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Evaluation of Anti-Obesity and Hypolipidemic Effects of Garcinia cambogia Extract in High-Fat Diet-Induced Obese Rats

V.Sandhya[1], Shaheena Sohi[2], J. Sangeetha[3]*, Bhushan Muley[4], Mahesh Kumar Posa[5], V. Amudhavalli[6], Jyothi Basini[7], Kanumaluri Lakshmi Prasanna[8]

[1]Department of pharmaceutical chemistry Faculty of Pharmacy, Sree Balaji Medical College and Hospital campus, Bharath Institute of Higher Education & Research, Chromepet.
Chennai - 44
[2]Universal College of Pharmacy, Lalru, Dera Bassi, Mohali, Punjab Pin code: - 140501
[3]Department of Pharmacognosy, Malla Reddy Institute of Pharmaceutical Sciences, A Constituent College of Malla Reddy Vishwavidyapeeth (Deemed to be University), Maisammaguda, Dhulapally, Secunderabad - 500100.
[4]Shri Rawatpura Sarkar Institute of Pharmacy, Kumhari, Dist Durg - 490 042, India.
[5]Department of Pharmaceutical Technology, School of Health and Medical Sciences, Adamas University, Barasat, Kolkata-700126, West Bengal, India.
[6]School of Pharmacy, Sathyabama institute of science and Technology, Jeppiaar nagar, Rajiv gandhi salai, Chennai 600119.
[7,8]Department of Pharmacology, Seven Hills College of Pharmacy, (Autonomous)
Venkatramapuram, R C Puram (Mandal) Tirupati-517561, Chittoor Dist., Andhra Pradesh, India.
Corresponding Author*
J. Sangeetha3*
Department of Pharmacognosy, Malla Reddy Institute of Pharmaceutical Sciences, A Constituent College of Malla Reddy Vishwavidyapeeth (Deemed to be University), Maisammaguda, Dhulapally, Secunderabad - 500100.
Email id san_geethaj@yahoo.co.in.

ABSTRACT

The present study investigates the anti-obesity and hypolipidemic potential of Garcinia cambogia methanolic extract in high-fat diet (HFD)-induced obese rats. Obesity was induced by feeding rats a high-fat diet for eight weeks, followed by oral administration of G. cambogia extract at doses of 200 mg/kg and 400 mg/kg for six weeks. Orlistat (30 mg/kg) served as the standard reference. Biochemical, molecular, and histopathological analyses were performed to evaluate treatment efficacy. The extract significantly reduced body weight gain and food intake in a dose-dependent manner compared to the HFD control. Serum lipid profile analysis showed a marked decrease in total cholesterol, triglycerides, LDL, and VLDL levels, along with elevated HDL levels. Furthermore, G. cambogia restored hepatic enzyme (ALT and AST) levels and improved liver morphology, indicating hepatoprotective effects. Enhanced antioxidant enzyme activities (SOD, CAT, GSH) and decreased MDA levels confirmed its oxidative stress mitigation potential. Molecular studies revealed downregulation of lipogenic genes (SREBP-1c, PPARγ) and upregulation of CPT-1, supporting enhanced fatty acid oxidation. Histopathological analysis showed reduced adipocyte size and hepatic steatosis in treated groups. These findings suggest that Garcinia cambogia exhibits potent anti-obesity and lipid-regulating activities through multiple mechanisms, offering a natural and safe alternative for obesity management. Future research should focus on clinical validation, standardized formulations, and long-term safety assessments to facilitate its therapeutic application in humans. These findings establish G. cambogia as a promising candidate for the development of natural, safe, and effective anti-obesity therapies.

KEYWORDS: Garcinia cambogia, Hydroxycitric acid, High-fat diet, Anti-obesity, Hypolipidemic, Antioxidant.

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INTRODUCTION

Obesity is a multifactorial metabolic disorder that has emerged as one of the most serious public health challenges of the twenty-first century. Characterized by an abnormal accumulation of body fat resulting from an imbalance between energy intake and expenditure, obesity significantly increases the risk of developing cardiovascular diseases, type 2 diabetes mellitus, hypertension, fatty liver disease, and certain types of cancer. The global prevalence of obesity has nearly tripled in the past four decades, and according to the World Health Organization, more than 650 million adults are currently classified as obese (Sarma et al., 2021). The condition not only affects physical health but also exerts a considerable burden on psychological well-being and socioeconomic productivity. Rapid urbanization, sedentary lifestyle patterns, and increased consumption of high-calorie, high-fat, and low-fiber diets have collectively contributed to the rise in obesity and associated metabolic complications worldwide (Geng et al., 2022).

The pathophysiology of obesity involves complex interactions between genetic, environmental, behavioral, and physiological factors. Central to this process is the disruption of energy homeostasis, which is regulated by neuroendocrine mechanisms involving hormones such as leptin, ghrelin, insulin, and neuropeptide Y. Chronic overnutrition leads to hypertrophy and

hyperplasia of adipocytes, resulting in increased lipid storage and expansion of adipose tissue. This excess fat accumulation not only alters metabolic pathways but also induces a pro-inflammatory state characterized by elevated levels of cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) (Lin & Li, 2021). These inflammatory mediators impair insulin signaling, enhance oxidative stress, and promote endothelial dysfunction, establishing a vicious cycle that sustains obesity-related metabolic disturbances. Furthermore, lipid dysregulation, particularly an increase in triglycerides, total cholesterol, and low-density lipoproteins (LDL), contributes to the development of hyperlipidemia and atherosclerosis, aggravating cardiovascular risks (Gadde et al., 2018).

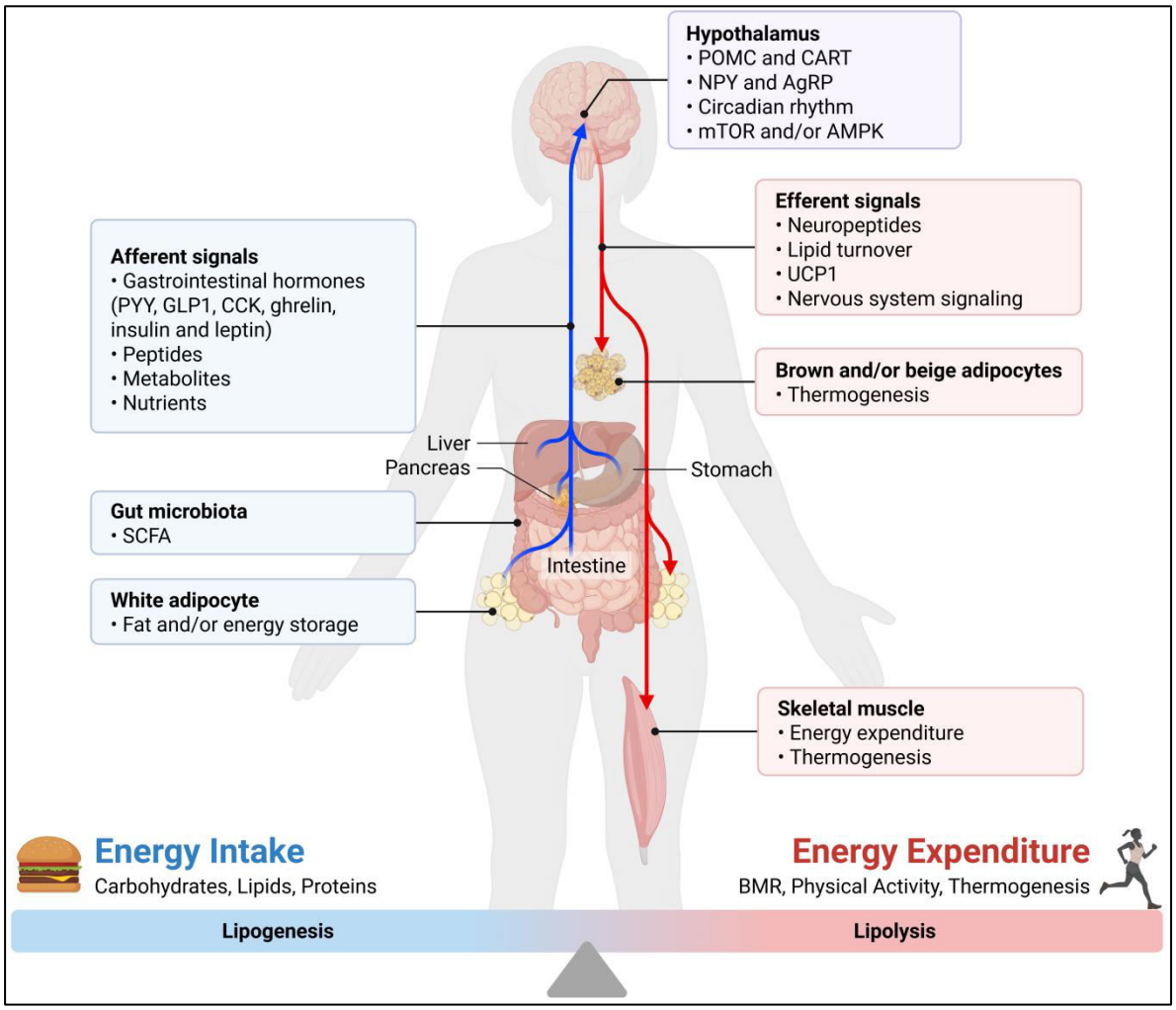


Figure 1: Key Metabolic Mechanisms on Body Weight Regulation

The management of obesity typically involves lifestyle modifications such as dietary restrictions, regular physical activity, and behavioral therapy. However, adherence to these approaches is often poor, and their effectiveness varies among individuals. Pharmacological treatments such as orlistat, sibutramine, and liraglutide have been used to promote weight loss through mechanisms like fat absorption inhibition or appetite suppression. Despite their efficacy, these drugs are associated with adverse effects including gastrointestinal discomfort, insomnia, hypertension, and mood alterations, which limit their long-term use (Gjermeni et al., 2021). Consequently, there is a growing interest in exploring natural alternatives derived from medicinal plants that offer safer and more sustainable solutions for weight management and lipid regulation. The search for plant-based therapeutics has gained momentum, particularly because of their multiple pharmacological activities, minimal side effects, and cost-effectiveness (Pigeyre et al., 2016).

Among various herbal remedies, Garcinia cambogia has attracted significant scientific attention for its potential role in the prevention and treatment of obesity and dyslipidemia. Garcinia cambogia, a tropical fruit belonging to the family Clusiaceae, is commonly found in Southeast Asia, India, and Africa. Its dried rind has been traditionally used as a flavoring agent and in folk medicine to aid digestion and weight reduction (Semwal et al., 2015b). The primary bioactive constituent of Garcinia cambogia is hydroxycitric acid (HCA), which has been identified as a potent inhibitor of the enzyme ATP-citrate lyase. This enzyme catalyzes the conversion of citrate to acetyl coenzyme A, a crucial precursor in fatty acid and cholesterol synthesis. By inhibiting this enzyme, HCA effectively suppresses de novo lipogenesis, thereby reducing the formation of new fat from carbohydrates. In addition, HCA is reported to increase glycogen synthesis in the liver and enhance serotonin levels in the brain, leading to reduced appetite and food intake (Semwal et al., 2015a).

Several preclinical and clinical studies have provided evidence supporting the anti-obesity and hypolipidemic properties of Garcinia cambogia extract. Animal studies have demonstrated that supplementation with HCA significantly decreases body weight gain, reduces visceral fat accumulation, and improves lipid profiles in diet-induced obese models. These effects are attributed to the compound's ability to modulate metabolic enzymes, enhance fatty acid oxidation, and downregulate lipogenic gene expression such as sterol regulatory element-binding protein-1c (SREBP-1c) and peroxisome proliferator-activated receptor gamma (PPARγ) (Onakpoya et al., 2011). Additionally, Garcinia cambogia exhibits antioxidant and anti-inflammatory properties, which further contribute to its beneficial effects on metabolic health. The extract has been shown to increase the activity of endogenous antioxidant enzymes including superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), thereby mitigating oxidative stress-induced cellular damage commonly associated with obesity and dyslipidemia (Tomar, Rao, Dorairaj, Koshta, Suresh, Rafiq, Kumawat, Paramesh, Babu, et al., 2019).

High-fat diet-induced obesity in animal models is widely recognized as an effective experimental approach to mimic human metabolic disorders. Feeding rats with a high-fat diet leads to increased caloric intake, body weight gain, hyperlipidemia, and hepatic lipid accumulation, closely resembling the pathophysiological conditions observed in obese individuals (Al-Omar et al., 2020). Such models provide an excellent platform for evaluating the efficacy of potential anti-obesity and hypolipidemic agents, as they allow the examination of biochemical, molecular, and histopathological changes induced by dietary interventions or pharmacological treatments. Garcinia cambogia extract, when tested in this model, has shown promising results in reducing body weight, improving lipid metabolism, and restoring liver function, thereby validating its therapeutic potential (Tomar, Rao, Dorairaj, Koshta, Suresh, Rafiq, Kumawat, Paramesh, V, et al., 2019). Apart from its role in reducing lipid synthesis, Garcinia cambogia may also influence energy expenditure by enhancing mitochondrial function and promoting β-oxidation of fatty acids. The upregulation of carnitine palmitoyltransferase, an enzyme essential for the transport of long-chain fatty acids into mitochondria for oxidation, supports this hypothesis. Moreover, HCA's ability to elevate serotonin levels may contribute not only to appetite suppression but also to improved mood and reduced emotional eating, which are important behavioral components of obesity management. The combination of metabolic and behavioral effects makes Garcinia cambogia a particularly appealing candidate for integrated obesity control (Lupala et al., 2020).

Despite these encouraging findings, some clinical trials have reported inconsistent results, with variations in outcomes possibly arising from differences in dosage, duration, extract composition, and study design. Nevertheless, the overall body of evidence supports the view that Garcinia cambogia exerts a multifaceted influence on body weight regulation and lipid metabolism. Continuous research focusing on standardized extracts, precise dosing strategies, and mechanistic insights is therefore essential to establish its efficacy and safety for human use (Abu Bakar, 2024). In the context of rising obesity prevalence and the limitations of current therapeutic options, natural products such as Garcinia cambogia offer valuable opportunities for developing safer, more holistic approaches to metabolic health management. Investigating its effects in high-fat diet-induced obese rats not only helps elucidate the biochemical and molecular mechanisms underlying its anti-obesity and hypolipidemic activities but also provides foundational data for future translational and clinical studies (Tian et al., 2021). The present research aims to evaluate the potential of Garcinia cambogia extract in controlling body weight, improving lipid profiles, enhancing antioxidant defenses, and regulating gene expression associated with lipid metabolism in an established model of diet-induced obesity. By exploring these parameters, the study seeks to contribute to the growing evidence base supporting the use of Garcinia cambogia as a natural, effective, and well-tolerated intervention for obesity and hyperlipidemia (Golzarand et al., 2020).

MECHANISM OF ANTI-OBESITY AND HYPOLIPIDEMIC EFFECTS

2.1. Inhibition of Lipogenesis

Hydroxycitric acid (HCA), the primary bioactive compound in *Garcinia cambogia*, plays a crucial role in inhibiting lipogenesis, which is the metabolic process responsible for synthesizing fatty acids from carbohydrates. HCA exerts this effect primarily by competitively inhibiting the cytosolic enzyme ATP-citrate lyase, a key catalyst that converts citrate to acetyl coenzyme A (acetyl-CoA), an essential precursor for fatty acid and cholesterol synthesis. By blocking this enzymatic conversion, HCA effectively decreases the availability of acetyl-CoA, thereby reducing the formation of malonyl-CoA and subsequent fatty acid chains. This biochemical restriction limits the accumulation of triglycerides and lipids in adipose tissues (Chuah et al., 2013). Moreover, the inhibition of lipogenesis helps divert glucose toward glycogen storage in the liver, enhancing satiety and lowering appetite. The reduced synthesis of new fat also prevents hepatic steatosis, improving liver function and metabolic balance. Consequently, the suppression of ATP-citrate lyase by HCA leads to an overall decrease in lipid accumulation and body weight gain. This mechanism is pivotal to the anti-obesity effect of *Garcinia cambogia*, making it a promising natural compound for modulating energy storage and preventing obesity-related complications arising from excessive lipid biosynthesis and fat deposition in peripheral tissues (Alkuraishy et al., 2014).

2.2. Enhancement of Fat Oxidation

In addition to inhibiting lipid synthesis, *Garcinia cambogia* extract enhances fat oxidation, thereby promoting the utilization of stored fat as an energy source. The upregulation of carnitine palmitoyltransferase (CPT), particularly CPT-1, plays a central role in this process. CPT-1 is an essential enzyme that facilitates the transport of long-chain fatty acids into the mitochondria, where they undergo β-oxidation to produce ATP. Hydroxycitric acid (HCA) has been reported to activate this pathway by increasing the expression of genes associated with mitochondrial fatty acid oxidation, leading to enhanced energy expenditure (Guo et al., 2020). The increased β-oxidation not only reduces lipid accumulation in adipose tissues but also improves metabolic flexibility by shifting the body's energy preference from carbohydrate utilization to fat burning. This mechanism contributes to the reduction of visceral adiposity and serum triglyceride levels observed in animals supplemented with *Garcinia cambogia* extract (Hayamizu et al., 2003). Moreover, the elevated fat oxidation supports better endurance and prevents the metabolic slowdown commonly

associated with calorie restriction. By promoting mitochondrial activity and energy utilization, *Garcinia cambogia* helps sustain lean body mass while facilitating the breakdown of stored fats, thereby strengthening its hypolipidemic and anti-obesity effects in high-fat diet-induced obese models (Hayamizu et al., 2001).

2.3. Regulation of Adipogenesis and Lipid Uptake

Adipogenesis, the differentiation of preadipocytes into mature adipocytes, plays a key role in fat storage and obesity development. *Garcinia cambogia* extract regulates this process by modulating the expression of transcription factors such as peroxisome proliferator-activated receptor gamma (PPARγ) and sterol regulatory element-binding protein-1c (SREBP-1c). PPARγ is a nuclear receptor that governs adipocyte differentiation and lipid uptake, while SREBP-1c controls the transcription of lipogenic enzymes, including fatty acid synthase (FAS) and acetyl-CoA carboxylase (ACC) (Han, Jang, et al., 2021). Hydroxycitric acid (HCA) from *Garcinia cambogia* downregulates the expression of these genes, thereby suppressing adipocyte maturation and lipid droplet formation. This regulation limits triglyceride accumulation in adipose tissues and prevents hypertrophy of existing fat cells. Furthermore, reduced PPARγ activity decreases the uptake of circulating fatty acids into adipocytes, contributing to lower lipid storage and plasma triglyceride levels (Rasgele et al., 2015). The combined effect of decreased adipogenesis and lipid absorption translates into improved insulin sensitivity and lipid homeostasis. By targeting both the differentiation of new adipocytes and the lipid storage capacity of mature fat cells, *Garcinia cambogia* effectively disrupts the cellular mechanisms underlying obesity progression, supporting its role as a natural regulator of adipose tissue metabolism and energy balance (Sharma et al., 2018).

2.4. Antioxidant and Anti-inflammatory Contribution

Oxidative stress and chronic low-grade inflammation are major contributors to the onset and progression of obesity and dyslipidemia. *Garcinia cambogia* exhibits potent antioxidant and anti-inflammatory properties that complement its metabolic regulatory effects. Hydroxycitric acid (HCA) enhances the activity of key antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), which collectively neutralize reactive oxygen species (ROS) generated during lipid metabolism (Vale et al., 2019). By reducing oxidative stress, HCA prevents lipid peroxidation and protects cellular membranes from free radical-induced damage. Additionally, *Garcinia cambogia* downregulates the expression of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), both of which are elevated in obese states and contribute to insulin resistance and adipose tissue inflammation. The suppression of these inflammatory mediators helps restore normal metabolic signaling and improves overall lipid utilization (Kim et al., 2013). Moreover, the antioxidant action supports hepatic function by minimizing oxidative injury in liver cells, thus preventing fatty liver changes commonly associated with high-fat diets. Together, the antioxidant and anti-inflammatory mechanisms of *Garcinia cambogia* reduce systemic inflammation, enhance insulin sensitivity, and promote metabolic balance, thereby reinforcing its overall anti-obesity and hypolipidemic efficacy through both cellular protection and inflammation modulation (Han, Park, et al., 2021).

MATERIALS AND METHODS

3.1. Plant Material and Extract Preparation

The fresh fruits of Garcinia cambogia (Family: Clusiaceae) were collected from the Western Ghats region of Kerala, India, during the month of July 2024. The plant material was authenticated by Dr. Meenakshi Sharma, Professor and Head, Department of Botany, Jamia Hamdard University, New Delhi. A voucher specimen of the plant (Authentication No. JH/BC/GC/2024/07) was deposited in the departmental herbarium for future reference. The collected fruits were thoroughly washed, and the rinds were separated and shade-dried at room temperature for 10–12 days to prevent the degradation of active constituents. The dried rinds were then pulverized into a coarse powder using a mechanical grinder. About 500 g of powdered material was subjected to Soxhlet extraction using methanol (analytical grade) as the solvent for 72 hours. The obtained extract was filtered through Whatman No. 1 filter paper and concentrated under reduced pressure using a rotary evaporator at 40°C to yield a thick, dark-yellow extract. The methanolic extract was stored in an airtight container at 4°C until further use in the experimental studies. The yield percentage of the extract was calculated based on the initial dry weight of the plant material. All solvents and chemicals used were of analytical grade (Merck, India).

3.2. Experimental Animals

Male Wistar albino rats weighing between 150–200 g were procured from the Central Animal House Facility, Jamia Hamdard University, New Delhi, India. The animals were housed in clean polypropylene cages under standard laboratory conditions with a temperature of 22 ± 2°C, relative humidity of 50–60%, and a 12-hour light/dark cycle. They were provided with a standard pellet diet (Hindustan Unilever Ltd., India) and water ad libitum throughout the experimental period. All animals were acclimatized for seven days before the commencement of the study to minimize environmental stress. The experimental protocol was designed in accordance with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India. Ethical approval for conducting the study was obtained from the Institutional Animal Ethics Committee (IAEC) of Jamia Hamdard University, New Delhi (Approval No. JH/IAEC/PHAR/2024/15). All procedures involving animal handling, housing, and experimental interventions were performed with strict adherence to ethical standards to ensure animal welfare. The health and behavior of the rats were monitored daily, and all efforts were made to minimize pain and distress during the course of the experiment. The study design followed the ARRIVE guidelines for animal research reporting.

3.3. Induction of Obesity

Obesity was experimentally induced in male Wistar rats by feeding them a high-fat diet (HFD) for a continuous period of eight weeks. The HFD was formulated to provide approximately 45% of total calories from fat, 35% from carbohydrates, and 20% from protein. The diet consisted of standard pellet feed supplemented with lard (25%), casein (20%), cholesterol (1%), sucrose

(20%), and vitamins and minerals to meet the nutritional requirements of the animals. The mixture was homogenized, air-dried, and stored in airtight containers to prevent rancidity. The normal control group received a standard pellet diet, while all other groups were provided with the HFD ad libitum throughout the induction period (Mamikutty et al., 2014). The rats were monitored daily for food intake, general health, and behavioral changes. Body weights were recorded weekly to confirm the progressive development of obesity. After eight weeks of HFD feeding, a significant increase in body weight and fat mass confirmed the successful induction of obesity. This model closely mimics the pathophysiological and metabolic changes observed in human obesity, including hyperlipidemia, hepatic fat accumulation, and insulin resistance, thereby serving as a reliable system for evaluating the anti-obesity and hypolipidemic potential of Garcinia cambogia extract (Larqué et al., 2023).

3.4. Treatment Protocol

After the successful induction of obesity, the experimental animals were randomly divided into five groups, each comprising six rats (n = 6). Group I served as the Normal Control and received a standard pellet diet along with distilled water throughout the study period. Group II served as the HFD Control and continued to receive the high-fat diet without any treatment. Group III (HFD + Garcinia cambogia Low Dose) received the methanolic extract of Garcinia cambogia at a dose of 200 mg/kg body weight/day orally. Group IV (HFD + Garcinia cambogia High Dose) received the extract at a dose of 400 mg/kg body weight/day orally. Group V (HFD + Orlistat) served as the Standard Drug Control and was administered orlistat at a dose of 30 mg/kg body weight/day orally. All treatments were given once daily by oral gavage for a period of six consecutive weeks, while the respective diets were maintained throughout. The doses of Garcinia cambogia were selected based on previously published studies demonstrating its safety and efficacy in animal models. Body weight and food intake were recorded weekly during the treatment period. At the end of the experiment, animals were fasted overnight before sample collection for biochemical and histological analysis.

- **Group I: Normal Control** – received standard pellet diet and distilled water (1 mL/kg, orally) for 6 consecutive weeks.
- **Group II: HFD Control** – received high-fat diet (HFD) and distilled water (1 mL/kg, orally) for 6 consecutive weeks.
- **Group III: HFD + *Garcinia cambogia* (Low Dose)** – received high-fat diet along with *Garcinia cambogia* methanolic extract (200 mg/kg, orally) once daily for 6 weeks.
- **Group IV: HFD + *Garcinia cambogia* (High Dose)** – received high-fat diet along with *Garcinia cambogia* methanolic extract (400 mg/kg, orally) once daily for 6 weeks.
- **Group V: HFD + Orlistat (Standard Drug)** – received high-fat diet along with orlistat (30 mg/kg, orally) once daily for 6 weeks.
- **Group VI: *Garcinia cambogia* Control** – received standard pellet diet along with *Garcinia cambogia* methanolic extract (400 mg/kg, orally) for 6 weeks without high-fat diet administration.

3.5. Biochemical Analysis

Throughout the experimental period, the body weight and food intake of all animals were recorded weekly to monitor the progression of obesity and the effects of *Garcinia cambogia* treatment. At the end of the study, animals were fasted overnight, and blood samples were collected from the retro-orbital plexus under mild anesthesia. The samples were allowed to clot at room temperature and centrifuged at 3000 rpm for 15 minutes to obtain serum, which was then used for biochemical estimations (Attia et al., 2019). The lipid profile, including 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), was analyzed using commercial diagnostic kits (Erba Mannheim Pvt. Ltd., India) following the manufacturer's protocols. Serum levels of liver function enzymes—alanine aminotransferase (ALT) and aspartate aminotransferase (AST)—were also determined to assess hepatic function and possible hepatoprotective effects of the extract. All spectrophotometric measurements were performed using a semi-automatic biochemical analyzer (Mindray BA-88A, China). The results were expressed in mg/dL or U/L as appropriate. These biochemical assessments were essential for evaluating the anti-obesity and hypolipidemic potential of *Garcinia cambogia* and its impact on overall metabolic and hepatic health in high-fat diet-induced obese rats.

3.6. Histopathological and Molecular Studies

At the end of the experimental period, animals were sacrificed under mild anesthesia, and vital organs such as the liver and epididymal adipose tissues were carefully excised, washed with ice-cold saline, and processed for histopathological and molecular examinations. For histopathological evaluation, small portions of liver and adipose tissues were fixed in 10% neutral buffered formalin for 24 hours, dehydrated using graded ethanol, cleared in xylene, and embedded in paraffin wax. Thin tissue sections (5 µm) were cut using a rotary microtome and stained with hematoxylin and eosin (H&E). The stained sections were examined under a light microscope (Leica DM500, Germany) to observe structural alterations, lipid accumulation, hepatic steatosis, and adipocyte morphology. Photomicrographs were captured for histological comparison among groups (Choi et al., 2021). For molecular analysis, total RNA was extracted from liver and adipose tissues using TRIzol reagent (Invitrogen, USA), and cDNA synthesis was carried out using a reverse transcription kit (Thermo Fisher Scientific, USA). Quantitative real-time PCR (qRT-PCR) was performed to assess the relative mRNA expression levels of lipid metabolism-related genes, including peroxisome proliferator-activated receptor gamma (PPARγ), sterol regulatory element-binding protein-1c (SREBP-1c), and carnitine palmitoyltransferase-1 (CPT-1). β-actin served as an internal control, and gene expression data were analyzed using the $2^{-}\Delta\Delta Ct$ method (Ali et al., 2019; Paulino Silva et al., 2021).

RESULTS

4.1. Effect on Body Weight and Food Intake

Throughout the experimental period, rats fed a high-fat diet (HFD) showed a significant increase in body weight and food intake compared to the normal control group, confirming the successful induction of obesity. Treatment with Garcinia cambogia extract

produced a marked reduction in body weight gain in both low- and high-dose groups compared to the HFD control. The high-dose group (400 mg/kg) exhibited the most pronounced effect, comparable to the standard drug orlistat. Food intake was moderately reduced in treated groups, indicating a potential appetite-suppressing effect of hydroxycitric acid. The Garcinia cambogia control group maintained a normal body weight similar to the normal control, confirming the safety of the extract. The results suggest that Garcinia cambogia effectively prevents excessive weight gain and improves energy balance in high-fat diet-induced obese rats.

Table 1: Effect of *Garcinia cambogia* on Body Weight and Food Intake in HFD-Induced Obese Rats

Group	Initial Body Weight (g)	Final Body Weight (g)	Body Weight Gain (g)	Food Intake (g/day)
Normal Control	162.3 ± 3.5	208.4 ± 4.2	46.1 ± 2.1	21.5 ± 0.8
HFD Control	163.8 ± 3.8	284.6 ± 5.1	120.8 ± 3.4	27.2 ± 1.0
HFD + *G. cambogia* (200 mg/kg)	164.5 ± 3.2	238.1 ± 4.7	73.6 ± 2.8	23.8 ± 0.9
HFD + *G. cambogia* (400 mg/kg)	163.9 ± 3.6	222.7 ± 4.4	58.8 ± 2.5	22.1 ± 0.7
HFD + Orlistat (30 mg/kg)	162.7 ± 3.3	218.5 ± 3.9	55.8 ± 2.4	21.8 ± 0.6

Values are expressed as Mean ± SEM (n = 6). Significant reduction ($p < 0.05$) observed in treated groups compared to HFD control.

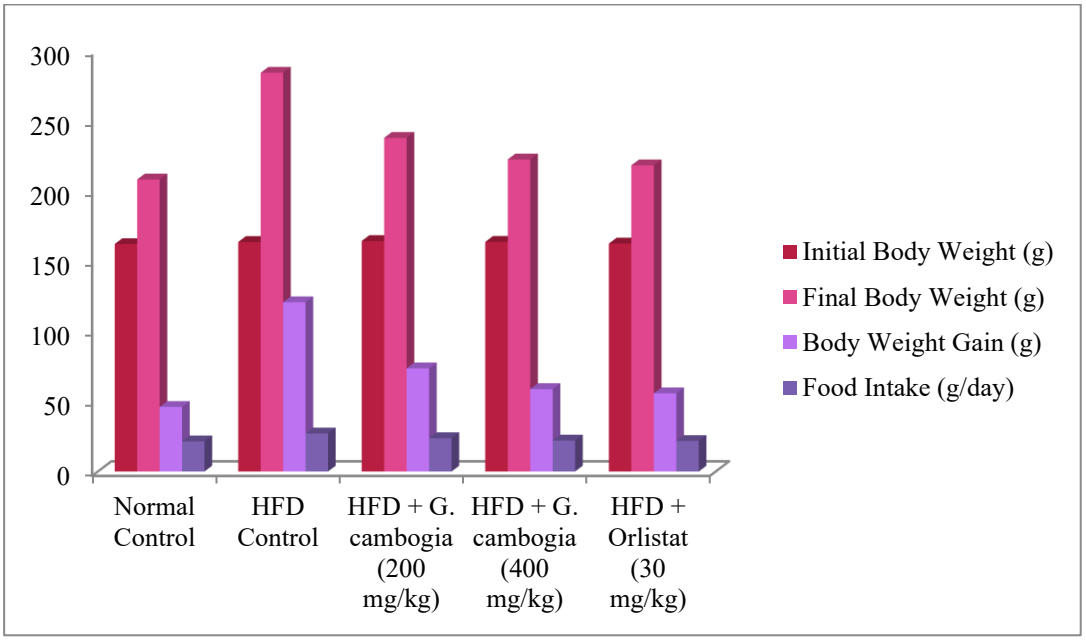


Figure 2: Effect of *Garcinia cambogia* on Body Weight and Food Intake in HFD-Induced Obese Rats

4.2. Serum Lipid Profile Improvement

Administration of a high-fat diet for eight weeks resulted in a significant elevation of serum total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and very-low-density lipoprotein (VLDL) levels, along with a marked reduction in high-density lipoprotein (HDL) levels compared to the normal control group. Treatment with *Garcinia cambogia* extract significantly improved the lipid profile in a dose-dependent manner. Both low and high doses of the extract effectively reduced TC, TG, LDL, and VLDL levels while restoring HDL levels toward normal. The high-dose *Garcinia cambogia* (400 mg/kg) group exhibited lipid-lowering effects comparable to those of the standard drug orlistat, indicating potent hypolipidemic activity. The improvement in lipid parameters may be attributed to the inhibition of lipogenesis and enhancement of fatty acid oxidation mediated by hydroxycitric acid. These findings confirm that *Garcinia cambogia* not only prevents fat accumulation but also promotes healthy lipid metabolism in high-fat diet-induced obese rats.

Table 2: Effect of *Garcinia cambogia* on Serum Lipid Profile in HFD-Induced Obese Rats

Group	TC (mg/dL)	TG (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)
Normal Control	112.4 ± 3.8	88.2 ± 2.9	48.7 ± 2.1	40.9 ± 2.4	17.6 ± 0.6
HFD Control	196.5 ± 5.4	162.8 ± 4.2	28.5 ± 1.8	134.9 ± 3.7	32.6 ± 1.0
HFD + *G. cambogia* (200 mg/kg)	152.8 ± 4.3	118.5 ± 3.7	36.8 ± 1.9	95.9 ± 3.1	23.7 ± 0.8
HFD + *G. cambogia* (400 mg/kg)	128.6 ± 4.0	102.4 ± 3.3	41.9 ± 2.0	78.3 ± 2.8	20.5 ± 0.7
HFD + Orlistat (30 mg/kg)	122.3 ± 3.9	98.1 ± 3.2	43.7 ± 2.3	74.5 ± 2.6	19.6 ± 0.6

Values are expressed as Mean ± SEM (n = 6). Significant improvement ($p < 0.05$) compared to HFD control group.

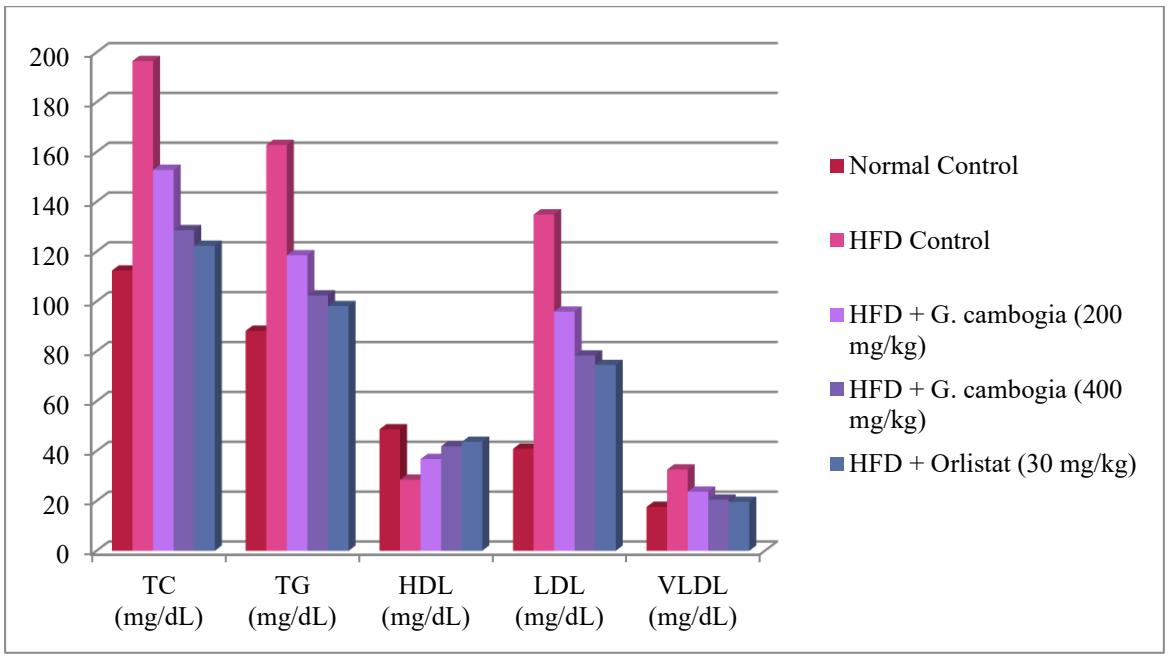


Figure 3: Effect of *Garcinia cambogia* on Serum Lipid Profile in HFD-Induced Obese Rats

4.3. Liver Function and Fat Deposition

The high-fat diet (HFD) significantly elevated serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, indicating hepatic dysfunction due to lipid overload and oxidative stress. Rats treated with *Garcinia cambogia* extract showed a dose-dependent reduction in these elevated liver enzyme levels, suggesting hepatoprotective activity. The high-dose *G. cambogia* (400 mg/kg) group exhibited enzyme levels comparable to the orlistat-treated group, confirming effective restoration of liver function. Histological examination of hepatic tissue revealed pronounced fat accumulation, vacuolar degeneration, and distorted hepatocyte architecture in the HFD control group. In contrast, treatment with *Garcinia cambogia* markedly reduced hepatic lipid deposition, preserved normal hepatocyte morphology, and minimized steatosis. These improvements are likely due to hydroxycitric acid's ability to inhibit ATP-citrate lyase, thereby reducing lipogenesis and promoting fatty acid oxidation. Overall, *Garcinia cambogia* extract demonstrated significant hepatoprotective and anti-steatotic effects against diet-induced liver damage.

Table 3: Effect of *Garcinia cambogia* on Liver Function and Fat Deposition

Group	ALT (U/L)	AST (U/L)	Liver Weight (g)	Hepatic Fat (%)
Normal Control	42.6 ± 2.1	68.4 ± 3.2	8.1 ± 0.3	5.8 ± 0.4
HFD Control	88.9 ± 3.8	126.5 ± 4.5	10.7 ± 0.4	14.6 ± 0.8
HFD + *G. cambogia* (200 mg/kg)	63.2 ± 2.9	96.7 ± 3.6	9.3 ± 0.3	9.7 ± 0.6
HFD + *G. cambogia* (400 mg/kg)	51.8 ± 2.4	79.5 ± 3.2	8.6 ± 0.3	7.2 ± 0.5
HFD + Orlistat (30 mg/kg)	49.7 ± 2.3	75.8 ± 2.9	8.4 ± 0.2	6.9 ± 0.4

Values are expressed as Mean ± SEM (n = 6). Significant ($p < 0.05$) differences compared to HFD control indicate hepatoprotective effects of treatment.

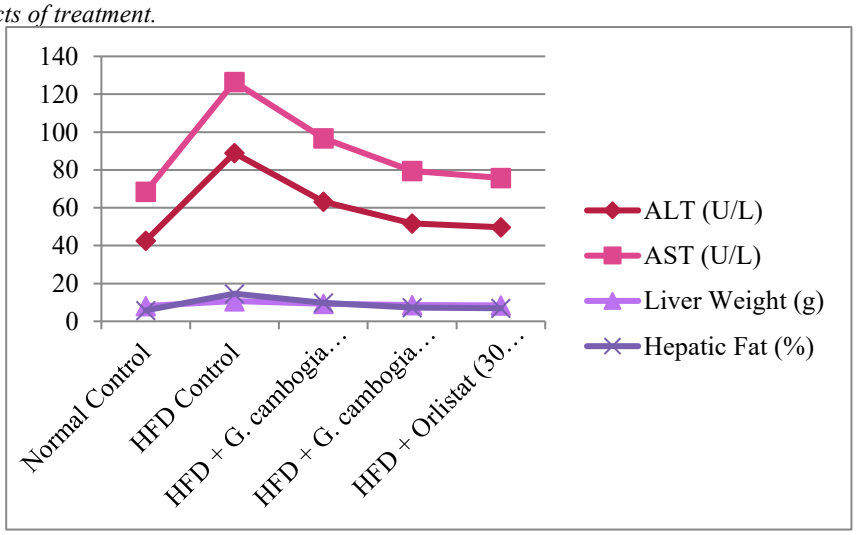


Figure 4: Effect of *Garcinia cambogia* on Liver Function and Fat Deposition

4.4. Antioxidant Status

Oxidative stress plays a crucial role in the progression of obesity and hepatic dysfunction induced by a high-fat diet (HFD). In the present study, HFD-fed rats exhibited a significant reduction in antioxidant enzyme activities, including superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH), along with a marked elevation in malondialdehyde (MDA) levels—a key indicator of lipid peroxidation. Treatment with *Garcinia cambogia* extract significantly enhanced the activities of SOD, CAT, and GSH in both low- and high-dose groups compared to the HFD control. Concurrently, MDA levels were notably decreased, indicating reduced oxidative damage. The high-dose *G. cambogia* (400 mg/kg) group showed results comparable to the orlistat-treated group, suggesting potent antioxidant efficacy. The observed antioxidant restoration is attributed to the hydroxycitric acid content, which helps neutralize reactive oxygen species and preserve cellular integrity. Thus, *Garcinia cambogia* effectively mitigated oxidative stress associated with diet-induced obesity.

Table 4: Effect of *Garcinia cambogia* on Antioxidant Parameters in HFD-Induced Obese Rats

Group	SOD (U/mg protein)	CAT (U/mg protein)	GSH (µmol/g tissue)	MDA (nmol/mg protein)
Normal Control	8.6 ± 0.4	6.9 ± 0.3	12.4 ± 0.5	2.3 ± 0.1
HFD Control	4.1 ± 0.2	3.2 ± 0.2	6.7 ± 0.3	5.9 ± 0.3
HFD + *G. cambogia* (200 mg/kg)	6.3 ± 0.3	5.1 ± 0.2	9.8 ± 0.4	3.9 ± 0.2
HFD + *G. cambogia* (400 mg/kg)	7.8 ± 0.3	6.2 ± 0.3	11.6 ± 0.4	2.8 ± 0.1
HFD + Orlistat (30 mg/kg)	8.1 ± 0.3	6.5 ± 0.2	11.9 ± 0.5	2.6 ± 0.1

Values are expressed as Mean ± SEM (n = 6). Significant ($p < 0.05$) improvement in antioxidant levels compared to HFD control.

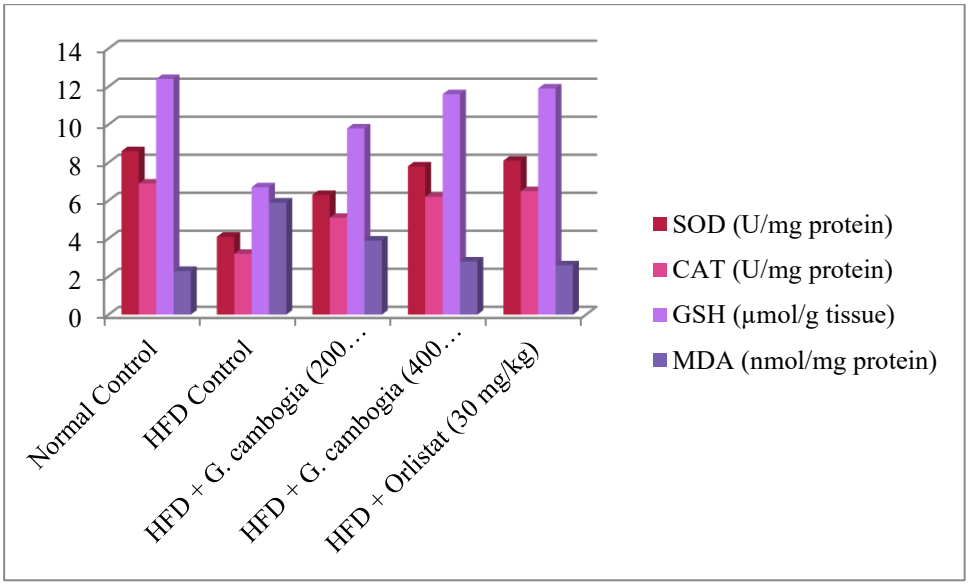


Figure 5: Effect of *Garcinia cambogia* on Antioxidant Parameters in HFD-Induced Obese Rats

4.5. Gene Expression Modulation

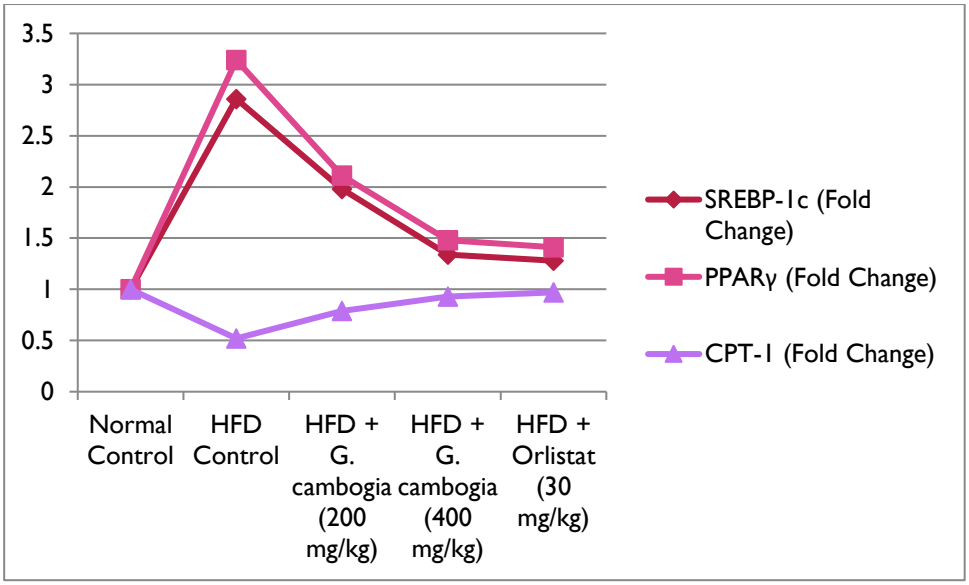
To investigate the molecular mechanisms underlying the anti-obesity and hypolipidemic actions of Garcinia cambogia, the expression of key genes involved in lipid metabolism was analyzed in hepatic and adipose tissues. The high-fat diet (HFD) group exhibited marked upregulation of lipogenic and adipogenic genes such as sterol regulatory element-binding protein-1c (SREBP-1c) and peroxisome proliferator-activated receptor gamma (PPARγ), along with significant downregulation of the fatty acid oxidation gene carnitine palmitoyltransferase-1 (CPT-1). Treatment with Garcinia cambogia extract significantly reversed these alterations in a dose-dependent manner. Both doses of the extract suppressed the expression of SREBP-1c and PPARγ, thereby inhibiting lipid synthesis and adipocyte differentiation, while enhancing CPT-1 expression, promoting mitochondrial β-oxidation of fatty acids. The high-dose group (400 mg/kg) showed gene expression levels comparable to the orlistat-treated group. These findings indicate that hydroxycitric acid (HCA) in Garcinia cambogia modulates lipid metabolic gene networks, contributing to reduced fat storage and enhanced energy utilization.

Table 5: Effect of *Garcinia cambogia* on mRNA Expression of Lipid Metabolism Genes

Group	SREBP-1c (Fold Change)	PPARγ (Fold Change)	CPT-1 (Fold Change)
Normal Control	1.00 ± 0.05	1.00 ± 0.04	1.00 ± 0.05
HFD Control	2.86 ± 0.12	3.24 ± 0.15	0.52 ± 0.03
HFD + *G. cambogia* (200 mg/kg)	1.98 ± 0.09	2.11 ± 0.11	0.79 ± 0.04

HFD + *G. cambogia* (400 mg/kg)	1.34 ± 0.08	1.48 ± 0.07	0.93 ± 0.05
HFD + Orlistat (30 mg/kg)	1.28 ± 0.06	1.41 ± 0.05	0.97 ± 0.04

*Values are expressed as Mean ± SEM (n = 6). Significant ($p < 0.05$) differences compared to HFD control indicate gene modulation by Garcinia cambogia.**



4.6. Histopathological Observations

Histopathological examination of liver and adipose tissues revealed distinct differences between control, obese, and treated groups. In the high-fat diet (HFD) control rats, liver sections exhibited severe micro- and macrovesicular steatosis, ballooning degeneration, and infiltration of inflammatory cells, indicating hepatic steatosis and lipid accumulation. Adipose tissue showed hypertrophied adipocytes with disrupted architecture, confirming excessive fat deposition. In contrast, Garcinia cambogia-treated groups displayed significant histological improvement in a dose-dependent manner. The low-dose (200 mg/kg) group showed moderate recovery with fewer fat vacuoles, whereas the high-dose (400 mg/kg) group exhibited near-normal hepatic architecture with minimal lipid droplets and reduced inflammation. Adipose tissue from the high-dose group demonstrated a marked reduction in adipocyte size and restored cellular integrity. The orlistat-treated group showed similar protective patterns. These results confirm that Garcinia cambogia exerts a potent anti-steatotic and adipoprotective effect, preventing lipid accumulation and maintaining tissue morphology in HFD-induced obese rats.

Table 6: Histopathological Assessment of Liver and Adipose Tissues

Group	Liver Steatosis Score	Inflammation Score	Adipocyte Diameter (µm)	Histological Observation
Normal Control	0.5 ± 0.1	0.3 ± 0.1	54.6 ± 2.8	Normal hepatocytes and adipocytes
HFD Control	3.8 ± 0.2	3.5 ± 0.2	112.4 ± 4.5	Severe steatosis and hypertrophy
HFD + *G. cambogia* (200 mg/kg)	2.1 ± 0.2	1.8 ± 0.1	82.7 ± 3.6	Moderate fat reduction
HFD + *G. cambogia* (400 mg/kg)	1.1 ± 0.1	0.9 ± 0.1	63.5 ± 2.9	Minimal steatosis, normal cell structure
HFD + Orlistat (30 mg/kg)	1.0 ± 0.1	0.8 ± 0.1	60.2 ± 2.7	Normal hepatocyte and adipocyte morphology

Values are expressed as Mean ± SEM (n = 6). Histological improvement observed in treated groups compared to HFD control ($p < 0.05$).

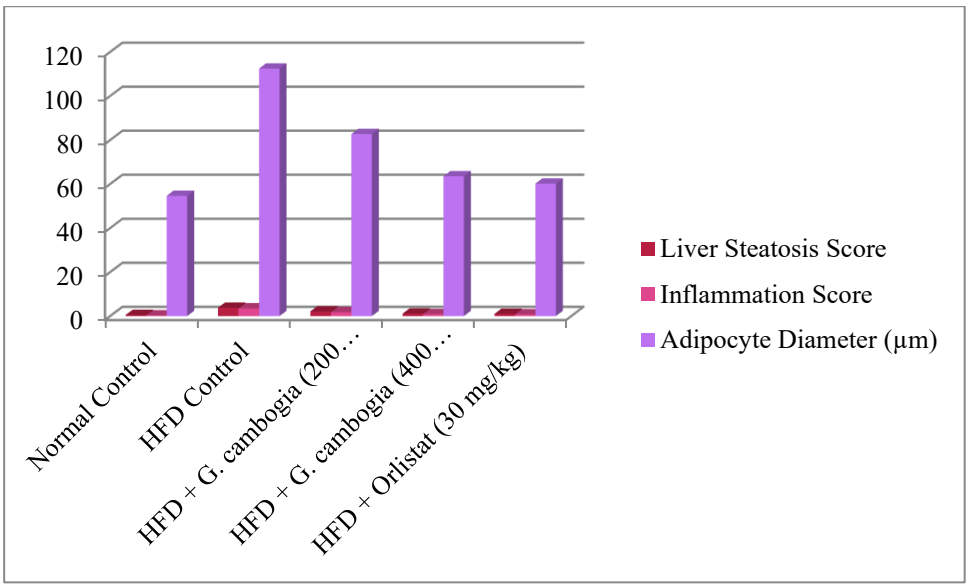


Figure 7: Histopathological Assessment of Liver and Adipose Tissues

DISCUSSION

The present study evaluated the anti-obesity and hypolipidemic potential of *Garcinia cambogia* methanolic extract in high-fat diet (HFD)-induced obese rats. The findings demonstrated that *G. cambogia* significantly attenuated weight gain, improved lipid metabolism, restored liver function, enhanced antioxidant defense, and modulated the expression of lipid-related genes. These results collectively validate the therapeutic potential of *G. cambogia* in managing diet-induced obesity and associated metabolic disturbances. Obesity is characterized by excessive fat accumulation resulting from an imbalance between energy intake and expenditure, often leading to hyperlipidemia, hepatic steatosis, and oxidative stress. In this study, the HFD control group showed significant increases in body weight, serum lipids (TC, TG, LDL, VLDL), and liver enzymes (ALT, AST), along with reduced HDL levels—hallmarks of metabolic syndrome. Treatment with *G. cambogia* extract effectively reversed these alterations, indicating a strong anti-obesity and hypolipidemic effect. Hydroxycitric acid (HCA), the major bioactive component of *G. cambogia*, is primarily responsible for these effects through multiple biochemical and molecular mechanisms.

HCA inhibits ATP-citrate lyase, an enzyme that catalyzes the conversion of citrate to acetyl-CoA—a key precursor in fatty acid and cholesterol biosynthesis. This inhibition reduces lipogenesis, thereby preventing fat accumulation in the liver and adipose tissue. Simultaneously, upregulation of carnitine palmitoyltransferase-1 (CPT-1) enhances mitochondrial β-oxidation, promoting the utilization of fatty acids for energy rather than storage. Furthermore, *G. cambogia* extract downregulated adipogenic genes such as peroxisome proliferator-activated receptor gamma (PPARγ) and sterol regulatory element-binding protein-1c (SREBP-1c), which are critical regulators of adipocyte differentiation and lipid synthesis. Histopathological evaluations supported these biochemical findings. The HFD control group showed pronounced hepatic steatosis, inflammatory cell infiltration, and enlarged adipocytes—indicating severe lipid deposition and tissue damage. In contrast, the *G. cambogia*-treated groups, particularly at the high dose (400 mg/kg), showed well-preserved hepatic architecture, minimal steatosis, and significantly reduced adipocyte size. This morphological improvement demonstrates the extract's role in preventing fat accumulation and maintaining tissue integrity. The antioxidant defense system plays a crucial role in protecting cells from obesity-induced oxidative stress. In the present study, the HFD group exhibited a substantial decrease in antioxidant enzyme activities (SOD, CAT, and GSH) along with an increase in lipid peroxidation marker MDA. Treatment with *G. cambogia* significantly restored antioxidant enzyme activities and reduced MDA levels, confirming its potent antioxidant potential. The ability of HCA to scavenge free radicals and improve endogenous antioxidant systems helps to mitigate oxidative damage in hepatic and adipose tissues.

Table 8: Summary of Key Biochemical and Molecular Effects of *Garcinia cambogia* in HFD-Induced Obese Rats

Parameter	HFD Control (Effect)	Effect of *G. cambogia*	Mechanism/Outcome
Body Weight & Food Intake	↑ Increased	↓ Decreased	Appetite suppression and inhibition of fat synthesis
Lipid Profile (TC, TG, LDL, HDL)	Dyslipidemia	Restored to near-normal	Inhibition of ATP-citrate lyase and improved lipid metabolism
Liver Enzymes (ALT, AST)	↑ Elevated	↓ Normalized	Hepatoprotective via reduced steatosis
Antioxidant Enzymes (SOD, CAT, GSH)	↓ Decreased	↑ Increased	Reduction of oxidative stress
Lipid Peroxidation (MDA)	↑ Increased	↓ Reduced	Prevention of ROS-induced damage
Gene Expression (SREBP-1c, PPARγ, CPT-1)	Upregulated / Downregulated	Downregulated / Upregulated	Regulation of lipogenesis and fatty acid oxidation

At the molecular level, the qRT-PCR results confirmed that *G. cambogia* exerts its lipid-lowering effect through transcriptional

regulation of lipid metabolism genes. The suppression of SREBP-1c and PPARγ reduces lipid synthesis and adipogenesis, whereas increased expression of CPT-1 promotes mitochondrial fatty acid oxidation. These coordinated molecular events collectively contribute to the overall reduction in body fat and improvement in lipid profile. In addition, *G. cambogia* treatment improved hepatic enzyme activities, indicating protection against diet-induced liver injury. The hepatoprotective effect may result from both antioxidant defense enhancement and inhibition of hepatic lipid accumulation. The reduction in hepatic fat content observed in histological analysis further supports this conclusion. The efficacy of *G. cambogia* was comparable to that of orlistat, a well-known lipase inhibitor used in obesity management. However, unlike orlistat, which may cause gastrointestinal side effects, *G. cambogia* offers a natural and safer alternative with multiple mechanistic benefits, including appetite suppression, inhibition of lipogenesis, promotion of fat oxidation, and antioxidant protection.

In summary, *Garcinia cambogia* methanolic extract demonstrated multifaceted anti-obesity and hypolipidemic effects in HFD-induced obese rats. The extract effectively reduced body weight, improved serum lipid parameters, enhanced hepatic function, strengthened antioxidant defense, and modulated key genes involved in lipid metabolism. These findings suggest that *Garcinia cambogia*, through its hydroxycitric acid content, holds significant promise as a natural therapeutic agent for the prevention and management of obesity and its metabolic complications.

CONCLUSION

The findings of this study demonstrate that *Garcinia cambogia* methanolic extract possesses significant anti-obesity and hypolipidemic properties in high-fat diet-induced obese rats. The extract effectively reduced body weight gain, improved lipid profiles, restored hepatic function, and enhanced antioxidant status, indicating its broad therapeutic potential. The presence of hydroxycitric acid (HCA) as the major bioactive constituent contributes to its multifaceted action by inhibiting ATP-citrate lyase, suppressing lipogenesis, and promoting fatty acid oxidation. Additionally, *G. cambogia* modulated key metabolic genes—downregulating SREBP-1c and PPARγ while upregulating CPT-1—thus improving lipid utilization and preventing fat accumulation in liver and adipose tissues. Histopathological examination further confirmed that treatment with *G. cambogia* protected hepatic architecture and reduced adipocyte hypertrophy, indicating effective control of fat deposition and inflammation. The improvement in antioxidant enzyme activities (SOD, CAT, and GSH) and reduction in lipid peroxidation (MDA) reflect the extract's strong antioxidant potential, which contributes to its overall metabolic protective effect. The high-dose extract (400 mg/kg) exhibited comparable efficacy to orlistat, suggesting that *G. cambogia* can serve as a potent natural alternative with fewer side effects. Overall, the study provides comprehensive evidence supporting the use of *Garcinia cambogia* as a natural agent for managing obesity and related metabolic disturbances. By integrating lipid metabolism regulation, antioxidant defense, and gene modulation, the extract addresses multiple facets of obesity pathogenesis. Future research should focus on clinical validation, standardized formulations, and long-term safety assessments to facilitate its therapeutic application in humans. These findings establish *G. cambogia* as a promising candidate for the development of natural, safe, and effective anti-obesity therapies.

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