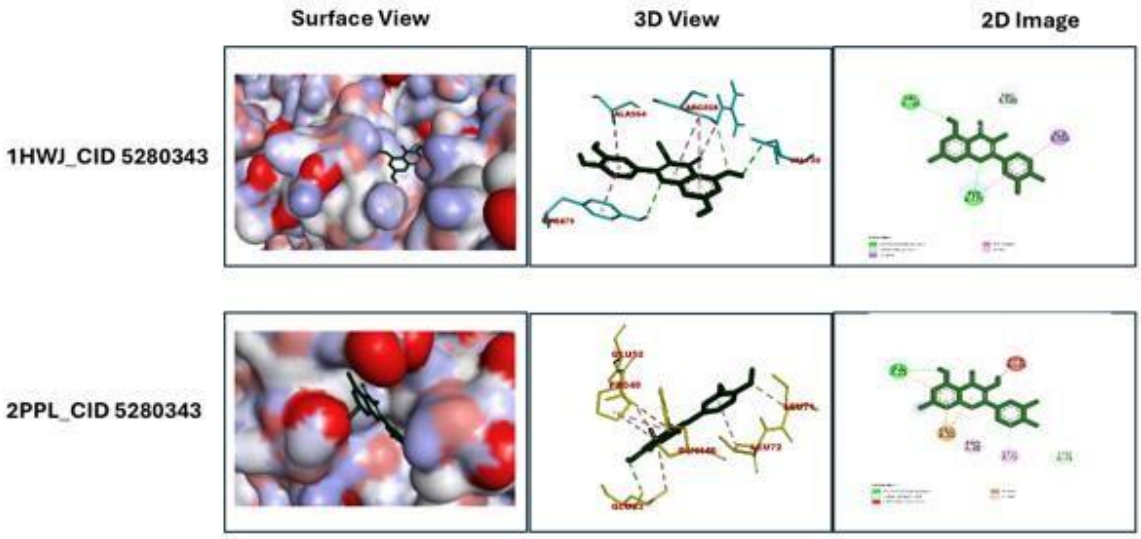

Figure 10: 2D, 3D, and Surface Binding View of Quercetin Human HMG-CoA reductase (1HWJ) & Pancreatic TAG Lipase (2PPL)

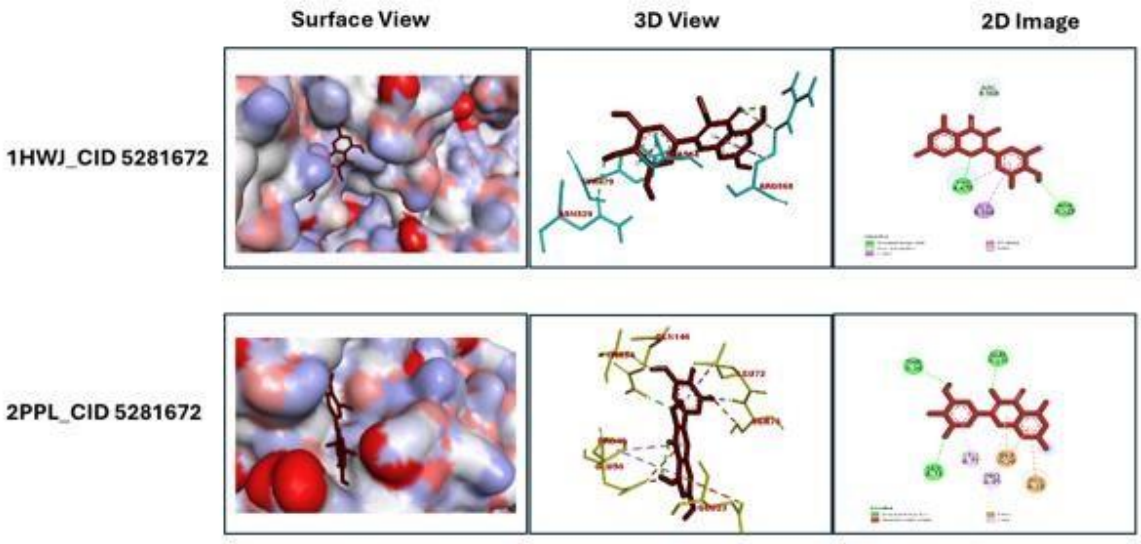

Figure 11: 2D, 3D, and Surface Binding View of Myricetin Human HMG-CoA reductase (1HWJ) & Pancreatic TAG Lipase (2PPL)

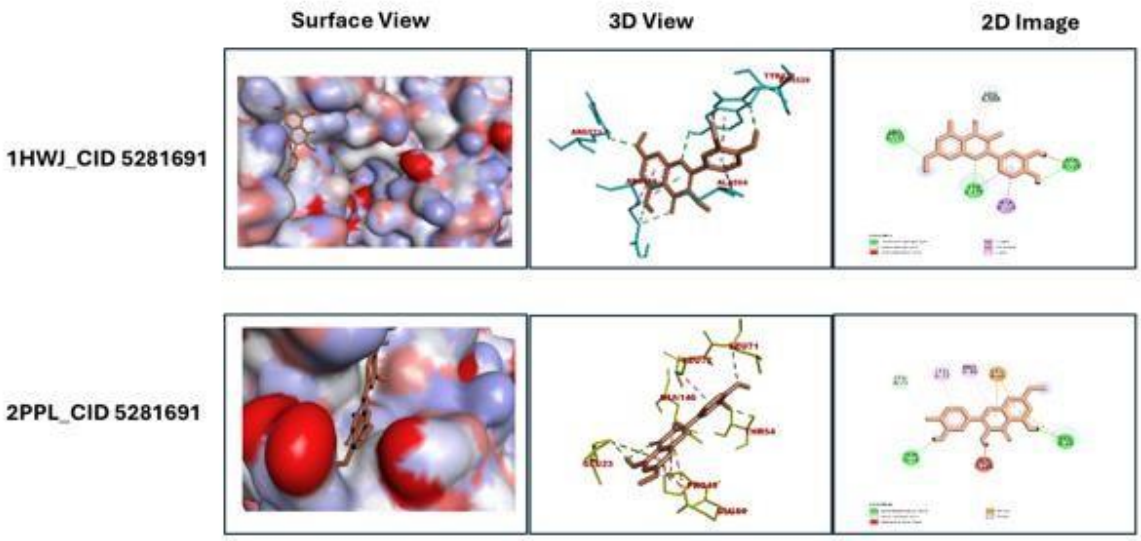

Figure 12: 2D, 3D, and Surface Binding View of Rhamnetin Human HMG-CoA reductase (1HWJ) & Pancreatic TAG Lipase (2PPL)

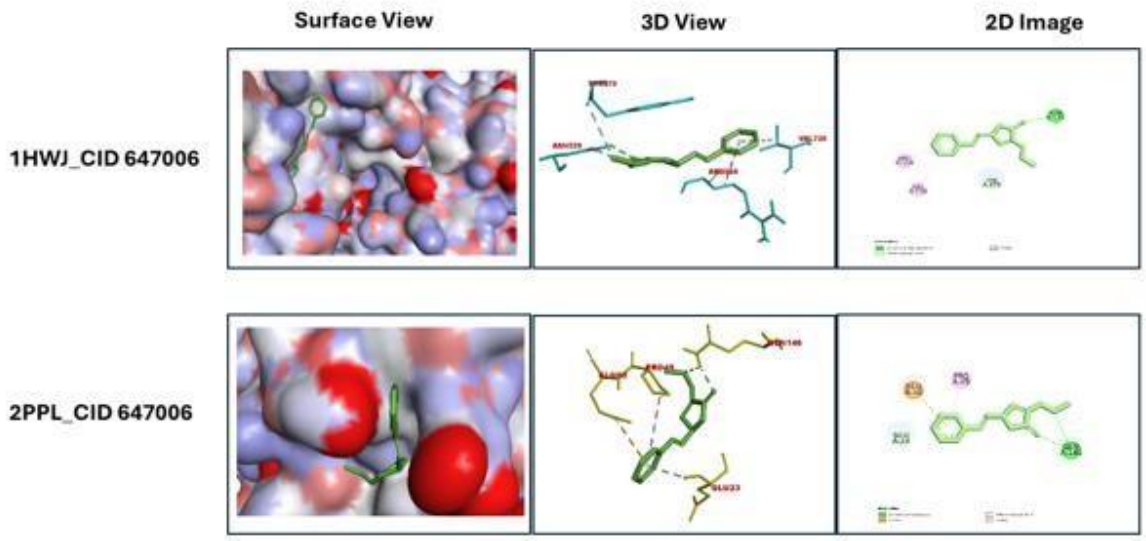

Figure 13: 2D, 3D, and Surface Binding View of beta-lactone Human HMG-CoA reductase (1HWJ) & Pancreatic TAG Lipase (2PPL)

4.2 Discussion

The proximate analysis of *Solanum aethiopicum* revealed a high content of carbohydrates and dietary fiber, with relatively lower levels of lipids, ash, and moisture. The abundance of dietary fiber is particularly relevant, as it has been shown to enhance satiety, bind lipids in the gastrointestinal tract, and reduce fat absorption, mechanisms that are central to weight management. These findings are consistent with the findings of Ofori *et al.* (2021) on African indigenous vegetables and support the nutritional value of the fruit as a functional food ingredient. The mineral content, inferred from ash levels, further suggests that the fruit could contribute to essential metabolic processes and enzymatic functions, aligning with studies on *Solanum* species (Peng *et al.*, 2020).

Phytochemical profiling using HPLC demonstrated that *S. aethiopicum* is rich in flavonoids, anthocyanins, and phenolic acids, with quercetin, delphinidin, caffeic acid, kaempferol, pelargonidin, myricetin, rhamnetin and chlorogenic acid being prominent. Flavonoids and anthocyanins are well-known for their antioxidant capacity and inhibitory effects on digestive and cholesterol-regulating enzymes, which may underpin the fruit's potential in obesity management. These observations support earlier studies that identified flavonoids as the predominant secondary metabolites in African eggplant varieties (Eze *et al.,* 2022) and highlight their pharmacological significance in lipid modulation (Bouyahya *et al.,* 2022; Okoye *et al.,* 2020).

Molecular docking revealed that several phytochemicals, particularly quercetin, delphinidin, and rhamnetin, exhibited strong binding affinities toward both human HMG-CoA reductase and pancreatic TAG lipase, comparable to standard inhibitors such as β-lactone and rosuvastatin. This dual binding potential suggests that these compounds could simultaneously reduce dietary fat absorption and inhibit cholesterol biosynthesis (Mursal *et al*., 2024). Similar dual inhibitory effects have been reported *in vitro* for flavonoids derived from other plant sources (Kumar *et al.*, 2019), indicating that such compounds may exert multifaceted anti-obesity actions.

Compounds like caffeic acid displayed comparatively weaker binding, which aligns with literature showing that simple phenolic acids generally exhibit lower enzyme inhibition than complex flavonoids (Sharma *et al.*, 2021). The interaction patterns, including hydrogen bonding and

hydrophobic contacts with key catalytic residues (e.g., TYR479 and ARG568 in TAG lipase), highlight the structural basis for the high binding affinity of certain phytochemicals (Modanwal *et al*., 2023). These interactions are consistent with previous molecular docking studies where anthocyanins and flavonoids showed preferential binding to enzyme active sites involved in lipid metabolism (Bouyahya *et al.,* 2022).

The observed interactions suggest significant implications for obesity management. Inhibition of pancreatic TAG lipase may decrease intestinal fat absorption, whereas inhibition of human HMG-CoA reductase could reduce endogenous cholesterol synthesis. Together, these effects have the potential to modulate lipid levels and prevent excessive fat accumulation, outcomes supported by *in vivo* studies on plant-derived polyphenols with similar binding properties.

The findings also underscore the potential of *S. aethiopicum* as both a functional food and a source of bioactive compounds for therapeutic development. Its nutritional composition, combined with the strong enzyme inhibitory potential of its phytochemicals, points to a dual mode of action in controlling obesity. Moreover, the study reinforces the relevance of natural products in drug discovery as safer alternatives or adjuncts to synthetic lipid-lowering agents, which are often associated with adverse effects.

While these results are promising, it is important to recognize that molecular docking provides in silico predictions. Future studies, including *in vitro* and *in vivo* experiments, are essential to validate bioactivity, absorption, metabolism, and safety. Nevertheless, the study establishes a scientific basis for the potential use of *S. aethiopicum* in obesity management and highlights the therapeutic relevance of its phenolic compounds.

CHAPTER FIVE

5.0 Summary of the findings

This study investigates the anti-obesity potential of phytochemicals from *Solanum aethiopicum* (African eggplant) through molecular docking analysis against human HMG-CoA reductase and pancreatic TAG lipase, key enzymes in lipid digestion and cholesterol biosynthesis. Despite the availability of synthetic anti-obesity drugs, challenges such as high cost, adverse effects, and limited accessibility highlight the need for safer, food-based alternatives. The study revealed that compounds such as quercetin and tannic acid exhibited strong binding affinities comparable to standard drugs, suggesting a dual inhibitory mechanism for obesity management. The paper includes Abstract, Introduction, Methodology, Results, Discussion, Conclusion, and Recommendations. Molecular docking revealed interactions with key catalytic residues of human HMG-CoA reductase and pancreatic TAG lipase, supporting the potential dual inhibitory effects of the compounds. Findings underscore the nutritional and pharmacological relevance of *S. aethiopicum* as a functional food and nutraceutical candidate for obesity prevention.

5.1 Conclusion

This study evaluated the nutritional composition, phytochemical profile, and molecular docking properties of *Solanum aethiopicum* fruits in relation to obesity management. Proximate analysis confirmed that the fruit contains appreciable levels of protein, fiber, and carbohydrates, underscoring its dietary relevance. HPLC identified several phenolic compounds, including quercetin, delphinidin, and rhamnetin, as major bioactive constituents. Molecular docking results revealed that these compounds demonstrated strong binding affinities with human HMG-CoA reductase and pancreatic TAG lipase, comparable to standard inhibitors. Such interactions suggest their potential as dual enzyme inhibitors in lipid metabolism and cholesterol biosynthesis. Collectively, the findings highlight the nutritional and pharmacological importance of *S. aethiopicum* fruits. This work supports its potential role as a natural therapeutic agent for managing obesity and related metabolic disorders.

5.2 Recommendations for Future Research

In vivo assays should be conducted to confirm the inhibitory effects of the selected phytochemicals on TAG lipase and HMG-CoA reductase.

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APPENDIX I

Grid Box Parameters Of Target Proteins

Exhaustiveness = 8

Dimensions	1HWJ	2PPL
center_x	28.97	27.57
center_y	15.57	-15.13
center_z	10.96	0.57
Size x	17.40	20.15
Size y	11.45	18.99
Size z	15.52	19.24