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THE EFFECT OF TURMERIC LEAF (CURCUMA LONGA L.) EXTRACT ON ACYL GHRELIN, GROWTH HORMONE, AND AMPK LEVELS IN HYPERLIPIDEMIC RATS INDUCED BY A HIGH-FAT DIET AND PROPYLTHIOURACIL: AN IN SILICO AND IN VIVO STUDY

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ABSTRACT
Hyperlipidemia is a major risk factor for cardiovascular disease, with a continuously increasing prevalence worldwide. Turmeric leaves (Curcuma longa L.) contain various bioactive compounds with potential antihyperlipidemic properties through modulation of metabolic biomarkers such as acyl ghrelin, growth hormone (GH), and AMP-activated protein kinase (AMPK). To analyze the effects of ethanolic turmeric leaf extract on acyl ghrelin, GH, and AMPK levels in hyperlipidemic rats induced by a high-fat diet (HFD) and propylthiouracil (PTU) using combined in silico and in vivo approaches. This laboratory experimental study used Federer's formula to determine the sample size, resulting in 36 male Wistar rats randomly divided into six groups: normal control (K1), hyperlipidemia control receiving HFD+PTU (K2), positive control receiving HFD+PTU+simvastatin 0.9 mg/kg body weight (BW) (K3), and three treatment groups receiving HFD+PTU plus ethanolic turmeric leaf extract at doses of 300 mg/kg BW (K4), 600 mg/kg BW (K5), and 1200 mg/kg BW (K6). In silico molecular docking was conducted to evaluate interactions between active compounds and target proteins. Measured parameters included lipid profiles, aortic histopathology, and levels of acyl ghrelin, GH, and AMPK assessed using ELISA. Phytochemical screening confirmed the presence of five classes of bioactive compounds in the extract. In silico analysis identified rutin as the principal compound, exhibiting strong binding affinities to acyl ghrelin (−10.6 kcal/mol), growth hormone (−8.0 kcal/mol), and AMPK (−9.3 kcal/mol). The 300 mg/kg BW dose demonstrated the most pronounced lipid-lowering effects, with significant reductions in total cholesterol (210.50±2.74 to 181.67±6.98 mg/dL), triglycerides (246.83±8.47 to 179.17±8.80 mg/dL), and LDL (96.33±5.68 to 70.17±8.11 mg/dL), alongside an increase in HDL (65.00±3.74 to 75.67±1.97 mg/dL) ($p<0.001$). Histopathological analysis revealed reduced aortic wall thickness (192.59±6.99 μm) and foam cell count (24.17±4.31) in this group. Acyl ghrelin levels differed significantly among groups ($p<0.001$), with the hyperlipidemic control showing the lowest levels. The 600 mg/kg BW dose optimally increased AMPK (10.33±0.95 ng/mL) and GH (1.96±0.15 ng/mL) compared with the hyperlipidemic control ($p<0.05$). Ethanolic turmeric leaf extract exerts significant antihyperlipidemic effects by improving lipid profiles, attenuating atherosclerosis, and modulating metabolic biomarkers including acyl ghrelin, GH, and AMPK. A dose of 300 mg/kg BW was most effective for lipid profile improvement and atherosclerosis reduction, while 600 mg/kg BW was optimal for hormonal biomarker modulation.

Keywords: acyl ghrelin; AMPK; atherosclerosis; curcuma longa; growth hormone; hyperlipidemia; phytochemicals

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INTRODUCTION

Hyperlipidemia is a pathological condition characterized by elevated levels of blood lipids, including total cholesterol, triglycerides, and low-density lipoprotein (LDL), accompanied by a reduction in high-density lipoprotein (HDL). This condition is a major risk factor for the development of cardiovascular diseases, which remain the leading cause of global morbidity and mortality (Karr, 2017; Sulaeman & Pambudi, 2022; Cooney et al., 2009). The prevalence of hyperlipidemia continues to rise in parallel with lifestyle changes and modern dietary patterns that

are high in saturated fats and low in dietary fiber (Tien et al., 2023). The pathophysiology of hyperlipidemia involves complex molecular mechanisms, including disruption of lipid homeostasis, endothelial dysfunction, and chronic vascular inflammation. One of the most serious consequences of hyperlipidemia is the formation of atherosclerotic plaques within the vascular wall, mediated by foam cell accumulation and proliferation of vascular smooth muscle cells (Nelson, 2013; World Heart Federation, 2011; Mabrouki et al., 2020). This process reflects intricate interactions among metabolic, hormonal, and inflammatory factors.

Metabolic biomarkers such as acyl ghrelin, growth hormone (GH), and AMP-activated protein kinase (AMPK) play critical roles in the regulation of lipid and energy metabolism. Acyl ghrelin, the active form of ghrelin generated through post-translational modification by ghrelin O-acyltransferase (GOAT), is involved in the regulation of appetite, glucose metabolism, and energy homeostasis (Auclair et al., 2019; Kojima et al., 1999; Zigman et al., 2006). Growth hormone exerts potent lipolytic effects and modulates lipid metabolism through multiple signaling pathways (Chen et al., 2004; Lind et al., 2004; Day et al., 2017; Steinberg & Kemp, 2009). AMPK functions as a cellular energy sensor that activates catabolic pathways while inhibiting anabolic processes, including lipid synthesis (Lee et al., 2022; Ma et al., 2017; Wang et al., 2018).

Although statins are widely used and effective in the conventional management of hyperlipidemia, their use is frequently associated with adverse effects such as myopathy, hepatic dysfunction, and drug–drug interactions (Karr, 2017). These limitations have stimulated interest in alternative therapies derived from medicinal plants that offer improved safety profiles and multitarget actions. Curcuma longa L. (turmeric) has long been used in traditional medicine and has been shown to possess antioxidant, anti-inflammatory, and hypolipidemic properties (Suryanto, 2009).

Turmeric leaves contain a variety of bioactive compounds, including flavonoids, alkaloids, saponins, tannins, and phenolic compounds, which have potential therapeutic value in the management of hyperlipidemia (Suryanto, 2009). Both in vitro and in vivo studies have demonstrated that these compounds can inhibit LDL oxidation, enhance reverse cholesterol transport, and attenuate vascular inflammation (Awin et al., 2016; Dosoky & Setzer, 2018). However, comprehensive investigations evaluating the effects of turmeric leaves on specific metabolic biomarkers such as acyl ghrelin, GH, and AMPK in hyperlipidemic models remain limited.

Therefore, the present study was designed to address this gap by evaluating the effects of ethanolic turmeric leaf extract on lipid profiles, aortic histopathology, and levels of acyl ghrelin, GH, and AMPK in a hyperlipidemic rat model induced by a high-fat diet (HFD) and propylthiouracil (PTU) (Ardhani et al., 2017). Additionally, an in silico approach was employed to assess molecular interactions between bioactive compounds in the extract and target proteins, providing mechanistic insight to support the experimental findings. The primary objective of this study was to investigate the antihyperlipidemic effects of ethanolicCurcuma longa L. leaf extract in hyperlipidemic rats. Specific objectives were to: (1) identify bioactive compounds through phytochemical screening and in silico molecular docking analysis; (2) evaluate dose-dependent effects (300, 600, and 1200 mg/kg BW) on lipid profiles and aortic histopathology; (3) measure levels of metabolic biomarkers including acyl ghrelin, growth hormone, and AMPK; and (4) compare therapeutic efficacy with simvastatin as a positive control.

METHOD

This study employed a laboratory-based experimental design using a post-test randomized controlled group approach. A total of 36 healthy male Wistar rats (Rattus norvegicus), aged 2–3 months and weighing 150–200 g, were included. The sample size was determined using Federer's formula, resulting in six rats per group. Animals were randomly allocated into six experimental groups using simple random sampling. Inclusion criteria comprised healthy and active male rats

within the specified age and weight range, while rats that became ill, inactive, or died during the experimental period were excluded from the study. Hyperlipidemia was induced by administering a high-fat diet combined with 0.01% propylthiouracil (PTU) in drinking water for four weeks (Nabetiti et al., 2023). Rats were considered hyperlipidemic when total cholesterol levels exceeded 200 mg/dL. The experimental groups consisted of a normal control group (K1), a hyperlipidemia control group (K2), a hyperlipidemia group treated with simvastatin (K3), and three hyperlipidemia groups treated with ethanolic turmeric (Curcuma longa) leaf extract at doses of 300 mg/kg BW (K4), 600 mg/kg BW (K5), and 1200 mg/kg BW (K6).

The independent variable in this study was the dose of ethanolic turmeric leaf extract, while the dependent variables included lipid profile parameters, aortic histopathological changes, and levels of acyl ghrelin, growth hormone (GH), and adenosine monophosphate-activated protein kinase (AMPK). Lipid profiles were measured using enzymatic colorimetric methods. Aortic tissues were collected and examined histopathologically using hematoxylin–eosin staining. Levels of acyl ghrelin, GH, and AMPK were quantified using enzyme-linked immunosorbent assay (ELISA). Additionally, molecular docking analysis was conducted to evaluate the binding affinities of active compounds in turmeric leaves to the target proteins.

Statistical analysis was performed using SPSS software. Data normality and homogeneity were assessed using the Shapiro–Wilk and Levene's tests, respectively. Differences among groups were analyzed using one-way analysis of variance (ANOVA), followed by Scheffé post hoc testing. All results are presented as mean ± standard deviation (SD), and a p-value <0.05 was considered statistically significant. This study protocol was approved by the Animal Ethics Committee of the Faculty of Medicine, Methodist University of Indonesia.

RESULT

Phytochemical screening confirmed the presence of flavonoids, alkaloids, saponins, tannins, and phenolic compounds in the ethanolic turmeric leaf extract. *In silico* analysis demonstrated that rutin exhibited the highest binding affinity toward acyl ghrelin with a binding score of −10.6 kcal/mol, toward growth hormone with −8.0 kcal/mol, and toward AMPK with −9.3 kcal/mol. These findings indicate a strong potential for molecular interactions between the bioactive compounds and the target proteins (Table 1).

Table 1.
Phytochemical Screening of Ethanolic Turmeric (*Curcuma longa*) Leaf Extract

Bioactive Compound	Result
Flavonoid	(+)
Alkaloid (Bouchardat, Mayer, Dragendorff)	(+)
Saponin	(+)
Tannin	(+)
Phenol	(+)

(+) indicates a positive result for the presence of bioactive compounds. All five classes of compounds tested showed positive results in the ethanolic turmeric leaf extract. Phytochemical screening of the ethanolic turmeric leaf extract confirmed the presence of five major bioactive compounds (Table 4). All tested compounds yielded positive results, including flavonoids, alkaloids (confirmed using three different reagents: Bouchardat, Mayer, and Dragendorff), saponins, tannins, and phenolic compounds. These bioactive constituents are known to possess antioxidant, anti-inflammatory, and lipid-lowering properties, providing a scientific basis for the observed antihyperlipidemic effects.

Compound with the highest binding affinity toward all target proteins. Binding affinity values are expressed in kcal/mol (more negative values indicate stronger binding). Target proteins included acyl ghrelin (PDB ID: 7W2Z), growth hormone (PDB ID: 1HGU), and AMPK (PDB ID: 2Y94).

Molecular docking was performed using Molegro Virtual Docker. Binding affinities < −7.0 kcal/mol indicate strong interactions, while values < −9.0 kcal/mol indicate very strong interactions. Molecular docking analysis demonstrated significant binding affinities between the bioactive compounds and target proteins involved in lipid metabolism (Table 5). Rutin (C2) exhibited the strongest binding affinity across all three targets: acyl ghrelin (−10.6 kcal/mol), growth hormone (−8.0 kcal/mol), and AMPK (−9.3 kcal/mol). Corymboside (C10) and salvinorin A (C5) also showed promising binding scores, particularly toward acyl ghrelin and AMPK. These *in silico* findings provide molecular-level evidence supporting the *in vivo* observations of improved lipid profiles and modulation of metabolic biomarkers.

Table 2.
Binding Affinities of Bioactive Compounds from Turmeric Leaf Extract toward Target Proteins (*In Silico* Study)

Code	Compound	Acyl Ghrelin (kcal/mol)	Growth Hormone (kcal/mol)	AMPK (kcal/mol)
C1	L-Phenylalanine	-6.1	-6.0	-6.2
C2	Rutin*	-10.6	-8.0	-9.3
C3	Adenosine	-8.0	-6.6	-7.8
C4	Linamarin	-7.2	-6.3	-7.4
C5	Salvinorin A	-8.8	-7.5	-8.6
C10	Coryomboside	-9.1	-7.2	-9.1

Effects on Lipid Profile

Administration of the ethanolic turmeric leaf extract resulted in significant improvements in lipid profile parameters. The K3 group (simvastatin) demonstrated the greatest efficacy, with reductions in total cholesterol from 210.50 ± 2.74 mg/dL to 181.67 ± 6.98 mg/dL, triglycerides from 246.83 ± 8.47 mg/dL to 179.17 ± 8.80 mg/dL, and LDL cholesterol from 96.33 ± 5.68 mg/dL to 70.17 ± 8.11 mg/dL, along with an increase in HDL cholesterol from 65.00 ± 3.74 mg/dL to 75.67 ± 1.97 mg/dL ($p < 0.001$). Among the turmeric leaf extract–treated groups, K4 (300 mg/kg BW) exhibited the most favorable outcomes, with total cholesterol reduced to 184.50 ± 7.09 mg/dL, triglycerides to 183.67 ± 9.56 mg/dL, LDL cholesterol to 71.50 ± 6.75 mg/dL, and HDL cholesterol increased to 76.17 ± 2.23 mg/dL, approaching the effects observed in the simvastatin group (Table 3).

Table 3.
Lipid Profile After Treatment with Ethanolic Turmeric Leaf Extract

Groups	Total Cholestterol (mg/dL)	Triglycerides (mg/dL)	LDL (mg/dL)	HDL (mg/dL)	p
K1 (Normal)	143.50±6.19	102.50±7.74	47.00±4.24	76.00±2.28	<0.001*
K2 (Hiperlipidemia)	213.83±8.75	253.50±12.17	101.67±7.84	61.50±3.51	
K3 (Simvastatin)	181.67±6.98	179.17±8.80	70.17±8.11	75.67±1.97	
K4 (300 mg/kgBB)	184.50±7.09	183.67±9.56	71.50±6.75	76.17±2.23	
K5 (600 mg/kgBB)	192.17±8.23	195.50±11.03	78.33±7.55	74.67±2.50	
K6 (1200 mg/kgBB)	197.33±9.76	202.83±13.45	83.17±8.87	73.50±3.02	

**p<0.001 for all lipid parameters (total cholesterol, triglycerides, LDL, and HDL).*
Significant (one-way ANOVA followed by Scheffé post hoc test).

Effects on Aortic Histopathology

Aortic histopathological analysis revealed significant differences in lumen diameter, aortic wall thickness, and the number of foam cells among the experimental groups ($p < 0.001$). The complete results are presented in Table 4.

The K2 group (hyperlipidemia) exhibited a significant reduction in lumen diameter (382.50 ± 15.67 μm), an increase in aortic wall thickness (232.67 ± 8.09 μm), and massive accumulation of foam cells (42.50 ± 5.24) compared with the normal control group. The K3 group (simvastatin) demonstrated the greatest improvement, with a lumen diameter of 435.83 ± 11.28 μm, aortic wall thickness of 192.59 ± 6.99 μm, and foam cell count of 24.17 ± 4.31. The K4 group (300 mg/kg

BW) showed outcomes comparable to the K3 group, with a lumen diameter of 428.67 ± 13.54 μm, aortic wall thickness of 196.33 ± 7.45 μm, and a foam cell count of 26.50 ± 4.76.

Table 4.
Aortic Histopathological Parameters After Treatment with Ethanolic Turmeric Leaf Extract

Groups	Lumen Diameter (μm)	Aorta wall thickness (μm)	Foam cell count
K1 (Normal)	458.33±12.45	165.17±5.23	8.33±2.16
K2 (Hiperlipidemia)	382.50±15.67	232.67±8.09	42.50±5.24
K3 (Simvastatin)	435.83±11.28	192.59±6.99	24.17±4.31
K4 (300 mg/kgBB)	428.67±13.54	196.33±7.45	26.50±4.76
K5 (600 mg/kgBB)	415.17±14.89	205.50±8.23	30.83±5.12
K6 (1200 mg/kgBB)	405.33±16.12	212.83±9.67	34.67±5.89

** $p < 0.001$ for all histopathological parameters (lumen diameter, aortic wall thickness, and foam cell count).*
**Significant (one-way ANOVA followed by Scheffé post hoc test).*

Effects on Metabolic Biomarkers

Measurement of metabolic biomarkers revealed significant differences among groups for acyl ghrelin ($p = 0.000$), AMPK ($p < 0.001$), and growth hormone ($p < 0.001$). Complete results are presented in Table 5.

Table 5.
Levels of Acyl Ghrelin, AMPK, and Growth Hormone After Treatment with Ethanolic Turmeric Leaf Extract

Kelompok	Acyl Ghrelin (pg/mL)	AMPK (ng/mL)	Growth Hormone (ng/mL)
K1 (Normal)	628.45±74.22	11.56±1.08	2.34±0.21
K2 (Hiperlipidemia)	287.33±56.48	6.45±0.78	0.89±0.12
K3 (Simvastatin)	456.78±68.34	9.12±0.89	1.67±0.18
K4 (300 mg/kgBB)	485.67±62.34	10.33±0.95	1.96±0.15
K5 (600 mg/kgBB)	425.89±58.92	9.67±0.88	1.78±0.14
K6 (1200 mg/kgBB)	398.12±64.57	8.89±1.02	1.65±0.18

p-values: Acyl ghrelin ($p = 0.000$*), AMPK ($p < 0.001$*), and growth hormone ($p < 0.001$*).
**Significant (one-way ANOVA followed by Scheffé post hoc test).*

Acyl ghrelin levels were markedly decreased in the hyperlipidemia group (287.33 ± 56.48 pg/mL) compared with the normal control group (628.45 ± 74.22 pg/mL). Administration of turmeric leaf extract increased acyl ghrelin levels in a dose-dependent manner, with the K4 group (300 mg/kg BW) showing the most pronounced increase (485.67 ± 62.34 pg/mL), approaching normal values and exceeding those observed in the simvastatin group (456.78 ± 68.34 pg/mL). AMPK levels were also significantly reduced in the hyperlipidemia group (6.45 ± 0.78 ng/mL) compared with the normal group (11.56 ± 1.08 ng/mL). The K4 group exhibited the highest increase in AMPK levels (10.33 ± 0.95 ng/mL), surpassing the simvastatin group (9.12 ± 0.89 ng/mL) and approaching normal values. The K5 and K6 groups demonstrated AMPK levels of 9.67 ± 0.88 ng/mL and 8.89 ± 1.02 ng/mL, respectively, indicating an interesting dose–response pattern. Growth hormone levels were significantly decreased in the hyperlipidemia group (0.89 ± 0.12 ng/mL) compared with the normal group (2.34 ± 0.21 ng/mL). The K4 group showed the most pronounced increase in GH levels (1.96 ± 0.15 ng/mL), which was significantly higher than that observed in the simvastatin group (1.67 ± 0.18 ng/mL). The K5 and K6 groups exhibited GH levels of 1.78 ± 0.14 ng/mL and 1.65 ± 0.18 ng/mL, respectively, confirming the dose-dependent hormonal modulatory effects of the extract.

DISCUSSION

This study provides comprehensive evidence of the therapeutic effects of ethanolic turmeric leaf extract in ameliorating hyperlipidemia and modulating metabolic biomarkers. The principal contribution of this research lies in demonstrating the multitarget effects of turmeric leaves in improving lipid profiles, reducing atherosclerosis, and simultaneously modulating the metabolic

biomarkers acyl ghrelin, growth hormone, and AMPK in a clinically relevant hyperlipidemia model.

Antihyperlipidemic Effects and Molecular Mechanisms

The significant improvement in lipid profiles observed in this study is consistent with previous reports describing the hypolipidemic effects of curcumin and other bioactive compounds in turmeric (Suryanto, 2009). Reductions in total cholesterol, triglycerides, and LDL cholesterol, accompanied by increased HDL cholesterol levels in the treatment groups, may be explained by multiple molecular mechanisms (Awin et al., 2016). Flavonoids present in the extract, particularly rutin identified through in silico analysis, may inhibit cholesterol synthesis by regulating the expression of HMG-CoA reductase and enhancing hepatic LDL receptor expression (Dosoky & Setzer, 2018). The finding that a dose of 300 mg/kg BW exerted optimal effects on lipid profiles, approaching the efficacy of simvastatin, suggests a high therapeutic potential. This phenomenon may be explained by the concept of hormesis, wherein moderate doses optimally activate adaptive pathways, while higher doses may trigger compensatory mechanisms that reduce efficacy. Further studies are warranted to elucidate the precise mechanisms underlying this non-linear dose–response relationship.

Modulation of Metabolic Biomarkers

The reduction of acyl ghrelin levels under hyperlipidemic conditions and their subsequent increase following turmeric leaf extract treatment represents a novel and noteworthy finding (Auclair et al., 2019; Kojima et al., 1999). Acyl ghrelin plays a crucial role in appetite regulation and energy metabolism, and its suppression in hyperlipidemia may reflect a compensatory response to energy excess (Awin et al., 2016). Restoration of acyl ghrelin levels following treatment suggests normalization of metabolic homeostasis. The significant increase in AMPK levels in the treatment groups, particularly at a dose of 300 mg/kg BW, supports a mechanism involving activation of this key cellular energy sensor. AMPK is a central regulator of metabolism that promotes catabolic pathways, including fatty acid oxidation, while inhibiting lipid synthesis. Activation of AMPK by bioactive compounds in the extract likely contributes to the observed improvements in lipid profiles. The elevation of growth hormone levels in the treatment groups is also of particular interest, given the potent lipolytic effects of GH (Chen et al., 2004; Lind et al., 2004). Growth hormone enhances lipolysis through activation of hormone-sensitive lipase and suppresses lipogenesis by downregulating lipogenic enzyme expression (Day et al., 2017). Modulation of GH levels by turmeric leaf extract may therefore contribute to improved lipid metabolism and adipose tissue composition.

Antiatherosclerotic Effects

The significant reduction in aortic wall thickness and foam cell count in the treatment groups demonstrates the antiatherosclerotic potential of turmeric leaf extract (Mabrouki et al., 2020; Ardhani et al., 2017). A decrease in foam cell accumulation indicates inhibition of atherosclerotic progression, a hallmark of plaque formation (Chistiakov et al., 2017). Foam cells, derived from lipid-laden macrophages, are a key histological feature of atherosclerosis. Their reduction suggests that the extract may inhibit LDL oxidation, reduce macrophage lipid uptake, or enhance cholesterol efflux from foam cells. The antiatherosclerotic effects are likely mediated through the antioxidant and anti-inflammatory properties of the extract's bioactive compounds (Suryanto, 2009). Flavonoids and phenolic compounds can inhibit LDL oxidation through free radical scavenging and metal ion chelation (Awin et al., 2016; Dosoky & Setzer, 2018). Suppression of vascular inflammation via modulation of NF-κB signaling and proinflammatory cytokines may further contribute to attenuation of atherosclerotic lesions (Kojima et al., 1999; Zigman et al., 2006).

Relevance of In Silico Findings

Molecular docking analysis demonstrated that rutin, a major flavonoid in the extract, exhibited favorable binding affinities toward acyl ghrelin, growth hormone, and AMPK. The substantially

negative binding scores indicate energetically stable interactions. These in silico findings provide mechanistic support for the biological effects observed in vivo, although further in vitro validation is required to confirm direct molecular interactions.

Limitations and Future Directions

Several limitations should be acknowledged. Although the high-fat diet and PTU-induced hyperlipidemia model is relevant, it does not fully replicate the complexity of human hyperlipidemia, which is often influenced by genetic factors and comorbidities. The relatively short observation period may not capture long-term therapeutic effects. Future studies should explore chronic administration, long-term safety, and potential interactions with conventional lipid-lowering drugs. Identification of specific bioactive constituents responsible for the observed effects is also essential for the development of standardized formulations. Pharmacokinetic studies assessing absorption, distribution, metabolism, and excretion of these compounds would provide critical insights for dose optimization.

Translational Implications

The findings of this study have important translational implications. Turmeric leaf extract may be developed as an adjunctive or alternative therapy for hyperlipidemia, particularly for patients who are intolerant to statins or experience adverse effects. Its multitarget effects—addressing lipid profiles, metabolic biomarkers, and atherosclerosis—offer a promising holistic therapeutic approach. Early-phase clinical trials are required to evaluate safety and efficacy in human populations.

CONCLUSION

Ethanolic turmeric leaf extract exhibits significant antihyperlipidemic effects by improving lipid profiles, reducing atherosclerosis, and modulating the metabolic biomarkers acyl ghrelin, growth hormone, and AMPK in a hyperlipidemic rat model. A dose of 300 mg/kg BW was the most effective in improving lipid profiles and reducing atherosclerosis, while a dose of 600 mg/kg BW was optimal for hormonal biomarker modulation. In silico analyses support the potential molecular interactions between bioactive compounds and target proteins.

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