RESEARCH PAPER

Modulatory Effects of Sesame (Sesamum indicum) Seeds on Metabolic, Biochemical, and Immune Functions in Experimentally Induced Hyperlipidemic Rats

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ABSTRACT

Background: Hyperlipidemia is a prevalent metabolic disorder associated with dyslipidemia, hepatic dysfunction, oxidative stress, and immune imbalance. Functional foods rich in bioactive compounds have gained increasing attention as supportive strategies for metabolic regulation. Sesame (Sesamum indicum) seeds contain lignans, unsaturated fatty acids, phytosterols, and antioxidant compounds that may contribute to metabolic homeostasis.

Objective: This study aimed to evaluate the effects of sesame seed supplementation on metabolic, biochemical, hepatic, and immune parameters in rats with experimentally induced hyperlipidemia.

Materials and Methods: Twenty-four male albino rats were randomly divided into four groups (n = 6). One group served as a normal control, while hyperlipidemia was induced in the remaining groups using a fat-enriched diet. Two hyperlipidemic groups received the same diet supplemented with sesame seed powder at levels of 7.5% and 12.5%, respectively. Growth performance indicators, serum lipid profile, glucose levels, liver enzyme activities, immunoglobulins, and uric acid concentrations were assessed.

Results: Hyperlipidemia induced significant metabolic and immunological disturbances. Sesame supplementation improved body weight regulation, favorably modulated lipid fractions, enhanced glycemic control, reduced liver enzyme elevations, and normalized immune and uric acid profiles, with the higher dose showing more pronounced effects.

Conclusion: Sesame seeds demonstrated significant regulatory potential against hyperlipidemia-associated metabolic alterations, supporting their role as a functional dietary component for metabolic health promotion.

Keywords: Sesame (Sesamum indicum); Hyperlipidemia; Lipid profile; Antioxidant activity; Metabolic regulation.

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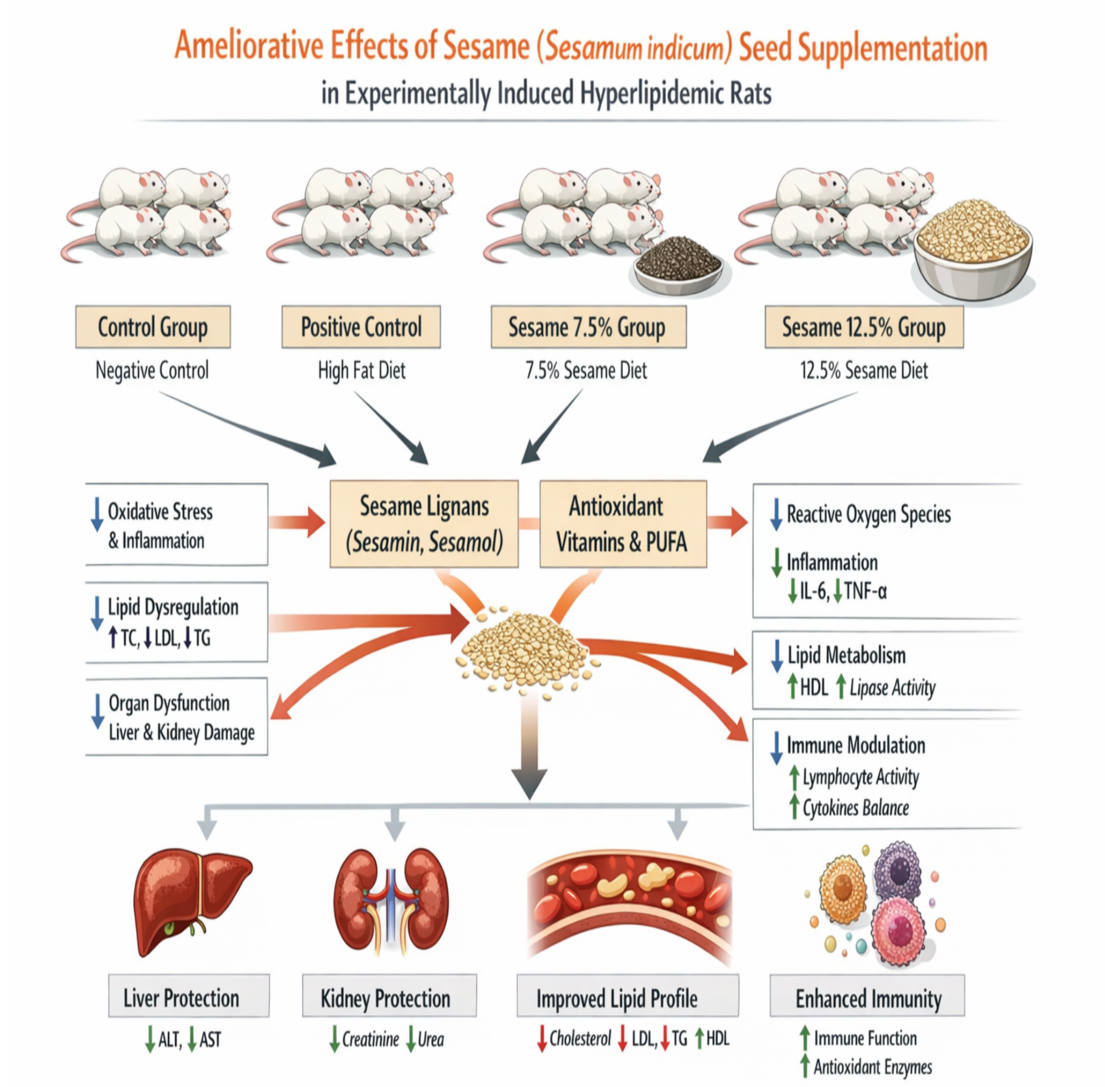

This graphical abstract shows the beneficial effects of sesame (Sesamum indicum) seed supplementation in high-fat diet–induced hyperlipidemic rats. Sesame (7.5% and 12.5%) improved lipid profile by lowering total cholesterol, LDL, and triglycerides while increasing HDL. It also reduced oxidative stress and inflammation, and supported liver, kidney, and immune function, highlighting its potential as a functional supplement against hyperlipidemia.

1- Introduction

Hyperlipidemia is a complex and highly prevalent metabolic disorder characterized by persistent elevations in plasma total cholesterol, triglycerides, and low-density lipoprotein cholesterol, alongside alterations in lipoprotein metabolism and reduced high-density lipoprotein functionality. It constitutes a central pathological driver in the development of atherosclerosis and cardiometabolic diseases and is increasingly recognized as a systemic condition that extends beyond lipid abnormalities. Accumulating evidence indicates that dyslipidemia is tightly interconnected with oxidative stress, endothelial dysfunction, mitochondrial impairment, and chronic low-grade inflammation (1). These intertwined mechanisms promote vascular damage, propagate inflammatory signaling cascades, and disrupt immune regulation, thereby amplifying the progression of metabolic complications. Consequently, effective strategies targeting multiple pathways simultaneously are of considerable scientific and clinical importance (2).

In recent years, nutritional modulation has emerged as a cornerstone in the prevention and adjunct management of metabolic disorders (3). Functional foods enriched with bioactive compounds offer a promising, evidence-based approach due to their capacity to influence lipid metabolism, redox homeostasis, inflammatory mediators, and gene expression profiles. Unlike single-target pharmacological agents, bioactive-rich dietary components may exert pleiotropic effects through the regulation of transcription factors, modulation of enzymatic activities involved in fatty acid oxidation and cholesterol biosynthesis, and enhancement of endogenous antioxidant defense systems. Such multi-dimensional actions align with contemporary perspectives in nutritional science, which emphasize systems-level interventions for complex metabolic diseases (4).

Plant-derived foods represent a particularly valuable source of naturally occurring phytochemicals with documented hypolipidemic and immunomodulatory properties. Among these, sesame seeds (*Sesamum indicum*) are distinguished by their unique composition of lignans (including sesamin and sesamolin), phytosterols, tocopherols, and polyunsaturated fatty acids (5). These constituents have been reported to influence hepatic lipid metabolism, enhance antioxidant enzyme activities such as superoxide dismutase and catalase, and attenuate lipid peroxidation processes (6). Moreover, sesame lignans have been implicated in the regulation of nuclear receptors and metabolic signaling pathways that govern cholesterol homeostasis and fatty acid catabolism (7,8). The combined presence of antioxidant and lipid-modulating compounds suggests a potential synergistic effect that may contribute to improved cardiometabolic outcomes (6).

Beyond metabolic regulation, dyslipidemia is increasingly recognized as a condition closely linked to immune dysregulation and inflammatory activation, where chronic low-grade inflammation plays a central role in disease progression (9). Excess lipid accumulation may contribute to oxidative stress and redox imbalance, processes that function as key signaling mechanisms but can become detrimental when dysregulated (10). Nutritional strategies have therefore gained attention as modulators of both immune responses and inflammatory pathways, highlighting the importance of diet in maintaining immune homeostasis (11). Plant-derived bioactive compounds, particularly dietary polyphenols, have demonstrated beneficial effects on cardiovascular and metabolic health through antioxidant and anti-inflammatory mechanisms (12).

In this context, sesame seeds (*Sesamum indicum*) represent a functional food rich in bioactive constituents with documented cardiometabolic benefits (6). However, further controlled experimental studies remain necessary to clarify their specific effects under defined pathological conditions. Experimental animal models provide a robust platform for evaluating the physiological effects of dietary interventions in a controlled and reproducible manner (13,14). Diet-induced hyperlipidemia models, particularly those utilizing cholesterol-enriched regimens, closely simulate metabolic alterations observed in dyslipidemic states, enabling comprehensive assessment of lipid profiles, biochemical indices, hepatic function, and immune-related parameters (15,16). Such models also allow exploration of dose-dependent responses and facilitate mechanistic interpretation of observed effects through integrated molecular and physiological analyses (17,18).

Given the growing global burden of metabolic disorders and the increasing demand for safe, accessible, and sustainable nutritional strategies, investigating the functional potential of sesame seeds is scientifically justified. Evidence from controlled clinical trials indicates that the consumption of sesame seeds and sesame products has favorable effects on blood glucose levels, supporting their potential role in metabolic health management (19). Evaluating graded dietary supplementation may further clarify the relationship between intake level and biological response, thereby contributing to evidence-based recommendations within the framework of functional nutrition research (20). Therefore, the present study was designed to investigate the modulatory effects of dietary sesame seed supplementation on metabolic, biochemical, and immune parameters in a cholesterol-induced hyperlipidemic rat model, with the aim of elucidating its potential as a multi-target functional food intervention in alignment with current priorities in translational nutrition science.

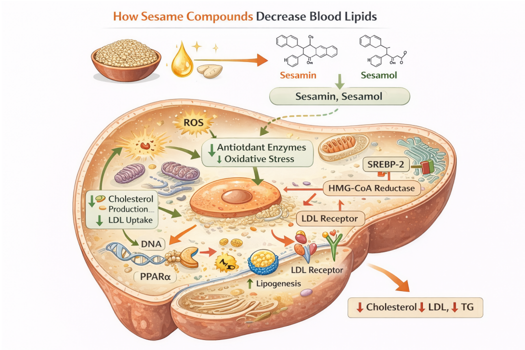

Figure 1. Mechanism of Sesame Compounds in Reducing Blood Lipids

2- Aim of study:

This study aims to investigate the potential regulatory effects of sesame seeds on metabolic, biochemical, and immune functions in rats with experimentally induced hyperlipidemia.

3- MATERIALS AND METHODS

3.1. Materials

3.1.1. Preparation of Sesame (Sesamum indicum) Seeds: Sesame seeds were obtained from a local market in Al-Baha City, Kingdom of Saudi Arabia. The seeds were carefully inspected and manually cleaned to remove foreign materials and debris. They were then dried under controlled conditions in a vacuum oven at 40 °C to achieve adequate moisture reduction while minimizing thermal and oxidative degradation. Subsequently, the seeds were ground into a fine, homogeneous powder using a laboratory grinder and passed through a standardized sieve to ensure uniform particle size distribution. The resulting powder was stored in airtight dark glass containers at temperatures below 30 °C to maintain the stability of heat- and light-sensitive bioactive compounds. All procedures were performed in accordance with standard protocols for the preparation of plant materials to preserve phytochemical integrity.

3.1.2. Lamb fat was purchased from a certified local butcher in Shibin El-Kom, Menoufia, Egypt, and utilized as part of the high-fat diet to induce hyperlipidemia in rats.

3.2. Biological experiment

3.2.1. Diet experiment

Dietary Composition The basal and experimental diets were formulated to be nutritionally balanced and isocaloric. The basal diet contained casein (20 g), corn oil (4.7 g), mineral mixture (3.5 g), vitamin mixture (1 g), cellulose (5 g), choline chloride (2 g), and sucrose (10 g), with corn starch added to complete the formulation to 100 g. For the experimental groups, sesame seeds (Sesamum indicum L.) were incorporated into the diet at levels of 7.5% and 12.5%, replacing an equivalent proportion of corn starch. Specifically, 7.5 g and 12.5 g of sesame seeds were added per 100 g of diet in the 7.5% and 12.5% groups, respectively, while maintaining the same amounts of casein, corn oil, mineral mix, vitamin mix, cellulose, choline chloride, and sucrose as in the basal diet. Corn starch was adjusted accordingly to maintain a total diet weight of 100 g. This formulation ensured controlled comparison between groups while isolating the effect of graded sesame seed supplementation.

3.2.2. Rats

Twenty-four clinically healthy adult male Wistar albino rats (150 ± 10 g) were obtained from the Animal House of the National Research Centre, Giza, Egypt. The sample size was determined with reference to previously published experimental studies utilizing comparable models of chemically induced hepatic injury, ensuring adequate statistical power while adhering to established ethical principles for the responsible use of laboratory animals. All procedures involving animals were carried out in accordance with internationally accepted standards for laboratory animal care and welfare, and the study protocol received ethical approval from the Research Ethics Committee of Al-Baha University (Approval No. 46123022; 17 April 2025). Following their transfer to the animal facility, the rats were individually maintained in adequately ventilated plastic cages under controlled laboratory conditions, with a regulated 12-hour light and 12-hour dark photoperiod. Before the initiation of the experiment, the animals underwent a one-week acclimation phase, during which they had unrestricted access to a standard basal diet and clean drinking water. Food was provided using spill-resistant feeders to reduce loss and cross-contamination, while water was supplied in bottles equipped with stainless-steel drinking spouts firmly secured to the cages. At baseline, all animals were confirmed to be clinically healthy. No animals were excluded from the study, and no mortality or unexpected adverse events occurred during the experimental period. Following acclimatization, rats were allocated to experimental groups using a simple random allocation method.

3.2.3. Animal Groups and Experimental Design:

After a one-week acclimatization period, baseline body weights were recorded for all animals prior to group allocation. No statistically significant differences in initial body weight were observed among the groups ($P > 0.05$). The rats were then randomly assigned, using a simple randomization method, into four experimental groups (n = 6 per group):

- Group 1 (Negative Control): Healthy rats fed the basal diet only and receiving no treatment.
- Group 2 (Positive Control): Hyperlipidemic rats fed a high-fat diet without any additional treatment.
- Group 3 (Hyperlipidemic + 7.5% Sesame): Hyperlipidemic rats fed a high-fat diet supplemented with 7.5% Sesamum indicum seeds (w/w of the total diet).
- Group 4 (Hyperlipidemic + 12.5% Sesame): Hyperlipidemic rats fed a high-fat diet supplemented with 12.5% Sesamum indicum seeds (w/w of the total diet).

Hyperlipidemia was induced by feeding the animals a high-fat diet throughout the experimental period. All rats had ad libitum access to food and tap water under controlled environmental conditions.

3.2.4. Determination of Total Phenolic and Flavonoid Contents in Sesame Seeds

The total phenolic content (TPC) of sesame seeds (Sesamum indicum) was measured using the Folin–Ciocalteu colorimetric method, while the total flavonoid content (TFC) was determined by the aluminum chloride ($AlCl_3$) assay. Both methods are widely applied to quantify bioactive compounds in plant materials and provide reliable estimates of antioxidant potential. All measurements were performed in triplicate and expressed as mg GAE/100 g dry weight (DW) for TPC and mg CE/100 g DW for TFC, following the procedures described by (21).

3.2.5. Blood sampling:

At the end of the study, blood samples were collected following a 12-hour fasting period. Blood was obtained using the retro-orbital method with specialized glass capillary tubes and transferred into clean, dry centrifuge tubes. The samples were allowed to clot for 30 minutes at room temperature in a water bath maintained at 37 °C. Subsequently, the clotted blood was centrifuged at 3000 rpm for 10 minutes to separate the serum prior to glucose analysis. The resulting serum was carefully aspirated, transferred into clean, tightly sealed polypropylene tubes, and stored at −20 °C until further analysis.

3.2.6. Biological evaluation:

Throughout the 28-day study period, daily food intake was recorded, while body weight was measured weekly. Based on these measurements, the feeding efficiency ratio (F.E.R.), body weight gain percentage (B.W.G.%), and organ weights were calculated according to the method described by (22).

3.2.7. Biochemical Analyses

- **Lipid Profile**

Serum total lipids were measured using a colorimetric method as described by (23). Triglycerides, total cholesterol, and high-density lipoprotein (HDL) levels were determined according to the methods of (23), (24), and (25), respectively. Low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) concentrations were calculated based on the method described by (26). The atherogenic index was determined according to (27).

- **Liver Function Tests**

Serum alanine aminotransferase (ALT) activity was measured according to (28). Aspartate aminotransferase (AST) activity was determined following the method of (29). Alkaline phosphatase (ALP) activity was assessed according to (30). Serum total protein and albumin concentrations were determined using the method described by (29).

- **Renal Function Tests**

Serum uric acid was assessed using the colorimetric method of (31).

- **Blood Glucose**

Serum glucose concentration was determined according to (32).

3.2.8. Ethical Approval

All experimental procedures involving live animals were performed in full compliance with the established institutional regulations governing the ethical care and use of laboratory animals. The complete study design and related experimental protocols received prior review and official approval from the Research Ethics Committee of Al-Baha University (Approval No. 46123022; 17 April 2025).

3.2.9. Statistical Analysis

Data are presented as mean ± standard deviation (SD). Statistical analysis was performed using one-way analysis of variance (ANOVA) for a completely randomized design **(33)**. Significant differences among group means were determined using Duncan's multiple range test at $p < 0.05$.

4. Results

4.1. Phytochemical Profile

As shown in Figure 2, Sesamum indicum seeds exhibited high levels of antioxidant-related phytochemicals. The total phenolic content (TPC) reached 520.7 mg gallic acid equivalents (GAE) per 100 g dry weight (DW), reflecting the richness of the seeds in phenolic constituents. These compounds are widely acknowledged for their redox properties, which enable them to scavenge free radicals and mitigate oxidative damage. The observed phenolic concentration highlights the potential contribution of sesame seeds to dietary antioxidant intake.

In parallel, the total flavonoid content (TFC) was recorded at 480.3 mg catechin equivalents (CE) per 100 g DW, indicating a substantial presence of flavonoid compounds within the seed matrix. Flavonoids are important secondary metabolites associated with multiple biological activities, including antioxidant and anti-inflammatory effects. Their considerable amount further supports the biofunctional properties of sesame seeds.

Collectively, these findings confirm that sesame seeds represent a valuable natural source of antioxidant phytochemicals with potential health-promoting effects.

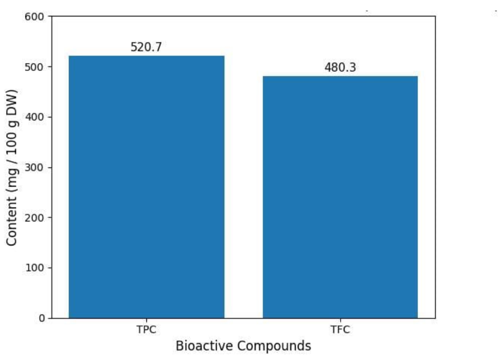

Figure 2. Total Phenolic and Flavonoid Contents of Sesame Seeds (Sesamum indicum)

4.2 Biological Evaluation

The results presented in Figure 3 illustrate the effects of dietary supplementation with sesame seeds on daily body weight gain (BWG), daily food intake (FI), and feed efficiency ratio (FER) in rats. The positive control group (+ve) exhibited the highest BWG (1.68 ± 0.020 g/day), whereas the negative control group (–ve) showed a BWG of 1.14 ± 0.003 g/day.

Rats supplemented with sesame seeds demonstrated a marked reduction in BWG. Specifically, the 7.5% sesame seed group recorded a BWG of –0.72 ± 0.010 g/day, while the 12.5% sesame seed group showed a further decrease to –1.04 ± 0.005 g/day, indicating a dose-dependent effect of sesame on weight reduction.

Regarding daily food intake (FI), the highest consumption was observed in the 12.5% sesame seed group (19.90 ± 0.040 g/day), compared to 17.00 ± 0.200 g/day in the negative control group. The 7.5% sesame seed group exhibited a moderate intake of 17.92 ± 0.10 g/day, suggesting a slight increase in food consumption with increasing sesame concentration.

Feed efficiency ratio (FER) decreased in the sesame-supplemented groups, with values of –0.040 ± 0.003 g/day for the 7.5% group and –0.052 ± 0.002 g/day for the 12.5% group, in comparison to 0.091 ± 0.008 g/day in the positive control and 0.067 ± 0.011 g/day in the negative control.

These findings indicate that dietary supplementation with sesame seeds reduces body weight gain and feed efficiency in rats, with more pronounced effects at higher supplementation levels (12.5%), while food intake remains relatively elevated in the high-dose group. Data are expressed as mean ± standard deviation, and different superscript letters denote statistically significant differences at $p \leq 0.05$.

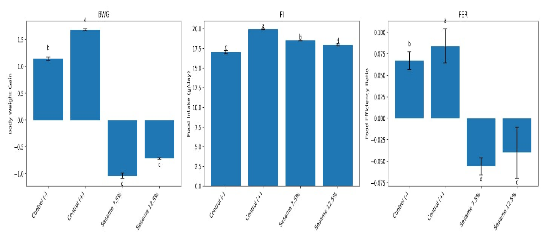

Figure (3): Effect of different levels of sesame (Sesamum indicum) seeds on BWG, FI and FER of Hyperlipidemic Rats

4.3 Biochemical Analysis

The effects of dietary supplementation with sesame seeds on lipid profile parameters in rats are presented in Figures 4 and 5. Total cholesterol (T.C) was highest in the positive control group (+ve, 237.80 ± 0.12 mg/dl) and lowest in the negative control group (–ve, 102.80 ± 0.01 mg/dl). Supplementation with sesame seeds reduced T.C in a dose-dependent manner, with values of 153.80 ± 0.03 mg/dl for the 7.5% sesame seed group and 131.00 ± 0.01 mg/dl for the 12.5% sesame seed group.

Triglyceride levels (T.G) followed a similar pattern. The +ve control exhibited the highest T.G (148.00 ± 0.090 mg/dl), while the –ve control showed the lowest (41.80 ± 0.011 mg/dl). The 7.5% sesame seed and 12.5% sesame seed groups recorded intermediate values of 89.80 ± 0.060 mg/dl and 71.20 ± 0.070 mg/dl, respectively, indicating a clear lipid-lowering effect of sesame supplementation.

Regarding high-density lipoprotein cholesterol (HDL-C), the –ve control group showed the highest level (52.60 ± 0.045 mg/dl), whereas the +ve control group had the lowest (37.00 ± 0.030 mg/dl). Supplementation with sesame seeds improved HDL-C levels, with 42.40 ± 0.011 mg/dl in the 7.5% group and 49.60 ± 0.091 mg/dl in the 12.5% group, suggesting a beneficial effect on protective cholesterol fractions.

Low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) were markedly elevated in the +ve control (171.20 ± 0.020 mg/dl and 29.60 ± 0.110 mg/dl, respectively) compared to the –ve control (41.84 ± 0.003 mg/dl and 8.36 ± 0.009 mg/dl). Sesame seed supplementation reduced LDL-C and VLDL-C levels in a dose-dependent manner, with values of 93.44 ± 0.003 mg/dl and 17.96 ± 0.016 mg/dl for the 7.5% group, and 67.16 ± 0.005 mg/dl and 14.24 ± 0.007 mg/dl for the 12.5% group.

The atherogenic index (AI) followed a similar trend. The +ve control exhibited the highest AI (5.43 ± 0.093), whereas the –ve control had the lowest (0.95 ± 0.017). Supplementation with sesame seeds reduced AI values to 2.63 ± 0.011 and 1.64 ± 0.009 in the 7.5% and 12.5% groups, respectively, indicating a decreased cardiovascular risk associated with sesame intake.

Data are expressed as mean ± standard deviation. Different superscript letters indicate statistically significant differences at $p \leq 0.05$. Overall, these findings demonstrate that sesame seed supplementation modulates lipid profile parameters in a dose-dependent manner, with more pronounced improvements at higher supplementation levels (12.5%).

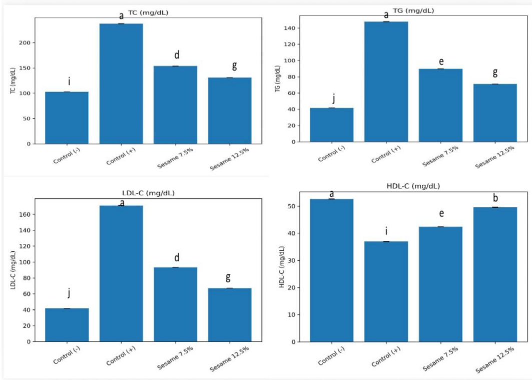

Figure 4. Effect of different levels of sesame (*Sesamum indicum*) seeds on the serum lipid profile (TC, TG, HDL-C, and LDL-C) in hyperlipidemic rats.

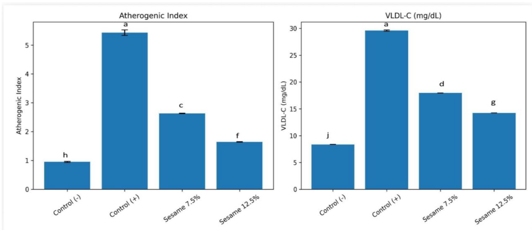

Figure 5. Effect of different levels of sesame (*Sesamum indicum*) seeds on serum VLDL-C levels and the atherogenic index in hyperlipidemic rats.

The effects of dietary supplementation with sesame seeds on blood glucose levels in rats are presented in Figure 6. The negative control group (–ve) exhibited the lowest glucose concentration (47.80 ± 0.020 mg/dL), whereas the positive control group (+ve) showed the highest level (92.00 ± 0.060 mg/dL), indicating a hyperglycemic condition. Rats supplemented with sesame seeds demonstrated a reduction in glucose levels in a dose-dependent manner. The 7.5% sesame seed group recorded a glucose concentration of 62.00 ± 0.040 mg/dL, while the 12.5% sesame seed group showed a further decrease to 60.20 ± 0.030 mg/dL. These results suggest that sesame seed supplementation effectively mitigates hyperglycemia, with higher doses producing slightly greater reductions in blood glucose.

Data are expressed as mean ± standard deviation. Different superscript letters indicate statistically significant differences at $p \leq 0.05$. Overall, the findings demonstrate the potential of sesame seeds to improve glucose regulation in a dose-dependent manner.

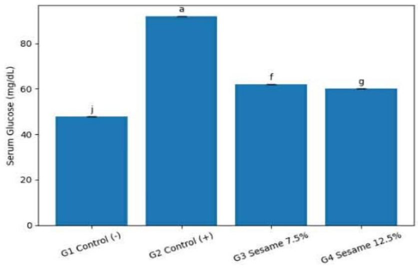

Figure 6. Effect of different levels of sesame (Sesamum indicum) seeds on serum glucose in hyperlipidemic rats.

As shown in Figure 7, significant differences in serum liver enzyme activities were detected among the experimental groups ($p \leq 0.05$). The positive control group (G2) exhibited substantially elevated levels of ALP (219.50 ± 54.50 U/L), AST (183.33 ± 3.79 U/L), and ALT (53.33 ± 1.53 U/L) compared with the negative control group (G1), indicating pronounced hepatic dysfunction.

Conversely, the negative control group demonstrated lower enzyme activities, with ALP (108.50 ± 3.50 U/L), AST (121.00 ± 3.00 U/L), and ALT (30.00 ± 4.36 U/L), consistent with normal liver function. Dietary supplementation with sesame seeds improved liver enzyme parameters in a dose-dependent manner. The 7.5% sesame group (G3) showed reductions in ALP, AST, and ALT relative to the positive control group. A greater improvement was observed in the 12.5% sesame group (G4), which exhibited further decreases in all measured enzymes.

Overall, these findings indicate that sesame seed supplementation attenuated hyperlipidemia-induced elevations in liver enzymes, with the higher dose demonstrating a more pronounced hepatoprotective effect. Data are expressed as mean ± standard deviation (SD), and different superscript letters within the same column indicate statistically significant differences at $p \leq 0.05$.

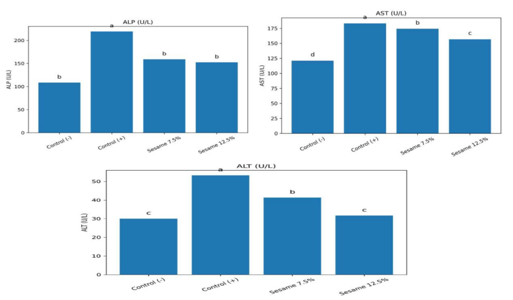

Figure 7. Effect of different levels of sesame (*Sesamum indicum*) seeds on serum liver enzymes (ALP, AST, and ALT) in hyperlipidemic rats.

As shown in Figure 8, significant variations in serum uric acid (UA) levels were detected among the experimental groups ($p \leq 0.05$). The positive control group (G2) recorded the highest UA concentration (3.13 ± 0.126 mg/dL) compared with the negative control group (2.03 ± 0.153 mg/dL), indicating an increase associated with hyperlipidemia.

Sesame seed supplementation significantly lowered serum UA levels relative to the positive control group. The 7.5% sesame group (G3) demonstrated a reduction in UA to 1.90 ± 0.045 mg/dL, whereas the 12.5% group (G4) showed a further decrease to 1.74 ± 0.010 mg/dL. The most pronounced improvement was observed in the higher-dose group, suggesting a dose-dependent beneficial effect.

Data are presented as mean ± standard deviation (SD) (n = 6). Different superscript letters within the same column denote statistically significant differences at $p \leq 0.05$.

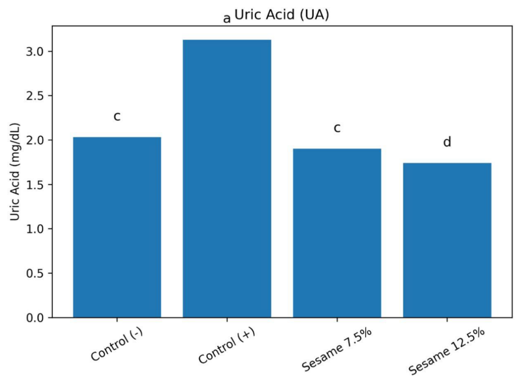

Figure 8. Effect of different levels of sesame (*Sesamum indicum*) seeds on serum uric acid (UA) in hyperlipidemic rats.

4.4 Immunological Results

As illustrated in Figure 9, statistically significant differences were detected among the experimental groups in serum immunoglobulin E (IgE) and immunoglobulin A (IgA) levels ($p \leq 0.05$). The positive control group (G2) showed significantly elevated IgE and IgA concentrations compared with the negative control group (G1), indicating immune dysregulation associated with hyperlipidemia.

Dietary supplementation with sesame seeds at 7.5% (G3) and 12.5% (G4) resulted in significant reductions in both IgE and IgA levels relative to the positive control group. IgE concentrations decreased to 89.67 ± 2.52 in G3 and 82.00 ± 2.00 in G4, while IgA levels declined to 111.67 ± 1.53 and 105.00 ± 1.00, respectively. The most pronounced improvements were observed in the 12.5% sesame group, suggesting a dose-dependent immunomodulatory effect.

Data are expressed as mean ± standard deviation (SD), and different superscript letters within the same column indicate statistically significant differences at $p \leq 0.05$.

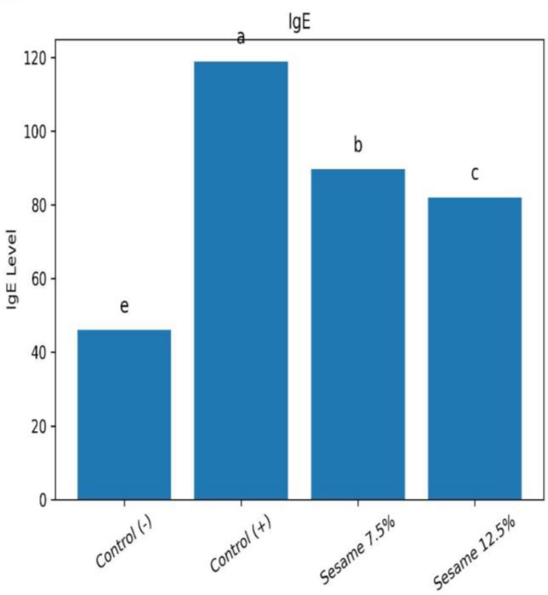

Figure 9. The effect of different experimental treatments on serum IgE and IgA levels in hyperlipidemic rats.

4.5 Histopathological Examination of Heart Tissue

The histopathological evaluation of cardiac tissues from the different experimental groups was performed to assess the potential protective effects of sesame (*Sesamum indicum*) seeds against hyperlipidemia-induced myocardial alterations.

Figure 10. "Photomicrographs of hematoxylin and eosin (H&E)-stained cardiac tissue sections reveal distinct histological differences across the experimental groups. **Panel (1)**, representing the negative control group (G1), displays remarkably preserved myocardial histology with a rare focus of mild circulatory disturbance (congestion). This confirms the overall integrity of cardiac structures under basal conditions. **Panel (2)**, corresponding to the positive control group (G2), demonstrates typical myocardial features without evident inflammatory or necrotic changes, indicating that the short-term high-fat diet may have induced biochemical changes preceding overt structural damage. Supplementation with **7.5% sesame seeds (Panel 3; G3)** and **12.5% sesame seeds (Panel 4; G4)** reveals a high degree of structural preservation. Both treatment groups exhibit pristine cardiac muscle morphology, with regularly arranged cardiomyocytes and intact nuclear features. The complete absence of pathological alterations in the treated groups underscores the potential cardioprotective role of dietary sesame seeds against metabolic challenges."

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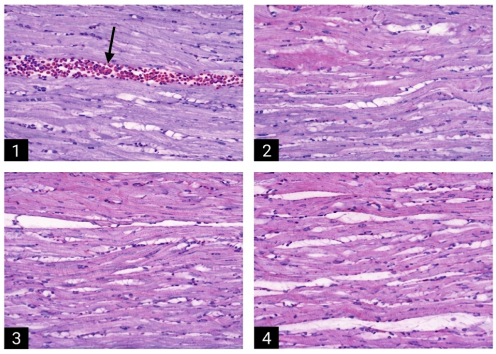

Figure 10. Histopathological sections of rat heart tissue from different experimental groups stained with H&E (×400).

5. Discussion

The findings of the present study demonstrate that sesame (Sesamum indicum) seed supplementation exerts comprehensive metabolic benefits in hyperlipidemic rats. The observed improvements across lipid profile, glycemic control, hepatic enzymes, immune markers, and uric acid levels indicate that sesame acts through multiple interconnected biological pathways rather than a single mechanism. One of the primary mechanisms underlying the lipid-lowering effects of sesame seeds is their high content of bioactive lignans, particularly sesamin and sesamolin. Recent experimental evidence indicates that sesamin enhances hepatic fatty acid oxidation and modulates lipid metabolism through activation of signaling pathways such as AMP-activated protein kinase (AMPK) and peroxisome proliferator-activated receptor-alpha (PPARα), leading to reduced lipid accumulation (34). In addition, systematic reviews and meta-analyses of human studies suggest that sesame-derived lignans improve lipid profiles, including reductions in total cholesterol and low-density lipoprotein cholesterol, potentially through PPAR-mediated regulation of lipid homeostasis (35). Through these molecular and metabolic pathways, sesame supplementation may decrease hepatic lipid deposition and improve systemic lipid distribution. Furthermore, sesame seeds are rich in unsaturated fatty acids, particularly linoleic and oleic acids, which have well-documented effects on improving plasma lipid composition. Dietary intake of linoleic acid, a major polyunsaturated fatty acid present in sesame oil, has been associated with significant reductions in low-density lipoprotein cholesterol levels compared with saturated fatty acids, indicating a beneficial role in lipid profile modulation (36). In addition, unsaturated fatty acids may facilitate reverse cholesterol transport mechanisms and promote a more favorable distribution of lipoproteins, contributing to cardiometabolic health (37). Sesame seeds also contain phytosterols and other bioactive compounds that can competitively inhibit intestinal cholesterol absorption, thereby reducing circulating cholesterol concentrations and lowering atherogenic risk. Collectively, these constituents contribute to the beneficial effects of sesame on blood lipid profiles and cardiovascular risk factors. The improvement in HDL-associated parameters is particularly important, as high-density lipoprotein (HDL) particles play a central role in reverse cholesterol transport, facilitating the removal of excess cholesterol from peripheral tissues to the liver for excretion. Recent evidence emphasizes that not only HDL cholesterol concentration but also HDL functionality is crucial for cardiovascular protection (38).Enhancement of HDL function may be associated with improved antioxidant status, since oxidative stress can alter HDL structure, reduce its anti-inflammatory properties, and impair its cholesterol efflux capacity (6). Sesame seeds contain natural antioxidants, including tocopherols and various phenolic compounds, which have been shown to protect lipoproteins from oxidative modification and help preserve their physiological activity. Through these mechanisms, sesame consumption may contribute to improved HDL quality and reduced atherogenic risk. The beneficial effect of sesame supplementation on glucose regulation suggests a potential role in improving insulin sensitivity. Hyperlipidemia is frequently associated with insulin resistance, which contributes to impaired glucose metabolism and increased cardiometabolic risk (39). Emerging evidence indicates that sesame bioactive compounds, including lignans and antioxidant constituents, may enhance insulin signaling pathways and improve peripheral glucose uptake by reducing oxidative stress and inflammatory responses in insulin-sensitive tissues. Oxidative stress plays a critical role in the progression of β-cell dysfunction, and antioxidants derived from dietary sources may help preserve pancreatic β-cell integrity and function (40). Through these mechanisms, sesame supplementation may contribute to improved glycemic control and metabolic homeostasis. The hepatoprotective effects observed in this study further highlight the therapeutic potential of sesame seeds. Elevated liver enzymes, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are commonly used biomarkers of hepatocellular injury and membrane damage (41). The reduction in these enzymes following sesame supplementation suggests improved hepatic integrity, stabilization of cell membranes, and decreased leakage of intracellular enzymes into circulation. Such protective effects may be attributed to the antioxidant and anti-inflammatory properties of sesame bioactive compounds, which can attenuate lipid-induced oxidative stress and mitochondrial dysfunction in liver tissues (42). By reducing oxidative damage and inflammatory signaling, sesame constituents may contribute to improved liver function and metabolic protection. Additionally, the immunomodulatory effects demonstrated by the reduction in immunoglobulin levels suggest that sesame seeds may help regulate inflammatory responses associated with metabolic disorders. Chronic low-grade inflammation is a hallmark of hyperlipidemia and metabolic syndrome and plays a central role in the development and progression of cardiometabolic diseases (43). Sesame phytochemicals, including lignans and phenolic compounds, have been reported to exert anti-inflammatory effects by suppressing pro-inflammatory cytokines and modulating immune cell signaling pathways. By attenuating inflammatory mediators and oxidative stress, sesame constituents may contribute to improved immune balance and metabolic homeostasis. The reduction in uric acid levels following sesame supplementation may reflect improved metabolic and oxidative status. Elevated serum uric acid is strongly associated with oxidative stress, systemic inflammation, insulin resistance, and increased cardiometabolic risk (6). Hyperuricemia is also linked to endothelial dysfunction and impaired renal and metabolic regulation, contributing to the progression of metabolic disorders (44).

Sesame seeds contain bioactive compounds with antioxidant and anti-inflammatory properties that may enhance endogenous antioxidant defenses and reduce inflammatory signaling pathways, thereby potentially supporting more balanced uric acid metabolism and lowering associated metabolic risk . Through these mechanisms, sesame supplementation may contribute to improved redox status and metabolic homeostasis.Importantly, the overall pattern of results suggests a dose-dependent response, with higher sesame intake generally producing more pronounced metabolic improvements. Dose–response relationships are a fundamental principle in nutritional interventions, indicating that the magnitude of physiological effects is related to the level of bioactive compound consumption. Evidence from recent systematic reviews and meta-analyses suggests that sesame-derived constituents exert measurable effects on lipid profile, inflammatory markers, and glycemic control in a manner consistent with increasing intake levels. Such findings reinforce the concept that the biological effects of sesame are attributable to its active components, including lignans, unsaturated fatty acids, phytosterols, and antioxidant compounds. Collectively, these data support the potential use of sesame seeds as a functional food ingredient with multi-target metabolic benefits (15). Nevertheless, while the present results are promising, further investigations are required to elucidate the underlying molecular mechanisms, including comprehensive gene expression analyses, enzymatic activity profiling, and assessment of inflammatory and oxidative stress markers. Modern nutrigenomic approaches are essential to better characterize how bioactive food constituents modulate metabolic pathways at the transcriptional and cellular levels (45). Additionally, although experimental and short-term studies provide supportive evidence, long-term randomized controlled trials in humans are necessary to confirm the translational and clinical relevance of these findings and to establish causality in metabolic outcomes . Such studies will strengthen the evidence base for the use of sesame as a functional food with metabolic benefits. In conclusion, sesame seed supplementation demonstrated significant protective effects against hyperlipidemia-induced metabolic disturbances, likely mediated through antioxidant, lipid-modulating, anti-inflammatory, and insulin-sensitizing mechanisms.

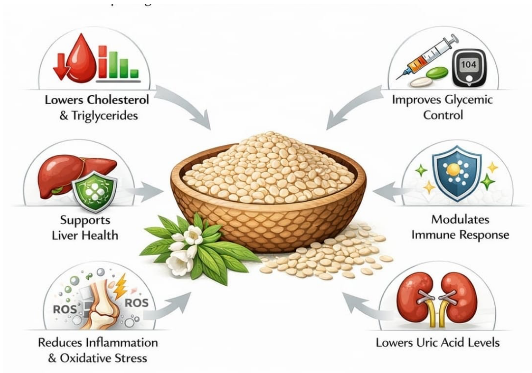

Figure 11. Proposed Mechanisms Underlying the Therapeutic and Protective Effects of Sesame Seed Supplementation.

6. Conclusion

The present study demonstrates that dietary supplementation with sesame (*Sesamum indicum*) seeds exerts significant beneficial effects on metabolic, hepatic, immunological, and oxidative parameters in hyperlipidemic rats. Sesame supplementation improved body weight regulation, enhanced lipid profile, reduced atherogenic risk, and positively modulated serum glucose levels. In addition, it attenuated liver enzyme elevations, normalized immunoglobulin levels, and reduced uric acid concentration, indicating hepatoprotective, immunomodulatory, and metabolic-regulating properties. These effects are likely attributed to the rich composition of sesame seeds, including lignans, unsaturated fatty acids, tocopherols, phytosterols, and phenolic compounds, which collectively contribute to antioxidant, anti-inflammatory, lipid-lowering, and insulin-sensitizing activities. The observed improvements were generally more pronounced at the higher supplementation level, suggesting a dose-dependent response. Overall, sesame seeds may represent a promising functional dietary component for the prevention and management of hyperlipidemia and its associated metabolic complications. Further mechanistic studies and clinical trials are recommended to confirm these findings and explore their translational potential in humans.

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