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The Hypolipidemic Property of Pomelo Fruit Extract on Sprague-Dawley Rats

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Abstract

This study evaluated the hypolipidemic activity of ethanolic pomelo (*Citrus maxima* [Burm.] Merr.) fruit extract in male Sprague-Dawley rats exposed to a high-fat diet. Guided by a bioactive-compound–lipid-regulation framework, the study examined whether the extract's phytochemical constituents could influence total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, and very-low-density lipoprotein. A randomized experimental design was employed using 15 rats assigned to pomelo-extract, positive-control, and negative-control groups, with five animals per group. The treatment group received 150 mg/kg body weight of the extract. Qualitative phytochemical screening and laboratory lipid-profile testing were conducted, while the data were analyzed using descriptive statistics, one-way analysis of variance, post hoc comparison, and the Kruskal–Wallis test. Flavonoids and coumarins were detected in the extract, whereas anthocyanins, phenols, saponins, steroids, tannins, and terpenoids were not detected. Compared with the untreated group, the pomelo-treated group had lower total cholesterol and LDL concentrations. The treated group also recorded the highest mean HDL concentration, although the reported HDL probability value and the stated significance threshold require clarification. No significant differences were observed in triglyceride and VLDL levels. The findings indicate that the extract demonstrated selective cholesterol-modulating activity rather than a uniform effect on the entire lipid profile. Further studies should use larger samples, multiple doses, longer treatment periods, quantitative phytochemical analysis, toxicity assessment, and pre- and post-treatment measurements. The research supports SDG 3 by contributing preliminary evidence related to cardiovascular-risk reduction and SDG 9 by promoting laboratory-based natural-product innovation. Its sustainability contribution lies in supporting public health research and the potential value-added use of a locally available agricultural resource, subject to further validation.

Keywords: Cardiovascular Risk, *Citrus Maxima*, Dyslipidemia, Flavonoids, Hypolipidemic Activity, Lipid Profile, Sprague-Dawley Rats

1. Introduction

Dyslipidemia is a metabolic disorder characterized by abnormal concentrations of circulating lipids and lipoproteins, commonly involving elevated total cholesterol, low-density lipoprotein cholesterol, triglycerides, or very-low-density lipoprotein cholesterol and, in some cases, reduced high-density lipoprotein cholesterol (Dybiec et al., 2023). These lipid abnormalities can impair endothelial function, promote lipid accumulation and inflammation within arterial walls, and contribute to the development of atherosclerosis and cardiovascular complications (Higashi, 2023). The World Health Organization (2025) identifies cardiovascular diseases as the leading cause of mortality worldwide and recognizes raised blood lipids as an important intermediate risk factor for heart attack, stroke, heart failure, and related complications. Although pharmacological agents remain central to dyslipidemia management, continuing research has examined plant-derived compounds as possible complementary sources of lipid-regulating agents. Pomelo, scientifically identified as *Citrus maxima* (Burm.) Merr., is a tropical citrus fruit containing flavonoids, coumarins, phenolic compounds, and other phytochemicals with potential antioxidant and pharmacological activities (Abiq et al., 2024). These bioactive constituents may influence oxidative stress, hepatic lipid synthesis, cholesterol transport, and fatty-acid metabolism. Preclinical investigations have reported that extracts, juices, fruit segments, leaves, and peels of *C. maxima* may modify selected lipid parameters under diabetic, high-fat-diet, and hepatic-steatosis conditions (Feksa et al., 2018; Ani & Ochu, 2020; Karthiga et al., 2021; Nunes et al., 2023). However, differences in the plant part used, extraction method, chemical composition, dosage, animal model, and treatment duration prevent direct generalization across studies. The present study therefore investigated the hypolipidemic property of ethanolic pomelo fruit extract in Sprague-Dawley rats exposed to a high-fat diet. It evaluated total cholesterol, triglycerides, HDL, LDL, and VLDL to determine whether the extract could produce favorable changes in the lipid profile. The study was designed as a preliminary preclinical evaluation and does not claim that the extract is clinically effective or that it can replace established lipid-lowering medications.

Cardiovascular diseases remain a major global public health burden. The World Health Organization (2025) reported that cardiovascular diseases accounted for an estimated 19.8 million deaths in 2022, representing approximately 32% of deaths

worldwide. A large proportion of these deaths resulted from heart attack and stroke, conditions strongly influenced by modifiable metabolic and behavioral risk factors, including unhealthy dietary patterns, obesity, physical inactivity, hypertension, diabetes, and elevated blood lipids. The Philippine situation reflects the same concern. According to the Philippine Statistics Authority (2026), ischemic heart diseases were the leading cause of registered deaths in the Philippines in 2024, accounting for 134,074 deaths or 19.1% of the national total. Cerebrovascular diseases ranked third, accounting for an additional 68,729 deaths. These figures demonstrate the continuing need for prevention strategies and research addressing modifiable cardiovascular risk factors such as abnormal lipid profiles. Dyslipidemia contributes to cardiovascular risk because excessive circulating LDL can promote cholesterol deposition within arterial walls. LDL oxidation, vascular inflammation, endothelial dysfunction, and progressive plaque formation may eventually restrict blood flow or trigger thrombotic events. HDL generally participates in reverse cholesterol transport by carrying cholesterol away from peripheral tissues toward the liver. Consequently, interventions that reduce total cholesterol and LDL while maintaining or increasing HDL may provide useful preliminary evidence of lipid-regulating activity. Pomelo is a potential source of natural bioactive compounds relevant to lipid metabolism. The uploaded study identified flavonoids and coumarins in its ethanolic fruit extract, supporting the biological plausibility of examining its effect on serum lipids. Inthachat et al. (2023) similarly demonstrated that *C. maxima* extracts may contain substantial concentrations of citrus flavonoids, including hesperidin and naringenin, although the concentration and composition of these substances depend on the plant part and extraction conditions used. Their findings emphasize that solvent concentration, extraction time, and temperature can substantially influence the phytochemical composition of the resulting extract. The potential lipid-modulating activity of pomelo should therefore be understood as an effect of a complex extract rather than of a single isolated compound. Flavonoids, coumarins, fiber-related substances, organic acids, and other constituents may act individually or interactively. Nevertheless, the mere presence of phytochemicals does not establish therapeutic effectiveness. Their biological relevance must be supported by controlled experiments evaluating measurable outcomes such as total cholesterol, triglycerides, HDL, LDL, and VLDL.

A consistent theme in recent literature is the phytochemical richness of different parts of *C. maxima*. Inthachat et al. (2023) optimized an aqueous-ethanolic extraction method for pomelo albedo and detected phenolic and flavonoid compounds, particularly naringenin and hesperidin. Their study also demonstrated that phytochemical yield is dependent on extraction conditions, indicating that results obtained from peel, albedo, pulp, juice, or whole-fruit preparations should not be treated as directly interchangeable. This distinction is important for the present study because it used an ethanolic fruit preparation. Evidence obtained from leaf, peel, or essential-oil extracts may support the broader pharmacological potential of the species but cannot independently establish the activity of the fruit extract tested in the present investigation. The biological effects of a preparation depend on the actual compounds extracted, their concentrations, stability, absorption, and interaction with the experimental model.

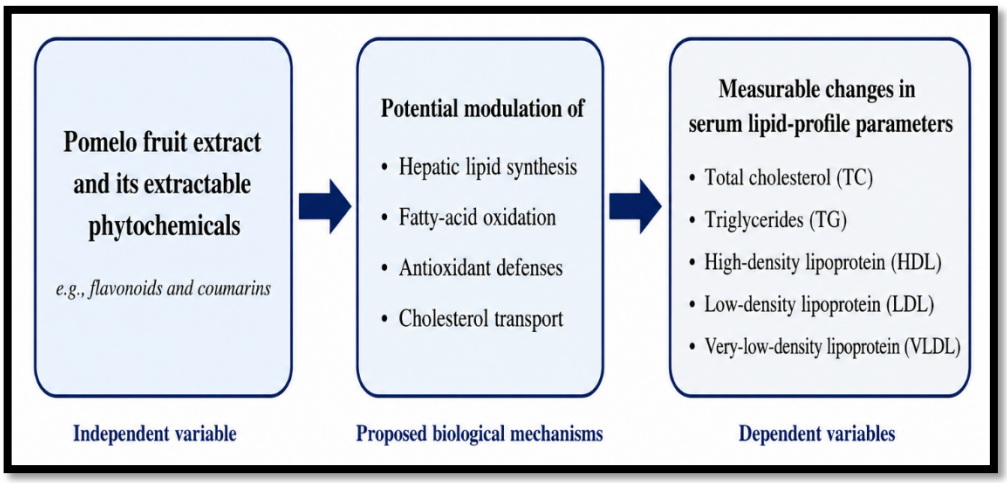
Feksa et al. (2018) evaluated a *C. maxima* leaf extract in Wistar rats subjected to fructose-associated hyperlipid-diet-induced hepatic steatosis. The authors reported hepatoprotective, hypolipidemic, antioxidant, and anti-inflammatory activity and associated these effects with the extract's phytochemical composition. Although their research involved leaves rather than fruit pulp, it provides evidence that compounds from *C. maxima* may influence interconnected processes involving lipid accumulation, oxidative stress, and hepatic function. Ani and Ochu (2020) examined *C. maxima* peel extract in alloxan-induced diabetic rats. Treatment with the higher tested dose increased HDL and reduced total cholesterol, triglycerides, and LDL relative to the diabetic condition. Their findings support the potential antihyperlipidemic activity of pomelo-derived preparations, but they also highlight the importance of dose because the reported effects were evaluated using peel extract at concentrations different from those applied in the present study. Karthiga et al. (2021) compared pomelo juice, naringin, and food products fortified with pomelo fruit segments in streptozotocin-induced diabetic rats. The interventions improved several biochemical outcomes and reduced serum lipids, although the effects varied according to the preparation administered. The results suggest that whole-fruit matrices and isolated flavonoids may not produce identical biological responses, further justifying the direct evaluation of a defined pomelo extract. More recently, Nunes et al. (2023) administered an aqueous pummelo pulp extract to Wistar rats with non-alcoholic fatty liver disease induced by a fructose-associated high-fat diet. The treated animals showed improvements in lipid-related biochemical parameters, hepatic fat accumulation, oxidative-stress indicators, and inflammatory markers. This study is particularly relevant because it evaluated pomelo pulp rather than only peel or leaves and demonstrated that the fruit portion may influence both circulating lipids and hepatic metabolic processes. Collectively, these studies support the investigation of *C. maxima* as a possible source of lipid-modulating compounds. However, they do not establish uniform effectiveness. Some investigations used diabetic models, while others used fatty-liver or high-fat-diet models. The interventions also differed in terms of plant part, solvent, duration, concentration, and comparator. These differences may explain why some preparations significantly affected triglycerides and VLDL, whereas the uploaded study found significant effects primarily in total cholesterol, LDL, and HDL.

Several biological pathways may explain the potential lipid-regulating effects of pomelo, although the present study did not directly measure molecular mechanisms. An et al. (2020) investigated mixtures of tea and *C. maxima* in lipid-loaded

HepG2 liver cells. The preparations activated the AMP-activated protein kinase and acetyl-CoA carboxylase pathway, increased proteins related to fatty-acid oxidation, and reduced the expression of proteins involved in lipid synthesis. These findings indicate that *C. maxima*-containing preparations may suppress hepatic fat synthesis while promoting fatty-acid utilization. Antioxidant and anti-inflammatory actions may provide additional explanations. Oxidative stress can promote lipid peroxidation and contribute to hepatic and vascular damage. In animal studies, *C. maxima* extracts have been associated with increased antioxidant-enzyme activity and reduced inflammatory markers under metabolically stressful dietary conditions (Feksa et al., 2018; Nunes et al., 2023). Nevertheless, these pathways should be treated as proposed explanatory mechanisms rather than confirmed mechanisms of the present study. The uploaded investigation measured the serum lipid profile and conducted qualitative phytochemical screening but did not measure AMPK activation, gene expression, hepatic cholesterol synthesis, fecal lipid excretion, oxidative-stress biomarkers, or inflammatory mediators.

Globally, the continuing burden of cardiovascular disease has encouraged research on preventive nutrition, functional foods, natural products, and complementary metabolic interventions. Raised blood lipids are modifiable cardiovascular risk factors; however, their management requires healthy dietary practices, regular physical activity, clinical monitoring, and appropriate medical treatment (World Health Organization, 2025). Research on plant extracts should therefore be positioned as an early stage of natural-product discovery rather than as evidence supporting unsupervised therapeutic use. Experimental studies have reported potentially beneficial biochemical effects of pomelo preparations, but the available evidence remains predominantly preclinical and varies according to the plant part, extraction method, dosage, and experimental model (Nunes et al., 2023). At the national level, the predominance of ischemic heart and cerebrovascular diseases among the leading causes of death in the Philippines gives practical relevance to studies addressing lipid abnormalities. The Philippine Statistics Authority (2026) reported that ischemic heart diseases accounted for 134,074 deaths or 19.1% of registered deaths in 2024, while cerebrovascular diseases accounted for 68,729 deaths or 9.8%. Research on locally available agricultural products may complement broader efforts to understand diet-related risk reduction and identify bioactive compounds for future pharmacological, nutraceutical, or functional-food development. At the local level, the pomelo fruits used in the study were obtained from a public market in Tuguegarao City and authenticated through the Department of Agriculture. Extraction and phytochemical analysis were conducted at Cagayan State University, while the animal experiment was undertaken using the authorized facilities and procedures described in the study. This context strengthens the research's relevance to Philippine natural-product investigation by examining an accessible tropical fruit through local laboratory and institutional resources. Nevertheless, local availability should not be equated with established safety, affordability, or clinical effectiveness. Extraction conditions can substantially affect the type and concentration of phytochemicals recovered from *Citrus maxima*, emphasizing the need for chemical characterization and standardized preparation procedures (Inthachat et al., 2023). Moreover, pomelo flavonoids may have variable bioavailability, and pomelo products may affect the pharmacokinetics of certain medicines, supporting the need to examine possible food–drug interactions before human application (Chen et al., 2018; Ding et al., 2022). Therefore, further research should establish toxicity, standardized composition, pharmacokinetics, safe and effective dosage, long-term effects, potential medication interactions, and reproducibility before pomelo extract is evaluated for clinical use.

The study may be anchored in a bioactive-compound-lipid-regulation framework. Under this framework, an ethanolic pomelo fruit extract serves as the independent intervention, while total cholesterol, triglycerides, HDL, LDL, and VLDL constitute the principal biochemical outcomes.



This conceptual framework illustrates how pomelo fruit extract, particularly its flavonoids and coumarins, may influence biological processes related to lipid metabolism. These phytochemicals may help regulate hepatic lipid synthesis, fatty-acid oxidation, antioxidant defenses, and cholesterol transport. Their potential effects are assessed through measurable changes in total cholesterol, triglycerides, HDL, LDL, and VLDL levels in the experimental rats.

Flavonoids and coumarins detected in the extract provide the phytochemical foundation of this proposed relationship. Evidence from An et al. (2020) suggests that *C. maxima*-containing preparations may influence AMPK/ACC signaling and proteins controlling fat synthesis and oxidation. Evidence from Feksa et al. (2018) and Nunes et al. (2023) further indicates possible relationships among pomelo-derived compounds, oxidative-stress regulation, inflammation, hepatic lipid accumulation, and serum lipid levels. The conceptual model does not assume that all lipid parameters will respond equally. Total cholesterol and LDL may be influenced through mechanisms different from those governing circulating triglycerides and VLDL. HDL may also respond independently depending on cholesterol transport, hepatic metabolism, treatment duration, and the physiological condition of the animals. This parameter-specific perspective is consistent with the uploaded findings, which demonstrated significant differences for total cholesterol, LDL, and HDL but no statistically significant differences for triglycerides and VLDL.

Despite increasing interest in pomelo-derived bioactive compounds, several gaps remain. First, many recent studies have evaluated pomelo peel, leaves, albedo, juice, isolated naringin, or mixed citrus formulations. Comparatively fewer investigations have focused specifically on ethanolic pomelo fruit extract in high-fat-diet-exposed Sprague-Dawley rats. Findings from other plant parts or animal models cannot automatically be applied to the preparation used in the current study. Second, extraction procedures remain poorly standardized across the literature. Ethanol concentration, solvent-to-sample ratio, extraction time, temperature, fruit variety, maturity, storage, and plant part may alter the concentration of active compounds. Inthachat et al. (2023) demonstrated the substantial role of extraction conditions in the recovery of pomelo flavonoids. This methodological variability limits comparisons among studies and indicates the need for future chemical quantification and extract standardization. Third, many studies assess combined metabolic conditions, such as diabetes or non-alcoholic fatty liver disease, rather than isolated dyslipidemia. While these models are relevant, they include alterations in glucose metabolism, insulin signaling, inflammation, and liver function that may affect lipid outcomes independently of the tested extract. Fourth, limited evidence is available concerning dose-response relationships. The present research evaluated one treatment concentration, making it possible to determine whether the selected preparation was associated with lipid-profile differences but not whether lower or higher doses would be more effective, safer, or biologically optimal. Fifth, serum lipid measurements alone cannot identify the exact mechanism of action. Molecular studies are needed to evaluate hepatic enzymes, lipid-regulating genes, cholesterol synthesis, bile-acid metabolism, intestinal lipid absorption, antioxidant activity, inflammation, and histopathological changes. Finally, evidence remains predominantly preclinical. Findings obtained in rats cannot be directly translated into recommendations for humans. The present investigation should therefore be interpreted as preliminary evidence supporting further experimental work rather than proof of clinical efficacy. These gaps justify the study because it contributes additional evidence regarding the effect of a locally prepared ethanolic pomelo fruit extract on multiple lipid-profile components in Sprague-Dawley rats. It also helps determine whether the observed activity is broad across all lipid parameters or selective for specific measures such as total cholesterol, LDL, and HDL.

The study directly aligns with SDG 3 because it addresses dyslipidemia, a modifiable risk factor associated with cardiovascular disease. By evaluating the lipid-regulating activity of a plant-derived extract, the research contributes to the preliminary evidence base needed for future preventive, nutritional, pharmaceutical, or functional-food investigations.
Its contribution remains preclinical. Therefore, its SDG 3 relevance lies in generating scientific knowledge and identifying possible research leads rather than providing an immediate treatment recommendation. This distinction is necessary to prevent the premature promotion of pomelo extract as an alternative to clinically prescribed lipid-lowering therapy. The research also aligns with SDG 9 through natural-product and laboratory-based innovation. It demonstrates how local agricultural materials may be subjected to extraction, phytochemical screening, animal experimentation, and biochemical analysis to identify potential value-added applications. With further validation, standardized pomelo-derived preparations may become subjects for functional-food, nutraceutical, pharmaceutical, or biotechnology research. However, such development would require reproducible extraction methods, quantitative chemical characterization, safety testing, dose optimization, regulatory evaluation, and eventual human studies.

The study contributes to public health sustainability by generating preliminary evidence related to dyslipidemia, a modifiable metabolic risk factor associated with cardiovascular disease (World Health Organization, 2025). Sustainable public health involves not only treating established diseases but also developing evidence-based preventive strategies and strengthening knowledge of dietary and metabolic risk factors. The study also contributes to biomedical and pharmaceutical sustainability by examining a plant-derived preparation as a potential source of biologically active compounds. Reviews of *Citrus maxima* have identified flavonoids, coumarins, limonoids, phenolic compounds, and other phytochemicals with potential antioxidant, anti-inflammatory, and lipid-regulating activities (Ding et al., 2022; Sapkota et al., 2022). Natural-product research may therefore expand the range of compounds available for functional-food, nutraceutical, and pharmaceutical investigation. Nevertheless, responsible biomedical innovation requires promising preclinical findings to be followed by toxicity assessment, quantitative chemical characterization, extract standardization, mechanistic investigation, and clinical validation (Inthachat et al., 2023; Nunes et al., 2023). The study also has potential relevance to

agricultural and socio-economic sustainability because pomelo is cultivated and consumed in several Asian countries, including the Philippines (Sapkota et al., 2022). Scientific investigation of its bioactive properties may support the future development of value-added products from locally available agricultural resources. Research on citrus materials and by-products has demonstrated their potential use as sources of bioactive compounds, essential oils, functional ingredients, and other high-value products, while also helping reduce agricultural and food-processing waste (Badalamenti et al., 2022; Russo et al., 2021). However, the present experiment did not evaluate commercial feasibility, production costs, agricultural supply, product stability, or market acceptance. From an institutional sustainability perspective, the study demonstrates the value of collaboration among academic laboratories, agricultural authorities, animal-research facilities, and clinical-testing services. Such collaboration can strengthen local capacity for natural-product investigation, experimental pharmacology, ethical animal research, and evidence-based innovation. Overall, the study's multidisciplinary significance arises from the intersection of nutrition, pharmacology, biochemistry, animal science, public health, agriculture, and sustainable innovation. Its primary contribution is not the immediate establishment of pomelo extract as a treatment but the generation of preliminary evidence that may guide more rigorous chemical, toxicological, mechanistic, and clinical investigations.

2. Material and methods

2.1 Research Design

The study used a randomized experimental research design to determine the effect of pomelo fruit extract on the lipid profiles of Sprague-Dawley rats. The animals were assigned to three experimental groups representing the pomelo extract treatment, positive control, and negative control conditions. The treatment group received pomelo fruit extract at a dosage of 150 mg/kg body weight. Differences in the measured lipid-profile parameters among the groups were subsequently evaluated using appropriate statistical tests.

2.2 Locale of the Study

Fresh pomelo fruits were obtained from a public market in Tuguegarao City and verified by the Department of Agriculture. The extraction and phytochemical analysis of the pomelo fruit were conducted at the Clinical Laboratory of Cagayan State University, Andrews Campus. The experimental rats were housed and managed at the Philippine Institute of Traditional and Alternative Health Care, where the animal treatment and blood-sample collection procedures were undertaken.

2.3 Respondents of the Study

The study did not involve human respondents. Its experimental subjects consisted of male Sprague-Dawley rats used to determine the effect of pomelo fruit extract on total cholesterol, triglycerides, HDL, LDL, and VLDL levels. Male rats were selected to maintain consistency among the experimental subjects and reduce biological variation associated with differences in sex.

2.4 Sample and Sampling Procedure

A total of 15 male Sprague-Dawley rats were obtained from a licensed breeder. The rats were randomly assigned to three groups, with five animals in each group. One group received the pomelo fruit extract, while the remaining groups served as the positive and negative controls. Before treatment, the rats were fed a high-fat diet for five days to induce hyperlipidemia.

2.5 Research Instrument

The study used laboratory materials and equipment for the preparation of the ethanolic pomelo fruit extract and the biochemical evaluation of the experimental animals. These included fresh pomelo fruit, a blender, a stoppered container, an orbital shaker, distilled water, ethanol, filters, Eppendorf tubes, a rotary evaporator, and refrigerated storage equipment. The pomelo extract underwent qualitative phytochemical analysis to determine the presence or absence of selected secondary metabolites. The effectiveness of the extract was assessed through laboratory measurements of total cholesterol, triglycerides, HDL, LDL, and VLDL in the blood samples collected from the experimental rats.

2.6 Data Gathering Procedure

Fresh pomelo fruits were purchased and authenticated before extract preparation. The fruit pulp was blended and subjected to maceration using a 75% ethanol solution at a sample-to-solvent ratio of 1:7. The mixture was placed in a stoppered container and soaked for 24 hours. It was subsequently filtered, concentrated using a rotary evaporator, and stored under refrigerated conditions until administration. Before receiving the intervention, the rats were fed a high-fat diet for five days to induce hyperlipidemia. The 15 rats were then randomly divided into three groups. The treatment group was administered pomelo fruit extract at a dosage of 150 mg/kg body weight, while the other groups served as positive and negative controls. Following treatment, blood samples were collected through cardiac puncture. The samples were placed in appropriate laboratory containers and analyzed to determine total cholesterol, triglycerides, HDL, LDL, and VLDL concentrations. The resulting measurements were used to evaluate the hypolipidemic activity of the pomelo fruit extract.

2.7 Data Analysis Techniques

Descriptive statistics, including the mean, median, standard deviation, and range, were used to summarize the lipid-profile measurements of the experimental groups. A one-way analysis of variance was performed to determine whether significant differences existed among the group means. Post hoc comparison was used to identify the specific groups that differed significantly after obtaining a significant overall result. The Kruskal–Wallis test was also applied as a nonparametric method for comparing the experimental groups. The level of statistical significance was set at $p<0.001p<0.001p<0.001$, as specified in the original methodology.

2.8 Ethical Considerations

The Sprague-Dawley rats were acquired and used under an approved animal-research permit issued through the Bureau of Animal Industry. The animals were housed at the Philippine Institute of Traditional and Alternative Health Care during the experiment. The procedures involving animal handling, treatment administration, and blood collection were conducted within the authorized research setting described in the study.

3. Results and Discussion

3.1 Phytochemical Profile of the Pomelo Fruit Extract

3.1.1 Detected and Undetected Phytochemical Constituents

Qualitative phytochemical screening showed that the ethanolic pomelo fruit extract tested positive for flavonoids and coumarins. Anthocyanins, phenols, saponins, steroids, tannins, and terpenoids were not detected using the applied screening procedures. Coumarins were examined using the procedure attributed to Muñoz et al (2021), while the other phytochemical classes were assessed through their respective qualitative tests. The detection of flavonoids and coumarins indicates that the ethanolic fruit extract contained selected secondary metabolites that may possess biological activity. Reviews of *Citrus maxima* have documented flavonoids, coumarins, phenolic compounds, limonoids, and other phytochemicals across its pulp, peel, leaves, and seeds, although their concentrations vary depending on the plant part, variety, maturity, solvent, and extraction procedure (Sapkota et al., 2022). Ding et al. (2022) identified naringin, hesperidin, narirutin, and neohesperidin among the principal flavonoids reported in *C. maxima*. These compounds have been investigated for their antioxidant, anti-inflammatory, and lipid-regulating properties. The current qualitative screening, however, established only the presence of general phytochemical classes and did not identify or quantify individual compounds. Therefore, the detected flavonoids cannot automatically be assumed to be naringin, hesperidin, or any specific flavonoid without chromatographic or spectrometric confirmation. Similarly, a negative qualitative result does not conclusively establish the complete absence of a compound because the concentration may have been below the detection limit of the applied assay. The findings should therefore be interpreted as preliminary evidence of the extract's phytochemical composition rather than a complete chemical characterization.

3.2 Lipid Profile of the Experimental Groups

3.2.1 Total Cholesterol

The pomelo extract group recorded a mean total cholesterol concentration of 2.620 mmol/L. The positive-control group had the lowest mean concentration at 1.474 mmol/L, while the untreated negative-control group had the highest mean at 3.620 mmol/L. The overall difference among the groups was statistically significant, with an F-value of 18.444 and a probability value below .001. Post hoc comparison showed that the pomelo extract group had significantly lower total cholesterol than the untreated negative-control group. The lower total cholesterol observed in the pomelo-treated group relative to the untreated group suggests that the extract attenuated the increase in cholesterol under the experimental conditions. However, the positive-control group produced a lower mean total cholesterol than the pomelo extract group. The findings therefore support a cholesterol-lowering effect relative to the untreated condition but do not indicate that pomelo extract was more effective than the positive-control intervention. The result is broadly consistent with previous animal investigations of *C. maxima*. Ani and Ochu (2020) reported reductions in serum total cholesterol following the administration of pomelo peel extract in diabetic rats. Karthiga et al. (2021) also found that pomelo fruit preparations and naringin improved selected serum lipid parameters in streptozotocin-induced diabetic rats. Moreover, Nunes et al. (2023) observed improved biochemical and hepatic outcomes after administering an aqueous pummelo pulp extract to rats with diet-induced non-alcoholic fatty liver disease. Although these studies support the lipid-regulating potential of pomelo, direct comparisons should be made cautiously because they used different plant parts, extracts, dosages, disease models, and treatment durations.

3.2.2 Triglycerides

The mean triglyceride concentration was 0.506 mmol/L in the pomelo extract group, 0.588 mmol/L in the positive-control group, and 0.384 mmol/L in the negative-control group. The difference among the three groups was not statistically significant, as indicated by an F-value of 0.350 and a probability value of .711. These results do not demonstrate a significant triglyceride-lowering effect of the pomelo fruit extract. Although the treatment group had a slightly lower mean than the positive-control group, it had a higher mean than the negative-control group, and the observed variations were not

statistically meaningful. Consequently, the study cannot conclude that the extract reduced triglycerides under the conditions tested. This finding differs from studies that reported lower triglyceride concentrations after treatment with certain pomelo preparations. Ani and Ochu (2020) observed reduced triglycerides following the administration of pomelo peel extract, while Karthiga et al. (2021) reported lipid-profile improvements from pomelo fruit preparations and naringin. Ding et al. (2022) further discussed evidence that flavonoids from *C. maxima* may affect triglyceride metabolism through pathways related to hepatic fatty-acid oxidation and lipid accumulation. The difference between the present findings and previous reports may be associated with variation in the extract composition, plant part, dosage, treatment period, metabolic model, and baseline lipid condition of the experimental animals. The lack of a significant triglyceride response also suggests that the extract did not influence all lipid components uniformly. Lipid-regulating substances may affect cholesterol synthesis, transport, absorption, or clearance without producing an equivalent change in circulating triglycerides. Therefore, the nonsignificant triglyceride result does not negate the significant total cholesterol and LDL findings, but it limits the claim to a selective rather than comprehensive hypolipidemic effect.

3.2.3 High-Density Lipoprotein

The pomelo extract group recorded the highest mean HDL concentration at 1.352 mmol/L. The negative-control group had a mean of 1.300 mmol/L, while the positive-control group had the lowest mean at 0.932 mmol/L. The overall difference was statistically significant, with an F-value of 4.378 and a probability value of .037. Post hoc analysis indicated that the pomelo extract group had significantly higher HDL than the positive-control group. However, no significant difference was found between the pomelo extract and negative-control groups. The result indicates that pomelo extract maintained a higher HDL concentration than the positive-control intervention. However, because the HDL level of the pomelo-treated group did not differ significantly from that of the untreated group, the findings do not establish that the extract significantly increased HDL relative to the negative control. The appropriate interpretation is that the effect was significant only in comparison with the positive-control group. Ani and Ochu (2020) similarly found that pomelo peel extract increased HDL in experimentally induced diabetic rats. Bioactive compounds in citrus fruits have been associated with lipid transport, hepatic lipid metabolism, and antioxidant activity, which may influence circulating lipoprotein concentrations (Ding et al., 2022; Sapkota et al., 2022). Nevertheless, the exact mechanism responsible for the HDL pattern in the present study cannot be determined because the research did not measure apolipoproteins, cholesterol transport proteins, hepatic enzymes, or gene expression.

3.2.4 Low-Density Lipoprotein

The mean LDL concentration was 0.838 mmol/L in the pomelo extract group, 0.618 mmol/L in the positive-control group, and 2.082 mmol/L in the untreated negative-control group. The overall difference among the groups was statistically significant, with an F-value of 37.436 and a probability value below .001. Post hoc analysis showed that the pomelo extract group had significantly lower LDL than the negative-control group. No significant difference was found between the pomelo extract and positive-control groups. The marked difference between the pomelo extract and untreated groups provides the strongest evidence of the extract's lipid-regulating activity in this investigation. The findings suggest that the extract helped limit LDL elevation following exposure to the experimental dietary condition. Although the mean LDL of the positive-control group remained numerically lower, the absence of a significant difference between the positive-control and pomelo-treated groups indicates that their LDL measurements were not statistically distinguishable in this sample. This result should not be interpreted as proof that both interventions were therapeutically equivalent because the study was not designed as an equivalence or noninferiority trial. The LDL result is consistent with Ani and Ochu (2020), who documented lower LDL following the administration of *C. maxima* peel extract in diabetic rats. Feksa et al. (2018) also reported hypolipidemic and hepatoprotective effects of a *C. maxima* leaf extract in rats with diet-induced hepatic steatosis. Similarly, Nunes et al. (2023) found that pummelo pulp extract improved biochemical and hepatic indicators in rats with non-alcoholic fatty liver disease. These studies support the possibility that pomelo-derived compounds can influence hepatic and circulating lipid metabolism despite differences in the type of extract and experimental model. Flavonoids may contribute to the observed LDL response through several possible pathways. An et al. (2020) found that a preparation containing *C. maxima* reduced lipid deposition in hepatic cells and affected the AMP-activated protein kinase and acetyl-CoA carboxylase signaling pathway. This pathway is involved in regulating fatty-acid synthesis and oxidation. Ding et al. (2022) also discussed the capacity of pomelo flavonoids to influence lipid accumulation, oxidative stress, and metabolic signaling. These mechanisms are biologically plausible explanations for the present findings, but they remain hypothetical because the current study measured serum lipid concentrations rather than molecular pathways.

3.2.5 Very-Low-Density Lipoprotein

The pomelo extract group recorded a mean VLDL concentration of 0.230 mmol/L. The mean was 0.264 mmol/L in the positive-control group and 0.174 mmol/L in the negative-control group. The differences were not statistically significant, as shown by an F-value of 0.335 and a probability value of .722. The nonsignificant VLDL result indicates that the pomelo fruit extract did not produce a measurable effect on this lipid parameter under the experimental conditions. The treatment mean was slightly lower than that of the positive-control group but remained higher than the negative-control mean. These numerical differences were insufficient to establish a treatment effect. Because VLDL primarily transports endogenously produced triglycerides, the absence of a significant VLDL response is consistent with the nonsignificant triglyceride

finding. This parallel pattern strengthens the conclusion that the tested extract did not significantly affect triglyceride-rich lipoproteins. Although Ding et al. (2022) discussed studies in which certain pomelo flavonoids reduced triglycerides and VLDL through lipid-regulating pathways, such effects may depend on the flavonoid concentration, bioavailability, dose, duration, and disease model. The current results therefore suggest that the administered extract and dosage were more influential on cholesterol-related parameters than on triglyceride-related measures.

3.3 Overall Hypolipidemic Pattern of Pomelo Fruit Extract

The inferential analysis demonstrated significant differences in total cholesterol, HDL, and LDL but not in triglycerides and VLDL. Compared with the untreated negative-control group, the pomelo extract group had significantly lower total cholesterol and LDL. The treatment group also had significantly higher HDL than the positive-control group, although its HDL concentration was not significantly different from the negative-control group. Triglycerides and VLDL remained statistically comparable across the three groups. Taken together, the findings support a selective hypolipidemic effect of the ethanolic pomelo fruit extract. Its clearest effects involved lower total cholesterol and LDL relative to the untreated condition. The results do not support claims that the extract significantly reduced triglycerides or VLDL, nor do they establish that it was superior to the positive-control intervention. The findings therefore indicate preliminary cholesterol-modulating activity rather than a uniform improvement across the complete lipid profile. The observed pattern is generally consistent with the reported biological activities of *C. maxima*. Recent experimental studies have linked pomelo extracts and flavonoids with changes in lipid metabolism, hepatic fat accumulation, oxidative stress, and inflammation (Feksa et al., 2018; Ani & Ochu, 2020; An et al., 2020; Karthiga et al., 2021; Ding et al., 2022; Nunes et al., 2023). However, differences across studies demonstrate that the effectiveness of pomelo preparations is dependent on the type of extract, chemical composition, dosage, treatment duration, and experimental condition. The presence of flavonoids and coumarins in the current extract provides a plausible phytochemical basis for the observed effects. Nevertheless, the findings do not establish which individual compounds were responsible or whether the compounds acted independently or synergistically. Further chemical characterization is required before the lipid changes can be attributed to specific substances.

3.4 Methodological and Interpretive Considerations

The results were derived from 15 male Sprague-Dawley rats, with five animals assigned to each experimental group. The limited sample size reduces statistical power and may have made small or moderate differences difficult to detect, particularly for triglycerides and VLDL. The use of only one extract dosage also prevents the determination of a dose-response relationship or the identification of an optimal effective dose. The study reported post-treatment lipid measurements for the three groups but did not present baseline lipid values in the Results section. Therefore, interpretation depends on differences among the groups after treatment rather than demonstrated within-animal changes from baseline. Future investigations should report pre-induction, post-induction, and post-treatment measurements to determine the magnitude of lipid changes over time. The qualitative phytochemical tests established the detected classes of compounds but did not quantify their concentrations. Standardized chemical analysis using high-performance liquid chromatography, liquid chromatography–mass spectrometry, or comparable techniques would help identify the active compounds and determine whether different batches contain consistent concentrations. The investigation also did not measure liver histology, hepatic lipid content, oxidative-stress markers, inflammatory indicators, fecal cholesterol, bile-acid excretion, or lipid-regulating enzymes. Consequently, the proposed biological mechanisms remain explanations supported by related literature rather than mechanisms demonstrated directly by the present experiment. The results should therefore be regarded as preliminary preclinical evidence and should not be translated directly into claims of safety or effectiveness in humans.

4. Conclusion & Recommendations

The findings indicate that the ethanolic pomelo (*Citrus maxima*) fruit extract exhibited a selective hypolipidemic effect in male Sprague-Dawley rats exposed to a high-fat diet. Compared with the untreated negative-control group, the pomelo-treated group recorded lower mean total cholesterol and LDL concentrations, and the reported statistical analysis confirmed significant group differences for these two parameters. The treated group also had the highest mean HDL concentration among the experimental groups, although this finding should be interpreted cautiously because the reported probability value of .037 must be reconciled with the methodology's stated significance level of p<.001p<.001p<.001. In contrast, no statistically significant differences were observed in triglyceride and VLDL concentrations, indicating that the extract did not produce a uniform improvement across all components of the lipid profile. The detected flavonoids and coumarins provide a plausible phytochemical basis for the observed cholesterol-related effects; however, the study did not identify or quantify the specific compounds responsible for these changes. Overall, the results provide preliminary preclinical evidence that ethanolic pomelo fruit extract may have potential for regulating total cholesterol and LDL, but they do not establish its clinical effectiveness, safety, or superiority over standard lipid-lowering treatment in humans.

Future investigations should evaluate pomelo fruit extract using larger animal samples, longer treatment periods, and several dosage levels to determine whether its lipid-regulating effects are dose-dependent, sustained, and reproducible. Pre-induction, post-induction, and post-treatment lipid measurements should be included to document changes within each

experimental subject more clearly. The extract should also undergo quantitative chemical characterization to identify and measure its principal flavonoids, coumarins, and other potentially active constituents and to ensure consistency across batches. Additional biochemical and histological assessments may be used to examine hepatic lipid accumulation, oxidative stress, inflammatory responses, and possible mechanisms involved in cholesterol metabolism. Other parts of the pomelo fruit, including the peel, albedo, and seeds, may likewise be investigated using standardized extraction procedures. Before any clinical or commercial application is considered, further studies should establish toxicity, safe dosage ranges, long-term effects, possible interactions with lipid-lowering medicines, and effectiveness in appropriately designed human trials.

The study was limited by its small sample of 15 male Sprague-Dawley rats, with only five animals assigned to each experimental group, which may have reduced the statistical power to detect smaller treatment effects. Only one extract dosage of 150 mg/kg body weight was tested, preventing the determination of a dose-response relationship or an optimal therapeutic level. The high-fat diet was administered for only five days, and the manuscript did not present baseline and post-induction lipid measurements; consequently, the analysis relied mainly on post-treatment comparisons among the groups rather than documented changes from each animal's initial condition. The phytochemical analysis was qualitative and identified only broad classes of compounds, without determining their concentration, purity, or specific chemical identity. The investigation also did not assess liver histology, hepatic lipid content, antioxidant markers, inflammatory indicators, molecular pathways, toxicity outcomes, or long-term physiological effects. In addition, the reported significance criterion of p<.001p<.001p<.001 is inconsistent with the classification of the HDL result at p=.037p=.037p=.037 as significant and should be corrected or clarified in the final manuscript. Because the experiment involved a limited preclinical animal model, the findings cannot be directly generalized to females, other animal strains, individuals with different metabolic conditions, or human populations.

Compliance with ethical standards

The study involved laboratory animals and was conducted under an approved animal research permit from the Bureau of Animal Industry, with the Sprague-Dawley rats housed and handled at the Philippine Institute of Traditional and Alternative Health Care in accordance with applicable animal-welfare and institutional research standards. As no human participants were involved, voluntary participation, informed consent, and confidentiality requirements were not applicable. The authors assume responsibility for the accuracy and integrity of the study, acknowledge all institutional and technical contributions, declare no conflict of interest, and affirm that the manuscript is original and subject to applicable copyright and publication policies.

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