Sahel Journal of Life Sciences FUDMA (SAJOLS)
March 2026 Vol. 4(1): 454-462
ISSN: 3027-0456 (Print)
ISSN: 1595-5915 (Online)
DOI: https://doi.org/10.33003/sajols-2026-0401-53

Research Article

Effect of Aqueous Extract of *Tapinanthus brunneus* leaves on diet-induced Hypercholesterolemia in Rats

Balogun, Abdul-Azeez[1], Adisa, Kazeem O.[2], Pama, Amina[1] Olutoye, Abdulquadri Funmbi[3], and Arole, Al-Ameen[1]

[1]Department of Biological Sciences, Al-Hikmah University, Ilorin, Kwara State, Nigeria
[2]Department of Biochemistry, Federal University of Health Sciences, Ila-Orangun, Osun State, Nigeria
[3]Department of Biochemistry, University of Ilorin, Ilorin, Kwara State, Nigeria
***Corresponding Author's email*: abalogun@alhikmah.edu.ng**

ABSTRACT
Hypercholesterolemia is a major contributor to cardiovascular diseases and is closely associated with oxidative stress. Plant-derived bioactive compounds have shown promise in modulating lipid metabolism and antioxidant defense systems. This study evaluated the hypolipidemic and antioxidant effects of aqueous leaf extract of *Tapinanthus brunneus* in hypercholesterolemic rats. Twenty albino rats were divided into four groups (n = 5): a normal control (standard diet), a high-fat diet (HFD) control, and two treatment groups administered *T. brunneus* extract (5 and 10 mg/kg body weight) orally for 28 days. Serum lipid parameters and hepatic antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT) were assessed. Treatment with *T. brunneus* significantly ($p < 0.05$) reduced serum total cholesterol, LDL-cholesterol, and triglycerides, while elevating HDL-cholesterol compared with HFD controls. Additionally, extract administration significantly enhanced hepatic SOD and CAT activities, indicating improved antioxidant status. *Aqueous leaf extract of Tapinanthus brunneus* exhibits significant hypolipidemic and antioxidant activities, suggesting its potential as a complementary therapeutic agent in the management of hypercholesterolemia and associated cardiovascular disorders.

Keywords: Antioxidant enzymes; Catalase; Cardiovascular disease; Hypercholesterolemia; Lipid profile; SOD; *Tapinanthus brunneus*

Citation: Balogun, A., Adisa, K.O., Pama, A., Olutoye, A.F., & Arole, A. (2026). Effect of Aqueous Extract of *Tapinanthus brunneus* leaves on diet-induced Hypercholesterolemia in Rats. *Sahel Journal of Life Sciences FUDMA*, 4(1): 454-462. DOI: https://doi.org/10.33003/sajols-2026-0401-53

INTRODUCTION

Hypercholesterolemia is a metabolic disorder defined by abnormally elevated concentrations of total cholesterol and low-density lipoprotein cholesterol (LDL-c) in the circulatory system. This pathological state plays a central role in the initiation and progression of atherosclerosis through multiple interconnected molecular mechanisms. These include the excessive generation of atherogenic biomolecules such as reactive oxygen species (ROS), pro-inflammatory cytokines, and growth factors, which collectively contribute to endothelial dysfunction and vascular inflammation. In addition, oxidative modification of LDL-c enhances its uptake by macrophages, leading to foam cell formation and plaque development. These processes are further exacerbated by the activation of redox-sensitive transcription factors such as nuclear factor-kappa-B (NF-κB), as well as the engagement of the advanced glycation end products (AGE)-receptor for AGE (RAGE) signaling axis and increased levels of C-reactive protein (CRP), all of which amplify inflammatory cascades and vascular injury (Prasad & Mishra, 2022). Consequently, hypercholesterolemia and atherosclerosis are widely recognized as major predisposing factors for cardiovascular diseases,

which remain a leading cause of global morbidity and mortality, accounting for nearly one-third of all deaths worldwide (El Rabey *et al*., 2025; Prasad & Mishra, 2022). This underscores the critical need for effective management of dyslipidemia as a major public health priority (Rachmawati *et al*., 2019).

Conventional pharmacological management of hypercholesterolemia primarily involves the use of statins, including atorvastatin and rosuvastatin, which exert their lipid-lowering effects through competitive inhibition of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme in endogenous cholesterol biosynthesis. While these agents have demonstrated significant efficacy in reducing serum lipid levels and cardiovascular risk, their long-term administration is frequently associated with adverse effects such as hepatotoxicity, skeletal muscle toxicity (myopathy), and an increased risk of new-onset diabetes mellitus. These limitations often compromise patient adherence and therapeutic outcomes (Afrose *et al*., 2019; El Rabey *et al*., 2025). Accordingly, there is a growing demand for alternative therapeutic approaches, particularly those derived from natural sources, that can provide comparable efficacy with improved safety profiles and reduced adverse effects.

Members of the genus *Tapinanthus* have attracted considerable scientific interest due to their diverse pharmacological properties, including hypoglycemic, hepatoprotective, anti-inflammatory, and antioxidant activities (Wang *et al*., 2022). Notably, *Tapinanthus dodoneifolius*, a closely related species, has been identified as a source of bioactive compounds such as dihydropyranone (Ouedraogo *et al*., 2007), whose derivatives have demonstrated potent anticancer properties through the induction of cell cycle arrest and apoptosis (Bignon *et al*., 2009). Despite the expanding body of evidence supporting the therapeutic potential of *Tapinanthus* species, there is a paucity of scientific data specifically addressing the antihyperlipidemic activity of *Tapinanthus brunneus*, thereby highlighting a significant gap in current knowledge.

Experimental models of diet-induced hypercholesterolemia, typically established through the administration of high-fat or cholesterol-enriched diets in rodents, are widely utilized for the preclinical evaluation of lipid-lowering agents. These models reliably recapitulate the key biochemical and physiological features of human dyslipidemia, including elevated levels of total cholesterol (TC), triglycerides (TG), and LDL-c, accompanied by a reduction in high-density lipoprotein cholesterol (HDL-c) (Ai et al., 2020; Ntchapda et al., 2021). Previous investigations have demonstrated that aqueous extracts of plant materials, such as *Ziziphus spina-christi* seeds and *Ipomoea batatas* leaves, exert significant antihypercholesterolemic effects in such models (Ai et al., 2020; Ntchapda et al., 2021). These findings support the continued exploration of aqueous extraction techniques for isolating bioactive compounds. Mechanistically, the beneficial effects of these plant extracts have been attributed to multiple pathways, including modulation of gut microbiota composition, attenuation of oxidative stress, and regulation of genes involved in cholesterol biosynthesis and fatty acid metabolism (Duan et al., 2024; Lv et al., 2024).

In light of these considerations, the present study was designed to investigate the effects of an aqueous extract of *Tapinanthus brunneus* leaves on diet-induced hypercholesterolemia in rats. The study aims to evaluate the capacity of the extract to restore lipid homeostasis and mitigate oxidative stress by assessing key biochemical parameters, including serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), and very-low-density lipoprotein cholesterol (VLDL-c), alongside hepatic antioxidant enzyme activities such as catalase (CAT) and superoxide dismutase (SOD). By providing experimental evidence on both lipid modulation and antioxidant defense, this study contributes to the expanding field of natural product-based therapeutics and offers preliminary insight into the potential development of *T. brunneus* or its bioactive constituents as a complementary strategy for the management of hypercholesterolemia and its associated complications.

MATERIALS AND METHODS

Plant Identification

The *leaves of Tapinanthus brunneus* were obtained from Kola nut plantation Ogbomosho, Oyo State, Nigeria. It was authenticated with a voucher number UIH001/1162 at the Faculty of Life Sciences, Department of Plant Biology, Herbarium Unit, University of Ilorin, Nigeria.

Reagent Materials: Diagnostic kits for cholesterol, HDL-cholesterol, triglycerides, and total cholesterol were purchased from RANDOX Laboratories Ltd., Anterim, United Kingdom. All other reagents were of analytical grade.

Experimental Animals: The rats used were obtained from the Department of Biochemistry, University of Ilorin, Ilorin, Nigeria.

Preparation of Aqueous Extract of *Tapinanthus brunneus*: Air-dried leaves were pulverized into powder, and 100 g was extracted in 1 L distilled water for 24 hours. The extract was filtered and concentrated using a water bath at 100°C, yielding 8.5% (w/w). The extract was reconstituted and stored under refrigeration until use.

Preparation of Diet: The hypercholesterolemic diet was prepared according to the method described by Ajiboye *et al*. (2014). The composition is shown below in Table 1.

Experimental Design

Twenty albino rats were obtained and acclimatized under standard laboratory conditions. The animals were randomly distributed into four groups of five (5) animals each as shown in table 2 below: Treatment lasted for 28 days.

Table 1: Composition of the Formulated Feeds

Feed Composition	Normal diet (g/kg)	High Fat Diet (g/kg)
Corn starch	406	406
Corn shaft	40	40
Lard	0	140
Soya beans	250	250
DL-Methionine	4	4
Lysine	10	10
Vitamin mix	50	50
Sucrose	100	100
Soya beans oil	140	0

Table 2: Animal grouping

Groups	Induction and treatment
Group A	Normal basal diet
Group B	High fat diet (HFD)
Group C	HFD + *Tapinanthus brunneus* (5 mg/kg mg/kg body weight)
Group D	HFD + *Tapinanthus brunneus* (10 mg/kg body weight)

Sample Collection and Tissue Preparation

At the end of the 4-week experimental period, animals were fasted overnight and humanely anesthetized using chloroform vapor. All procedures were conducted in accordance with standard ethical guidelines for the care and use of laboratory animals and in compliance with institutional regulations. Blood samples were collected via jugular vein incision using sterile instruments, and additional samples were obtained by cardiac puncture into plain tubes containing clot activator. The collected blood was allowed to clot at room temperature (30–60 min) and subsequently centrifuged at 3,000 × g for 15 min to obtain serum. The separated serum was stored at −18°C until further biochemical analysis of lipid profile parameters, including total cholesterol, triglycerides, HDL-cholesterol, and LDL-cholesterol.

Liver tissues were promptly excised, rinsed in ice-cold physiological saline to remove blood residues, blotted dry, and weighed. Liver homogenates were prepared for antioxidant enzyme assays by homogenizing the tissue in ice-cold sucrose buffer (pH 7.4) to obtain a 10% (w/v) homogenate. The homogenate was centrifuged at 3,000 × g for 10–15 min at 4°C, and the supernatant was collected and used for the determination of antioxidant enzymes, including superoxide dismutase and catalase.

Biochemical Assays

Biochemical parameters were determined using standard analytical methods. Serum total cholesterol was measured enzymatically following Allain *et al*. (1974), while triglycerides were determined colorimetrically according to Trinder (1969). High-density lipoprotein cholesterol (HDL-c) was estimated using the method of Lopes-Virella *et al*. (1977). Low-density lipoprotein cholesterol (LDL-c) and very low-density lipoprotein cholesterol (VLDL-c) were calculated using the Friedewald equation (Friedewald *et al*., 1972). Concentrations of lipid parameters were derived from absorbance ratios of samples to standards using appropriate conversion factors.

Determination of Antioxidant Enzyme Activity

Hepatic antioxidant enzyme activities were assessed using 10% tissue homogenates prepared by homogenizing frozen liver samples in ice-cold sucrose buffer (pH 7.4). Catalase (CAT) and superoxide dismutase (SOD) activities were determined spectrophotometrically according to the methods of Sinha *et al*. (1972) and Sun and Zigma (1978) at 240 nm and 480 nm, respectively.

Data Analysis

Statistical analysis was performed using SPSS (version 10.0; SPSS Inc., Chicago, IL, USA). Data were expressed as mean ± SD. Statistical significance was determined using one-way ANOVA followed by Duncan's multiple range test ($p < 0.05$).

RESULTS

Oral administration of *Tapinanthus brunneus* aqueous leaf extract significantly modulated lipid and antioxidant parameters in high-fat diet (HFD)-induced hypercholesterolemic rats. HFD feeding resulted in a significant ($p < 0.05$) increase in serum total cholesterol (TC) and triglycerides (TAG) compared to the control group. Treatment with the extract (5 and 10 mg/kg body weight) significantly reduced TC and TAG levels, with the 10 mg/kg dose producing values comparable to the control as shown in Figure 1.

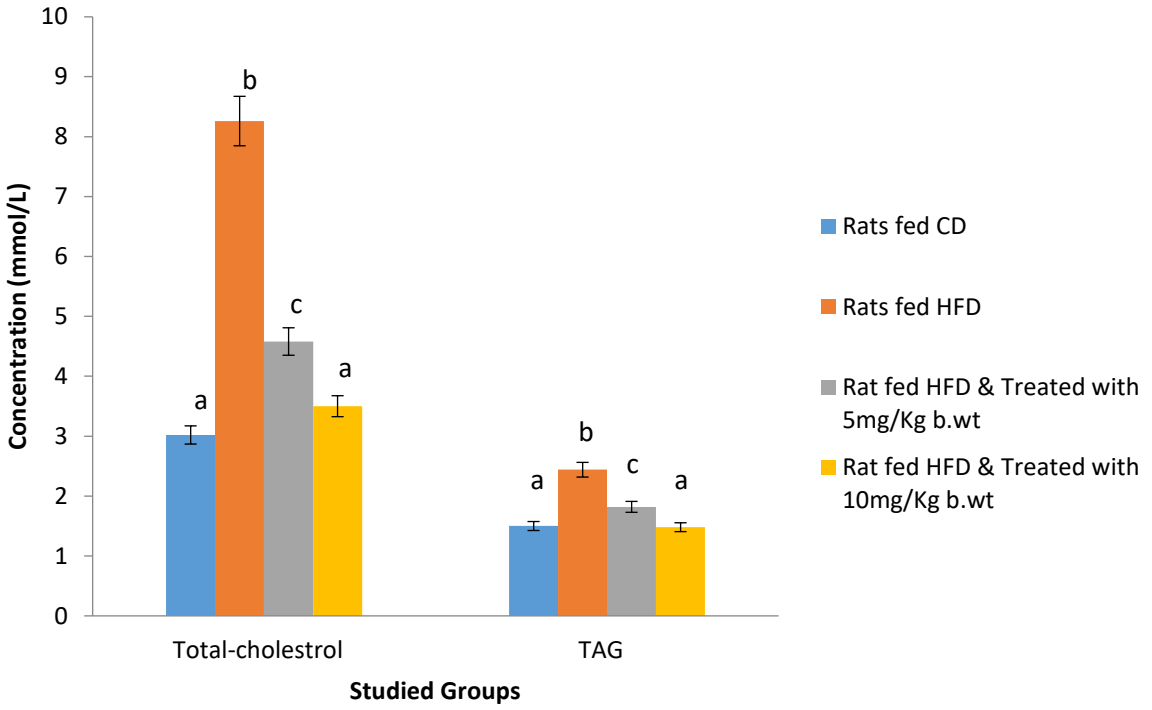

Figure 1: Effect of oral administration of *Tapinanthus brunneus* aqueous leaf extract on serum total cholesterol and triglyceride concentration in fed high-fat diets

Note: CD (control diet), HFD (high-fat diet), TAG (triglycerides). The values with different superscript letters in the same column indicate significant differences at $p < 0.05$

Similarly, HFD significantly elevated LDL-c and VLDL-c levels while reducing HDL-c ($p < 0.05$) (Figure 2). Administration of the extract significantly reversed these alterations, decreasing LDL-c and VLDL-c and increasing HDL-c levels. The 10 mg/kg dose showed the most pronounced effect, with lipid parameters closely approximating control values as depicted in Figure 2.

HFD also significantly reduced hepatic catalase (CAT) and superoxide dismutase (SOD) activities, indicating oxidative stress. Treatment with *T. brunneus* extract significantly ($p < 0.05$) restored CAT and SOD activities in a dose-dependent manner (Figures 3 and 4). The 10 mg/kg dose normalized enzyme activities, while the 5 mg/kg dose showed moderate improvement shown in Figures 3 and 4.

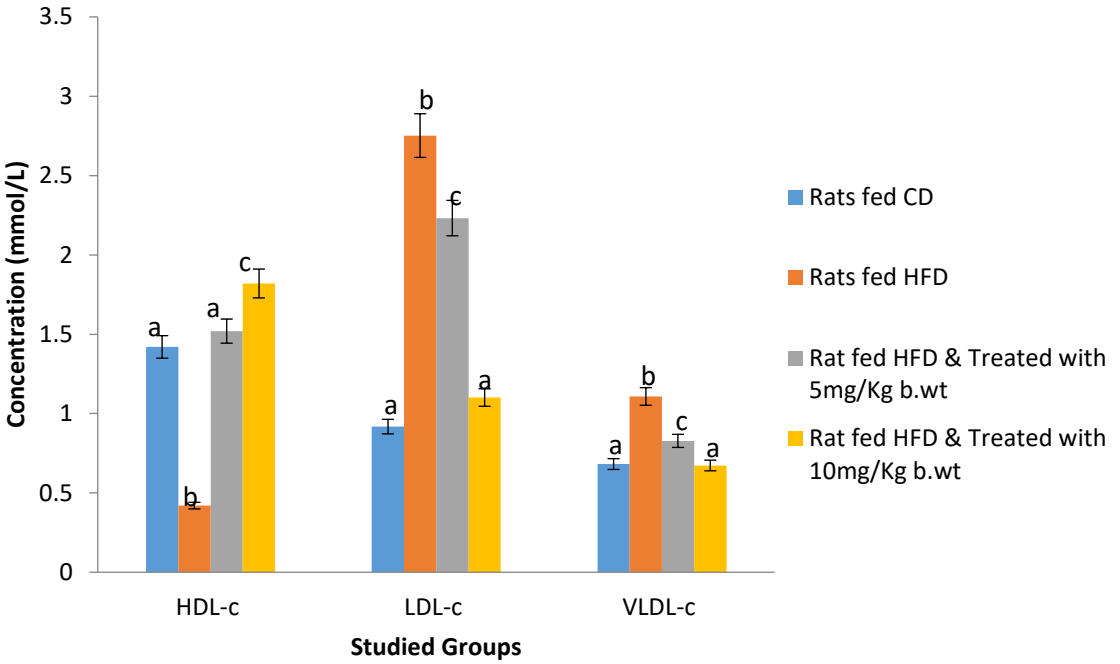

Figure 2: Effect of oral administration of *Tapinanthus brunneus aqueous* leaf extract on serum lipoprotein fractions concentration in fed high-fat diets

Note: CD (control diet), HFD (high-fat diet), VLDL-c (very low-density lipoprotein cholesterol), HDL-c (high-density lipoprotein cholesterol), LDL-c (low-density lipoprotein cholesterol), TAG (triglycerides). The values with different superscript letters in the same column indicate significant differences at $p < 0.05$

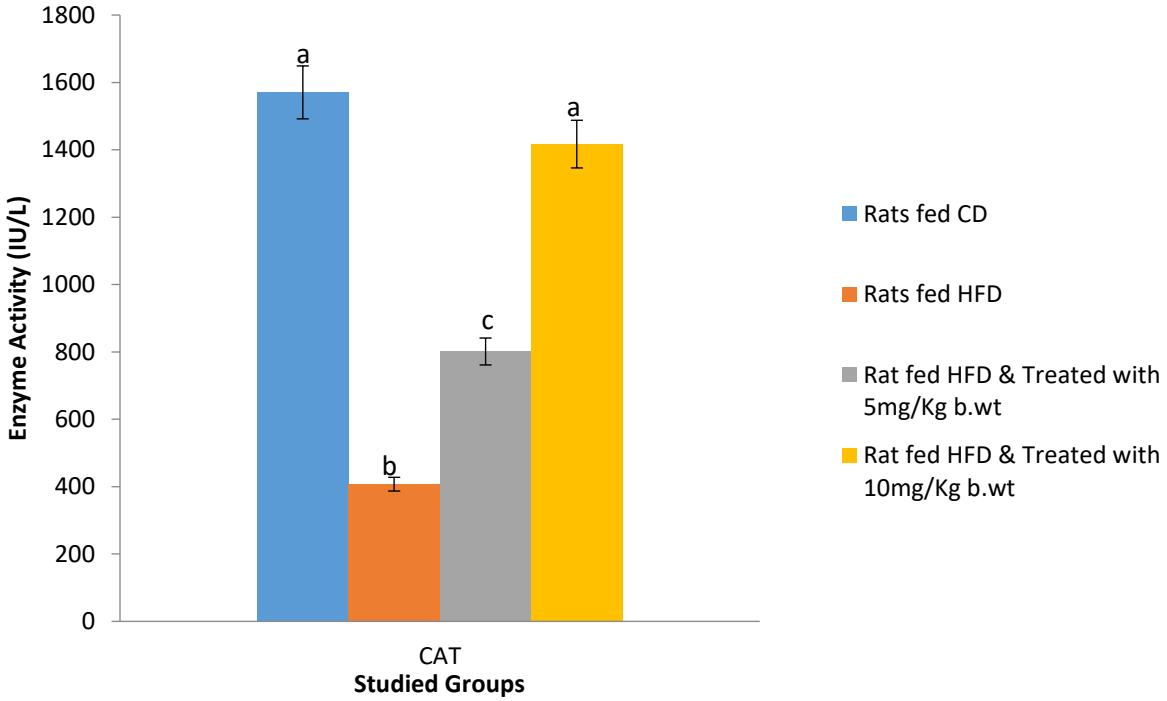

Figure 3: Effect of oral administration of *Tapinanthus brunneus* aqueous leaf extract on liver homogenate catalase (CAT) activity in hypercholesterolemic rats

Note: CD (control diet), HFD (high-fat diet), and CAT (catalase). The values with different superscript letters in the same column indicate significant differences at $p < 0.05$

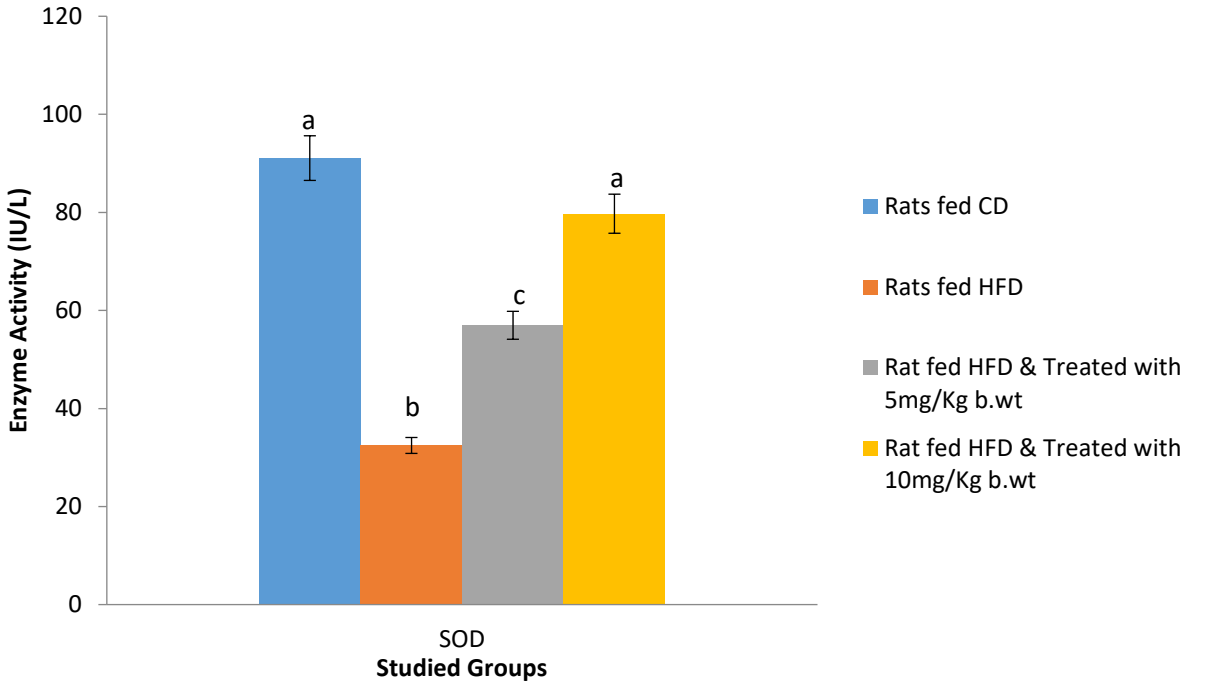

Figure 4: Effect of oral administration of *Tapinanthus brunneus* aqueous leaves extract on liver homogenate level of Superoxide dismutase (SOD) in hypercholesterolemic rats

Note: CD (control diet), HFD (high-fat diet), SOD (superoxide dismutase). The values with different superscript letters in the same column indicate significant differences at $p < 0.05$.

DISCUSSION

The present study provides compelling evidence that the aqueous leaf extract of *Tapinanthus brunneus* exerts significant antihyperlipidemic and antioxidant effects in a model of diet-induced hypercholesterolemia. The high-fat diet (HFD) employed in this study successfully induced a dyslipidemic state, as reflected by elevated serum total cholesterol (TC), triglycerides (TAG), low-density lipoprotein cholesterol (LDL-c), and very-low-density lipoprotein cholesterol (VLDL-c), alongside a reduction in high-density lipoprotein cholesterol (HDL-c). These alterations are consistent with the established biochemical phenotype of experimental hypercholesterolemia (Fidèle *et al*., 2017) and reflect a disruption in lipid homeostasis driven by increased intestinal cholesterol absorption, enhanced hepatic lipogenesis, and impaired reverse cholesterol transport (Fidèle *et al*., 2017). Such metabolic disturbances are central to the pathogenesis of atherosclerosis and cardiovascular disease.

The significant attenuation of TC and TAG levels following administration of *T. brunneus* extract suggests a potent hypolipidemic effect, may be attributed to modulation of key regulatory pathways involved in lipid metabolism. Previous studies have established that plant-derived hypocholesterolemic agents may exert their effects through multiple mechanisms, including inhibition of intestinal lipid absorption, upregulation of hepatic LDL receptor expression, and suppression of cholesterol biosynthesis via inhibition of rate-limiting enzymes such as HMG-CoA reductase (Ibrahim *et al*., 2020). In addition, activation of AMP-activated protein kinase (AMPK), a critical energy sensor, may contribute to the observed effects by suppressing lipogenic gene expression and promoting fatty acid oxidation. AMPK activation is known to downregulate sterol regulatory element-binding protein-1c (SREBP-1c), a transcription factor that controls the expression of genes involved in fatty acid and triglyceride synthesis (Fang *et al*., 2022). Consequently, suppression of SREBP-mediated pathways could reduce hepatic lipogenesis and VLDL production, thereby lowering circulating lipid levels (Fang *et al*., 2022).

Furthermore, upregulation of hepatic LDL receptor expression may enhance clearance of circulating LDL-c, contributing to the observed reduction in atherogenic lipoproteins (Zegeye *et al*., 2023). Although the specific phytochemical constituents of *T. brunneus* were not characterized in this study, the lipid-lowering effects observed are consistent with those reported for flavonoid-rich plant extracts,

suggesting that polyphenolic compounds may play a central role in mediating these effects.

In addition to dyslipidemia, hypercholesterolemia is known to induce oxidative stress through excessive generation of reactive oxygen species (ROS), leading to lipid peroxidation and cellular damage. This oxidative burden often overwhelms endogenous antioxidant defense systems, including enzymes such as superoxide dismutase (SOD) and catalase (CAT) (Olorunnisola *et al*., 2012). In the present study, HFD feeding significantly reduced hepatic SOD and CAT activities, indicating a state of oxidative imbalance. This reduction may be attributed to increased utilization of these enzymes in detoxifying ROS generated under hyperlipidemic conditions (Jiangwei *et al*., 2011), as well as impaired regeneration of antioxidant systems (Venkateshan *et al*., 2016).

Interestingly, treatment with *T. brunneus* extract significantly restored SOD and CAT activities, with the higher dose (10 mg/kg body weight) producing effects comparable to the control group. This suggests that the extract possesses potent antioxidant properties, likely mediated through both direct and indirect mechanisms. Direct scavenging of ROS by phytochemicals such as flavonoids and phenolic acids may reduce oxidative damage, which is supported by the findings of Salvamani *et al*. (2016), who reported the presence of flavonoids such as quercetin and catechin in *Amaranthus viridis* leaf extract, contributing to its hypocholesterolemic and anti-atherosclerotic properties. While indirect mechanisms may involve activation of endogenous antioxidant pathways for instance, plant-derived compounds have been shown to activate nuclear factor erythroid 2–related factor 2 (Nrf2), a transcription factor that regulates the expression of antioxidant enzymes, thereby enhancing cellular defense against oxidative stress (Wu *et al*., 2022). By reducing ROS accumulation and limiting lipid peroxidation, the antioxidant action of *T. brunneus* may prevent oxidative modification of LDL particles, thereby mitigating atherogenesis. This dual modulation of lipid profile and oxidative stress provides a strong mechanistic basis for its protective effects against diet-induced metabolic disturbances.

In addition to oxidative stress, inflammatory signaling pathways play a crucial role in the progression of hypercholesterolemia-induced vascular damage. Activation of nuclear factor-kappa B (NF-κB) under oxidative conditions leads to increased expression of pro-inflammatory cytokines and adhesion molecules, thereby promoting endothelial dysfunction and atherogenesis. It is plausible that the antioxidant activity of *T. brunneus* extract may indirectly suppress NF-κB activation by reducing ROS levels, thereby attenuating inflammatory responses. Although this mechanism was not directly investigated in the present study, it provides a potential link between the antioxidant and anti-atherogenic effects of the extract.

Furthermore, the observed increase in HDL-c levels in extract-treated groups further supports its cardioprotective potential. HDL-c plays a critical role in reverse cholesterol transport, facilitating the removal of excess cholesterol from peripheral tissues and its delivery to the liver for excretion. In addition, HDL exhibits anti-inflammatory and antioxidative properties, contributing to vascular protection (Nagao *et al*., 2018). The elevation in HDL-c may be mediated by increased synthesis of apolipoprotein A-I (apo A-I) and enhanced activity of lecithin-cholesterol acyltransferase (LCAT), which are essential for HDL maturation and function (Kontush & Chapman, 2006).

The dose-dependent effects observed in this study, with the 10 mg/kg body weight group demonstrating superior efficacy, highlight the importance of optimizing dosage to achieve maximal therapeutic benefit. This observation is consistent with pharmacokinetic and pharmacodynamic principles governing drug action (Brossard *et al*., 2013). However, extrapolation of these findings to human application requires careful consideration of interspecies differences in metabolism, body surface area, and pharmacokinetics.

Importantly, the multi-targeted mode of action exhibited by *T. brunneus* distinguishes it from conventional lipid-lowering agents such as statins, which primarily inhibit cholesterol biosynthesis. While statins are effective, their long-term use is associated with adverse effects, underscoring the need for alternative therapies with improved safety profiles. The ability of *T. brunneus* to simultaneously modulate lipid metabolism, enhance antioxidant defense, and potentially attenuate inflammatory signaling suggests a broader therapeutic spectrum.

In conclusion, the present study provides mechanistic insight into the antihyperlipidemic and antioxidant effects of *Tapinanthus brunneus*, highlighting its potential as a complementary therapeutic agent for the management of hypercholesterolemia. Future studies should focus on identifying the bioactive constituents responsible for these effects, elucidating molecular pathways such as AMPK/SREBP and NF-κB signaling in greater detail, and evaluating long-term safety and efficacy in clinical settings.

REFERENCES

Afrose, S., Khan, M. I., Eva, E. O., & Mahbub, M. I. (2019). Comparison of Lipid Lowering Effect of Aqueous Extract of Cinnamon (Cinnamomum Cassiae) with that of Rosuvastatin on Experimentally Induced Hypercholesterolaemic Rats. *TAJ: Journal of Teachers Association*, *31*(1), 52–61. https://doi.org/10.3329/taj.v31i1.41573

Ai, A.-S., Ha, E.-R., & Mn, A.-S. (2020). The aqueous extract of Christ's thorn (Ziziphus spina-christi) seed modulates hyperlipidemia in hypercholesterolemic male rat. *Biomed Res*, *31*(3).

Bignon, J., Bénéchie, M., Herlem, D., Liu, J.-M., Pinault, A., Khuong-Huu, F., & Wdzieczak-Bakala, J. (2009). A novel iodomethylene-dimethyl-dihydropyranone induces G2/M arrest and apoptosis in human cancer cells. *Anticancer Research*, *29*(6), 1963–1969.

Brossard, P., Derendorf, H., Xu, J., Maatouk, H., Halabi, A., & Dingemanse, J. (2013). Pharmacokinetics and pharmacodynamics of ponesimod, a selective $S1P_1$ receptor modulator, in the first-in-human study. *British Journal of Clinical Pharmacology*, *76*(6), 888–896. https://doi.org/10.1111/bcp.12129

Duan, Y., Guo, F., Li, C., Xiang, D., Gong, M., Yi, H., Chen, L., Yan, L., Zhang, D., Dai, L., Liu, X., & Wang, Z. (2024). Aqueous extract of fermented Eucommia ulmoides leaves alleviates hyperlipidemia by maintaining gut homeostasis and modulating metabolism in high-fat diet fed rats. *Phytomedicine*, *128*, 155291. https://doi.org/10.1016/j.phymed.2023.155291

El Rabey, H. A., Attia, E. S., Bakry, N., Rezk, S. M., & Sharfeldin, A. Y. (2025). Comparison between the protective effect of the orally administered atorvastatin and safflower (Carthamus tinctorius) in hypercholesterolemic male rats. *Frontiers in Pharmacology*, *16*, 1663717. https://doi.org/10.3389/fphar.2025.1663717

Fang, C., Pan, J., Qu, N., Lei, Y., Han, J., Zhang, J. and Han, D., (2022). The AMPK pathway in fatty liver disease. *Frontiers in physiology*, *13*, p.970292.

Fidèle, N., Joseph, B., Emmanuel, T., & Théophile, D. (2017). Hypolipidemic, antioxidant and anti-atherosclerogenic effect of aqueous extract leaves of Cassia. Occidentalis Linn (Caesalpiniaceae) in diet-induced hypercholesterolemic rats. *BMC Complementary and Alternative Medicine*, *17*(1), 76. https://doi.org/10.1186/s12906-017-1566-x

Ibrahim, A., Shafie, N. H., Mohd Esa, N., Shafie, S. R., Bahari, H., & Abdullah, M. A. (2020). Mikania micrantha Extract Inhibits HMG-CoA Reductase and ACAT2 and Ameliorates Hypercholesterolemia and Lipid Peroxidation in High Cholesterol-Fed Rats. *Nutrients*, *12*(10), 3077. https://doi.org/10.3390/nu12103077

Jiangwei, M., Zengyong, Q., & Xia, X. (n.d.). *Aqueous extract of Astragalus mongholicus ameliorates high cholesterol diet induced oxidative injury in experimental rats models*.

Kontush, A., & Chapman, M. J. (2006). Functionally Defective High-Density Lipoprotein: A New Therapeutic Target at the Crossroads of Dyslipidemia, Inflammation, and Atherosclerosis. *Pharmacological Reviews*, *58*(3), 342–374. https://doi.org/10.1124/pr.58.3.1

Lv, C., Liu, X., Chen, S., Yi, Y., Wen, X., Li, T., & Qin, S. (2024). Extract of Gardenia jasminoides Ellis Attenuates High-Fat Diet-Induced Glycolipid Metabolism Disorder in Rats by Targeting Gut Microbiota and TLR4/Myd88/NF-κB Pathway. *Antioxidants*, *13*(3), 293. https://doi.org/10.3390/antiox13030293

Nagao, M., Nakajima, H., Toh, R., Hirata, K., & Ishida, T. (2018). Cardioprotective Effects of High-Density Lipoprotein Beyond its Anti-Atherogenic Action. *Journal of Atherosclerosis and Thrombosis*, *25*(10), 985–993. https://doi.org/10.5551/jat.RV17025

Ntchapda, F., Tchatchouang, F. C., Miaffo, D., Maidadi, B., Vecchio, L., Talla, R. E., Bonabe, C., Seke Etet, P. F., & Dimo, T. (2021). Hypolipidemic and anti-atherosclerogenic effects of aqueous extract of Ipomoea batatas leaves in diet-induced hypercholesterolemic rats. *Journal of Integrative Medicine*, *19*(3), 243–250. https://doi.org/10.1016/j.joim.2021.02.002

Olorunnisola, O. S., Bradley, G., & Afolayan, A. J. (2012). Protective Effect of T. violacea Rhizome Extract Against Hypercholesterolemia-Induced Oxidative Stress in Wistar Rats. *Molecules*, *17*(5), 6033–6045. https://doi.org/10.3390/molecules17056033

Ouedraogo, M., Carreyre, H., Vandebrouck, C., Bescond, J., Raymond, G., Guissou, I.-P., Cognard, C., Becq, F., Potreau, D., Cousson, A., Marrot, J., & Coustard, J.-M. (2007). Structure Elucidation of a Dihydropyranone from *Tapinanthus dodoneifolius*. *Journal of Natural Products*, *70*(12), 2006–2009. https://doi.org/10.1021/np070355x

Prasad, K., & Mishra, M. (2022). Mechanism of Hypercholesterolemia-Induced Atherosclerosis. *Reviews in Cardiovascular Medicine*, *23*(6), 212. https://doi.org/10.31083/j.rcm2306212

Rachmawati, N. A., Wasita, B., & Kartikasari, L. R. (2019). Basil Leaves (Ocimum sanctum linn.) Extract

Decreases Total Cholesterol Levels in Hypercholesterolemia Sprague Dawley Rats Model. *IOP Conference Series: Materials Science and Engineering*, *546*(6), 062020. https://doi.org/10.1088/1757-899X/546/6/062020

Salvamani, S., Gunasekaran, B., Shukor, M. Y., Abu Bakar, Md. Z., & Ahmad, S. A. (2016). Phytochemical investigation, hypocholesterolemic and anti-atherosclerotic effects of Amaranthus viridis leaf extract in hypercholesterolemia-induced rabbits. *RSC Advances*, *6*(39), 32685–32696. https://doi.org/10.1039/C6RA04827G

Srinivasan, K. (2013). Dietary spices as beneficial modulators of lipid profile in conditions of metabolic disorders and diseases. *Food & Function*, *4*(4), 503. https://doi.org/10.1039/c2fo30249g

Venkateshan, S., Subramaniyan, V., Chinnasamy, V., & Chandiran, S. (2016). Anti-oxidant and anti-hyperlipidemic activity of Hemidesmus indicus in rats fed with high-fat diet. *Avicenna Journal of Phytomedicine*, *6*(5), 516–525.

Wang, L., Kong, D., Tian, J., Zhao, W., Chen, Y., An, Y., Liu, X., Wang, F., Cai, F., Sun, X., Liu, Q., Zhang, W., Tian, J., & Zhou, H. (2022). Tapinanthus species: A review of botany and biology, secondary metabolites, ethnomedical uses, current pharmacology and toxicology. *Journal of Ethnopharmacology*, *296*, 115462. https://doi.org/10.1016/j.jep.2022.115462

Wu, X., Wei, J., Yi, Y., Gong, Q. and Gao, J., (2022). Activation of Nrf2 signaling: A key molecular mechanism of protection against cardiovascular diseases by natural products. *Frontiers in pharmacology*, *13*, p.1057918.

Zegeye, M.M., Nakka, S.S., Andersson, J.S., Söderberg, S., Ljungberg, L.U., Kumawat, A.K. and Sirsjö, A., (2023). Soluble LDL-receptor is induced by TNF-α and inhibits hepatocytic clearance of LDL-cholesterol. *Journal of Molecular Medicine*, *101*(12), pp.1615-1626.