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Effects of Dietary Sesame Seed Supplementation on Alleviating Oxidative Stress–Induced Damage and Restoring Immune Homeostasis in Experimental Rats

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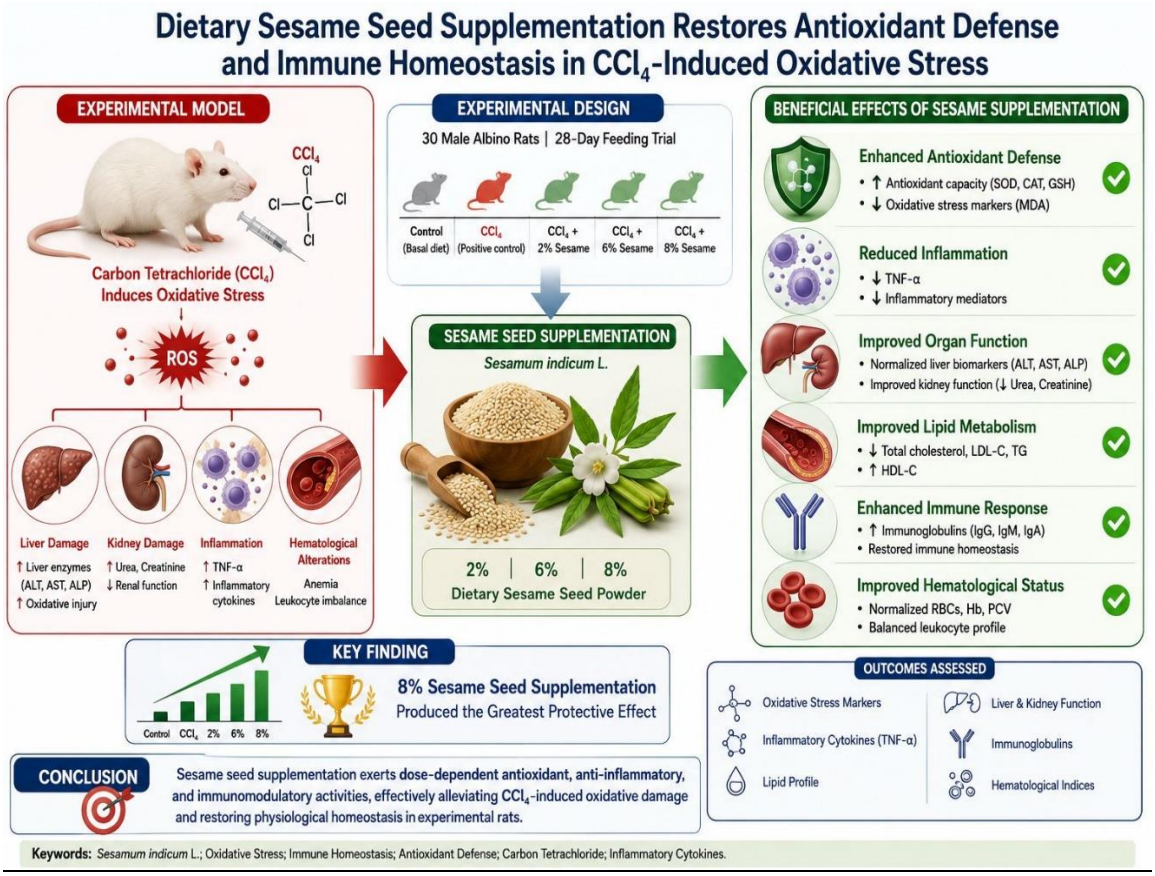
ABSTRACT: This study aimed to investigate the potential protective effects of dietary sesame seed supplementation against oxidative stress-induced biochemical and immunological alterations in experimental rats. Thirty adult male albino rats (150 ± 10 g) were randomly allocated into five groups (n = 6 per group). Group 1 served as the negative control and received a standard basal diet without any intervention. Group 2 represented the positive control group, in which oxidative stress was induced and animals were maintained on a basal diet without supplementation. Groups 3, 4, and 5 consisted of oxidatively stressed rats fed a basal diet supplemented with sesame seed powder at concentrations of 2%, 6%, and 8%, respectively. The experimental period lasted 28 days. At the end of the study, animals were sacrificed, and blood samples were collected for biochemical and immunological analyses to evaluate oxidative stress markers and immune function parameters. Dietary sesame seed supplementation significantly and dose-dependently ameliorated these alterations. The 8% sesame group demonstrated the most pronounced effects, restoring antioxidant defenses, reducing oxidant and inflammatory marker (including Tumor Necrosis Factor-alpha), improving lipid profile, and normalizing liver and kidney function parameters. In addition, sesame supplementation improved hematological indices and enhanced immunoglobulin levels toward normal values. In conclusion, sesame seed exerts dose-dependent antioxidant, anti-inflammatory, and immunomodulatory effects, effectively mitigating Carbon Tetrachloride-induced oxidative damage and restoring physiological homeostasis in experimental rats.



Graphic abstract: Sesame Seed Supplementation Counteracts CCl_4-Induced Oxidative Stress and Restores Immune Homeostasis in Experimental Rats.

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1. INTRODUCTION

Oxidative stress is a critical biological phenomenon implicated in the pathogenesis of numerous chronic and degenerative diseases. It arises from an imbalance between the generation of reactive oxygen species (ROS) and the capacity of the antioxidant defense system to neutralize them . As illustrated in Figure 1, excessive accumulation of ROS can lead to lipid peroxidation, protein modification, DNA damage, and ultimately cellular dysfunction (Halliwell & Gutteridge, 2015). In experimental and clinical settings, oxidative stress has been closely associated with immune dysregulation, where both innate and adaptive immune responses may become impaired or excessively activated, resulting in pathological inflammation and disruption of immune homeostasis.. Disturbance of redox balance may affect cytokine secretion, lymphocyte activation and proliferation, and macrophage-mediated immune responses, thereby compromising host defense mechanisms. Consequently, restoring redox homeostasis has emerged as a promising therapeutic strategy for managing oxidative stress-associated immune dysfunction (Manoharan et al., 2024; Perpinan et al., 2023).

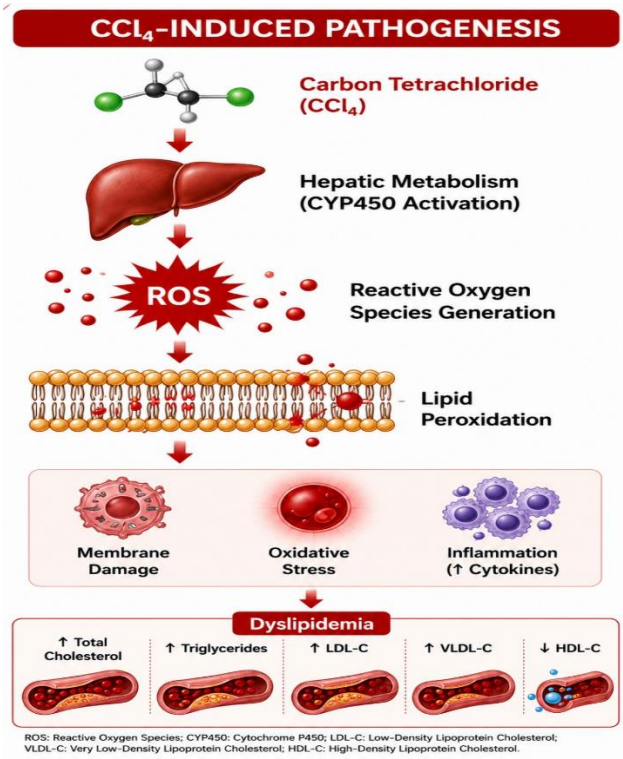

Figure 1. Schematic Illustration of the Pathogenesis of Carbon Tetrachloride (CCl_4)-Induced Liver Injury Through CYP450-Mediated Reactive Oxygen Species Generation, Lipid Peroxidation, Inflammation, and Dyslipidemia.

In recent years, there has been growing interest in natural dietary antioxidants as potential modulators of oxidative stress and immune responses (Pisoschi, & Pop,2015). Plant-derived bioactive compounds, particularly polyphenols, flavonoids, and lignans, have demonstrated significant antioxidant and anti-inflammatory properties. These compounds not only scavenge free radicals but also enhance endogenous antioxidant defense systems, contributing to improved cellular resilience against oxidative injury (Shaito et al., 2022; Durazzo et al., 2019). Sesame seeds (*Sesamum indicum* L.) are among the richest natural sources of bioactive lignans, primarily sesamin, sesamolin, and sesamol. These compounds have been extensively investigated for their antioxidant, anti-inflammatory, and immunomodulatory activities (Elleuch et al., 2007). Sesamin has been shown to enhance antioxidant enzyme activities and reduce lipid peroxidation, while sesame lignans may modulate inflammatory signaling pathways, including NF-κB, thereby reducing the production of pro-inflammatory cytokines and attenuating inflammatory responses (Majdalawieh et al., 2019).A dietary supplementation with sesame seeds and their lignans can improve oxidative stress biomarkers by enhancing the activities of endogenous antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), while reducing malondialdehyde (MDA) levels, a major marker of lipid peroxidation. These antioxidant effects may contribute to improved immune regulation and maintenance of cellular homeostasis (Majdalawieh et

al., 2019; Elmeged & Albaggar, 2026). Beyond their antioxidant properties, sesame seeds are recognized as nutrient-rich functional foods due to their diverse nutritional composition, including high-quality proteins, dietary fiber, essential minerals, and unsaturated fatty acids. They are particularly rich in minerals such as calcium, magnesium, phosphorus, zinc, and selenium, which play important roles in various physiological processes, including cellular metabolism, enzymatic activity, and immune function. In addition, sesame seeds contain substantial amounts of mono- and polyunsaturated fatty acids, which are important components of cellular membranes and may contribute to maintaining cellular integrity and protecting against oxidative stress. The combination of these nutritional and bioactive constituents highlights the potential of sesame seeds as a valuable dietary component for supporting antioxidant defenses and reducing the risk of oxidative stress-related disorders (Durazzo et al., 2019; Wei et al., 2022) Among the bioactive constituents of sesame seeds, lignans have attracted particular attention because of their ability to interact with molecular pathways involved in oxidative stress and inflammation (Wei et al., 2022). Previous studies have demonstrated that sesamin can regulate gene expression associated with antioxidant defense mechanisms and may enhance the activity of endogenous detoxification enzymes (Labban et al., 2026). Moreover, sesamol has been shown to protect biological membranes against oxidative injury through direct free-radical scavenging activity and inhibition of lipid peroxidation processes.

These observations suggest that the beneficial effects of sesame seeds extend beyond simple antioxidant activity and may involve complex regulatory actions at the cellular and molecular levels. Another important mechanism through which sesame-derived compounds exert their biological effects involves the regulation of redox-sensitive transcription factors (Majdalawieh et al .,2017). Given the increasing prevalence of disorders associated with oxidative stress and immune dysfunction, the identification of safe, affordable, and naturally occurring dietary interventions has become a major focus of biomedical and nutritional research. Sesame seeds offer considerable promise in this regard due to their unique combination of antioxidant lignans, essential nutrients, and immunomodulatory properties. However, further investigation is required to determine the extent to which different levels of dietary supplementation can influence oxidative stress biomarkers and immune responses under experimentally induced conditions. Understanding these relationships may contribute to the development of evidence-based nutritional strategies aimed at improving health and preventing disease. Despite the growing body of evidence supporting the antioxidant and immunomodulatory properties of sesame seeds, there remains a need for dose-dependent in vivo studies that evaluate their efficacy in experimentally induced oxidative stress models (Alzahrani et al., 2026). In particular, the relationship between varying dietary concentrations of sesame seed supplementation and immune homeostasis restoration has not been fully elucidated.

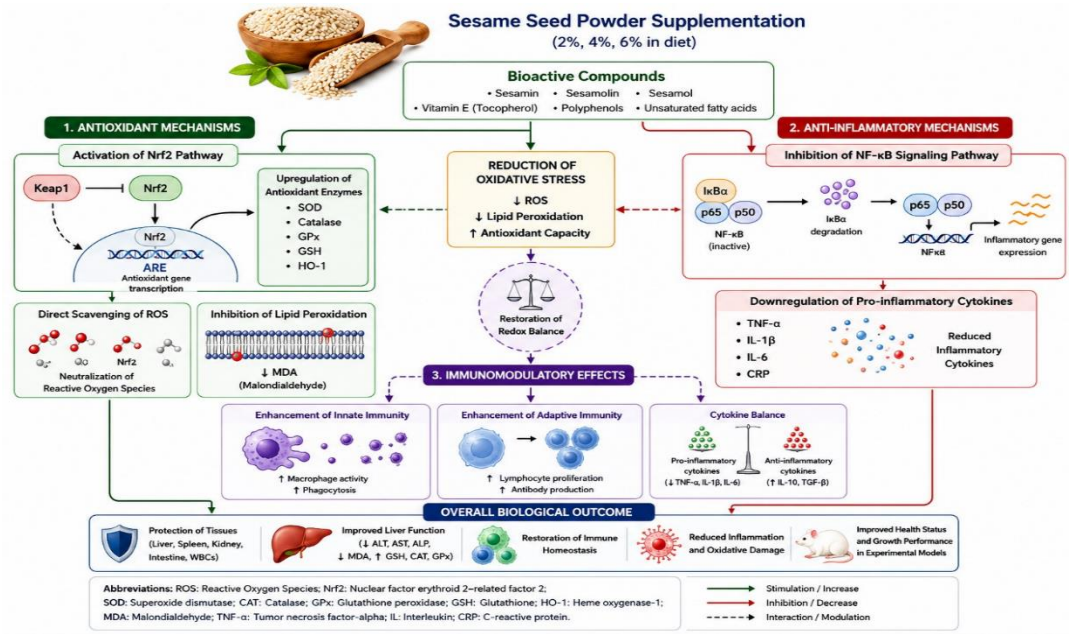

Figure 2. Proposed Mechanisms Underlying the Protective Effects of Dietary Sesame Seed Powder Against Oxidative Stress and Immune Dysfunction in Experimental Rats.

2. AIM OF STUDY

The present study was designed to investigate the potential protective effects of dietary sesame seed supplementation at different concentrations (2%, 6%, and 8%) on oxidative stress-induced biochemical alterations and immune dysfunction in albino rats. The study aims to provide further insight into the dose-dependent antioxidant and immunomodulatory effects of sesame seeds in an experimental model of oxidative stress.

3. MATERIALS AND METHODS

3.1. Materials

3.1.1. Preparation of Sesame (Sesamum indicum L.) Seed Powder

Sesame seeds (*Sesamum indicum* L.) were purchased from a certified local agricultural market in Menoufia Governorate, Egypt. The seeds were manually cleaned to remove dust, damaged seeds, and foreign materials. After cleaning, the seeds were washed with distilled water and air-dried under laboratory conditions. To preserve their bioactive constituents, the seeds were further dried in a forced-air oven at 40°C until constant weight was achieved. The dried seeds were finely ground using a laboratory grinder and sieved to obtain a homogeneous powder. The resulting powder was stored in airtight amber-colored glass containers at room temperature until dietary formulation.

3.1.2. Chemicals and Reagents

All chemicals and analytical reagents used in the present study were of analytical grade. Diagnostic kits used for biochemical and immunological analyses were obtained from certified commercial suppliers (El-Gomhoria Company for Medical Supplies, Cairo, Egypt) and were used according to the manufacturers' instructions.

3.1.3. Carbon Tetrachloride (CCl_4)

Carbon tetrachloride (CCl_4) was obtained from El-Gomhoria Company for Chemicals and Medical Supplies, Cairo, Egypt. The compound was supplied as a 10% liquid preparation and stored according to the manufacturer's recommendations. Prior to administration, CCl_4 was freshly diluted in paraffin oil to obtain the required concentration for oxidative stress induction. Carbon tetrachloride was selected because of its well-established ability to generate reactive oxygen species and induce oxidative tissue damage in experimental animals (Weber et al., 2003).

3.2. Biological Experiment

3.2.1. Experimental Animals and Housing Conditions

Thirty healthy adult male albino rats weighing 150 ± 10 g were obtained from the Animal House of the National Research Centre, Giza, Egypt. The animals were housed in polypropylene cages under controlled laboratory conditions (22 ± 2°C, 50–60% relative humidity, and a 12 h light/12 h dark cycle). Food and drinking water were provided ad libitum throughout the study. Before the commencement of the experiment, all rats were acclimatized to the laboratory environment and basal diet for seven days. During this period, animals were monitored daily to ensure normal health status.

3.2.2. Experimental Diet

The basal diet was prepared according to the recommendations of the American Institute of Nutrition (AIN-93M) (Reeves et al., 1993). The diet consisted of casein, corn starch, sucrose, cellulose, corn oil, vitamin mixture, mineral mixture, and choline chloride.

For the treatment groups, sesame seed powder was incorporated into the basal diet at concentrations of 2%, 6%, and 8% (w/w), replacing equivalent amounts of corn starch to maintain nutritional balance among all experimental diets.

3.2.3. Induction of Oxidative Stress

Oxidative stress was induced using CCl_4 according to a modified protocol based on Weber et al. (2003). Rats in the oxidative stress groups received intraperitoneal injections of CCl_4 diluted in paraffin oil at a dose of 2 mL/kg body weight twice weekly for two consecutive weeks. The hepatotoxic effect of CCl_4 results from its metabolic activation by cytochrome P450 enzymes, leading to the formation of trichloromethyl (CCl_3) and trichloromethyl peroxyl ($OOCCl_3$) radicals. These reactive intermediates

initiate lipid peroxidation and oxidative cellular damage, causing disturbances in antioxidant defense systems and promoting inflammatory responses.

3.2.4. Experimental Design

Following acclimatization, rats were randomly allocated into five groups (n = 6 rats per group) as shown below and the experimental period continued for 28 consecutive days:

- Group 1 (Negative Control): Healthy rats fed the basal diet without CCl_4 administration.
- Group 2 (Positive Control): Oxidative stress-induced rats fed the basal diet without sesame supplementation.
- Group 3 (Sesame 2%): Oxidative stress-induced rats fed the basal diet supplemented with 2% sesame seed powder.
- Group 4 (Sesame 6%): Oxidative stress-induced rats fed the basal diet supplemented with 6% sesame seed powder.
- Group 5 (Sesame 8%): Oxidative stress-induced rats fed the basal diet supplemented with 8% sesame seed powder.

3.2.5. Blood Sampling and Serum Preparation

At the end of the experimental period, animals were fasted overnight prior to blood collection. Blood samples were collected from the retro-orbital venous plexus using sterile capillary tubes. Samples were allowed to clot at room temperature and subsequently centrifuged at 3000 rpm for 15 min. The separated serum was carefully transferred into sterile Eppendorf tubes and stored at −20°C until biochemical and immunological analyses were performed.

3.2.6. Determination of Total Phenolic and Flavonoid Contents of Sesame Seeds

The total phenolic content (TPC) of sesame seed powder was determined using the Folin–Ciocalteu colorimetric method (REFERNCE), while total flavonoid content (TFC) was measured using the aluminum chloride ($AlCl_3$) assay (REFERENCE). Results were expressed as mg gallic acid equivalents (GAE)/100 g dry weight for TPC and mg catechin equivalents (CE)/100 g dry weight for TFC.

3.2.7. Analytical Biochemistry

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities were determined using spectrophotometric kits (BioMérieux, France) according to the method of Reitman and Frankel (1957). Alkaline phosphatase (ALP) activity was measured colorimetrically following the method described by Roy (1970). Serum total bilirubin concentration was determined colorimetrically at 578 nm according to Doumas et al. (1973).

For lipid profile analysis, total cholesterol was determined as described by Ratliff and Hall (1973). Triglycerides and high-density lipoprotein (HDL) cholesterol were measured using enzymatic colorimetric methods (Jacobs & Van Denmark, 1960). Very-low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) concentrations were calculated according to the method of Lee and Nieman (1996). For kidney function assessment, serum creatinine and uric acid concentrations were determined according to the methods described by Bartels et al. (1972) and Haisman and Muller (1977), respectively. Whole blood samples were used for the determination of hematological parameters, including red blood cell (RBC) count, white blood cell (WBC) count, platelet (PLT) count, hemoglobin (Hb) concentration, and packed cell volume (PCV), as well as differential leukocyte counts. All measurements were performed according to Dacie and Lewis (2017).

3.2.8. Determination of Total Antioxidant Status (TAS) and Total Oxidant Status (TOS)

- **Total Antioxidant Status (TAS)**

Total Antioxidant Status (TAS) was measured using commercially available diagnostic kits (Rel Assay Diagnostics, Gaziantep, Turkey). The assay is based on the ability of antioxidants present in the sample to reduce the colored 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical to its colorless reduced form. Absorbance was measured spectrophotometrically at 660 nm. Calibration was performed using Trolox (a vitamin E analog), and results were expressed as mmol Trolox equivalents per liter (mmol Trolox eq./L), as described by Erel (2004).

- **Total Oxidant Status (TOS)**

Total Oxidant Status (TOS) was determined using commercially available kits (Rel Assay Diagnostics, Turkey) according to the method described by Erel (2005). This assay is based on the oxidation of ferrous ions, pre-complexed with a chelator, to ferric ions in the presence of oxidants in the sample. In an acidic medium, the ferric ions form a colored complex with a chromogen, the intensity of which is measured spectrophotometrically at 530 nm. Calibration was performed using hydrogen peroxide (H_2O_2), and results were expressed as μmol H_2O_2 equivalents per liter (μmol H_2O_2 eq./L).

3.2.9. Immunological Analyses

Serum immunoglobulin M (IgM) and immunoglobulin G (IgG) levels were determined using enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturer's instructions. Absorbance was measured at 450 nm, and concentrations were calculated from standard curves and expressed as mg/dL (Engvall, 1980). Serum levels of tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and interleukin-10 (IL-10) were determined using commercially available enzyme-linked immunosorbent assay (ELISA) kits .

3.2.10. Ethical Approval

All experimental procedures involving animals were conducted in accordance with the institutional guidelines for the care and use of laboratory animals. The study protocol was reviewed and approved by the Research Ethics Committee of Al-Baha University, Saudi Arabia (Approval No. 46123022; approved on 17 April 2025).

3.2.11. Statistical Analysis

Data were expressed as mean ± standard deviation (SD). Statistical analyses were performed using SPSS software (IBM Corp., Armonk, NY, USA). Differences among experimental groups were assessed using one-way analysis of variance (ANOVA), followed by Duncan's multiple range test for post hoc comparisons. Statistical significance was accepted at $P < 0.05$.

4. RESULTS

4.1. Phytochemical Profile

The phytochemical composition and antioxidant potential of the ethanolic extract of Sesamum indicum seeds were evaluated, as presented in Figure (3). The results indicated a considerable presence of bioactive constituents, particularly phenolic and flavonoid compounds. The total phenolic content (TPC) was found to be 420.00 mg GAE/100 g, suggesting a substantial contribution of phenolic metabolites to the overall phytochemical profile of the extract. In addition, the total flavonoid content (TFC) reached 610.00 mg CE/100 g, reflecting a notable abundance of flavonoid compounds, which are widely recognized for their antioxidant properties. The extract also contained low levels of carotenoids and β-carotene, recorded at 2.50 mg/100 g and 0.85 mg/100 g, respectively, indicating that these compounds play a minor role in comparison to phenolic constituents. The antioxidant activity of the ethanolic sesame seed extract, evaluated using the DPPH radical scavenging assay, demonstrated an IC_{50} value of 120.00 μg/mL, indicating a moderate free-radical scavenging activity. This activity may be associated with the presence of phenolic and flavonoid compounds in the extract. Overall, the findings suggest that *Sesamum indicum* seeds represent a valuable source of bioactive phytochemicals, particularly phenolic and flavonoid constituents, which may contribute to their antioxidant potential.

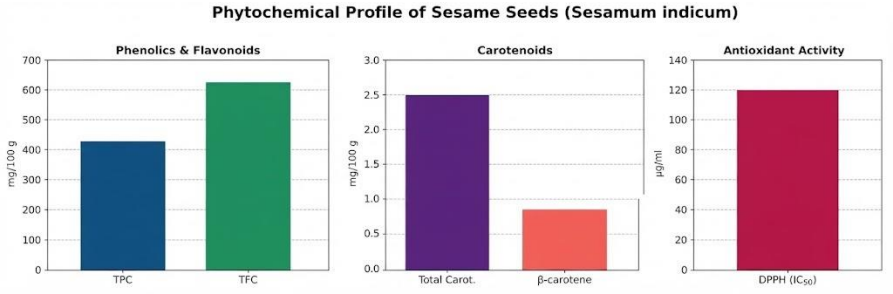

Figure 3. Phytochemical profile and antioxidant activity of the ethanolic extract of *Sesamum indicum* seeds. Data are expressed as mean ± SD (n=3). TPC: Total phenolic content; TFC: Total flavonoid content

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4.2 Biochemical Analysis

Figure (4) shows the effect of different concentrations of sesame seeds on serum lipid profile parameters, including total cholesterol (TC), triglycerides (TG), HDL-c, LDL-c, and VLDL-c (mg/dl). The negative control group (G1) recorded the most favorable lipid profile, with low levels of TC (88.42 ± 3.85 mg/dl), TG (65.20 ± 4.55 mg/dl), LDL-c (30.55 ± 8.50 mg/dl), and VLDL-c (13.05 ± 0.65 mg/dl), in addition to the highest HDL-c level (41.25 ± 2.10 mg/dl). This indicates normal lipid metabolism and a healthy biochemical status. In contrast, the positive control group (G2) showed a significant deterioration in lipid parameters, with elevated TC (122.50 ± 8.60 mg/dl), TG (110.80 ± 9.20 mg/dl), LDL-c (81.20 ± 7.10 mg/dl), and VLDL-c (22.15 ± 2.40 mg/dl), accompanied by a marked reduction in HDL-C (23.40 ± 2.50 mg/dL). These changes clearly indicate the development of CCl_4-induced dyslipidemia. Regarding the treated groups, sesame supplementation produced a gradual improvement in the lipid profile. In G3 (2% sesame), TC decreased to 114.75 ± 7.90 mg/dl, TG to 92.45 ± 5.80 mg/dl, LDL-c to 64.30 ± 6.20 mg/dl, and VLDL-c to 18.50 ± 0.75 mg/dl, while HDL-c increased to 29.80 ± 3.10 mg/dl, compared with the positive control.

A more pronounced improvement was observed in G4 (6% sesame), where TC further decreased to 102.30 ± 6.50 mg/dl, TG to 81.15 ± 4.90 mg/dl, LDL-c to 51.40 ± 4.10 mg/dl, and VLDL-c to 16.20 ± 1.10 mg/dl, with an increase in HDL-c to 33.45 ± 2.80 mg/dl.

The most significant effect was recorded in G5 (8% sesame), which showed TC of 96.80 ± 7.20 mg/dl, TG of 75.60 ± 5.10 mg/dl, LDL-c of 42.15 ± 3.90 mg/dl, and VLDL-c of 15.45 ± 0.35 mg/dl, along with the highest HDL-c level among treated groups (38.90 ± 2.30 mg/dl).

Overall, sesame seed supplementation demonstrated a clear dose-dependent hypolipidemic effect, improving lipid profile parameters progressively with increasing concentration and partially restoring values toward those observed in the negative control group.

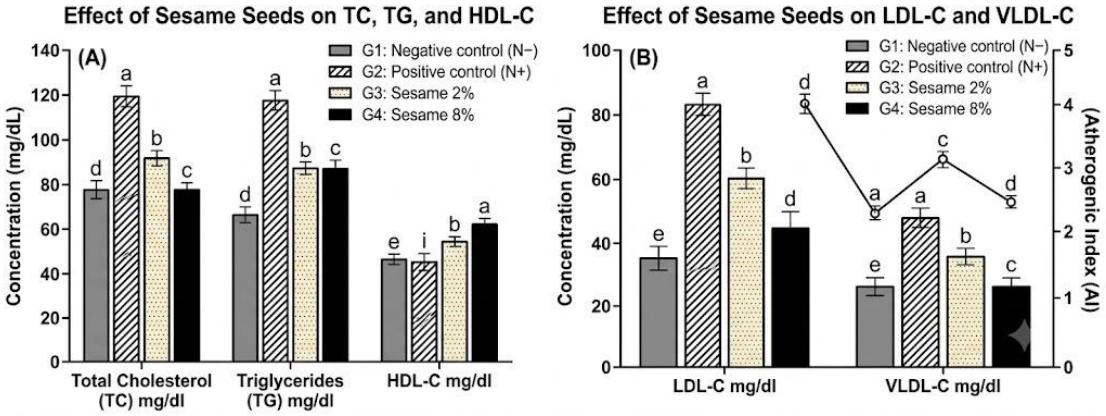

Figure 4. Effect of dietary sesame seed supplementation on lipid profile parameters and the calculated atherogenic index in experimental rats. Different superscript letters (a, b, c, etc.) indicate statistically significant differences among the experimental groups at $p < 0.05$, whereas groups sharing the same superscript letter are not significantly different.

Figure (5) presents the effect of different concentrations of sesame seeds on liver function enzymes, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) in experimental rats. The results revealed that the negative control group (G1) exhibited normal liver function enzyme levels, with AST recorded at 43.50 ± 4.20 µ/ml, ALT at 14.10 ± 1.50 µ/ml, and ALP at 32.40 ± 4.80 µ/ml. These values indicate normal hepatic cellular integrity and physiological liver activity. In contrast, the positive control group (G2) showed a marked elevation in liver enzyme activities, with AST increasing to 78.20 ± 8.40 µ/ml, ALT to 31.20 ± 2.90 µ/ml, and ALP to 55.60 ± 5.20 µ/ml. This significant rise suggests liver damage or hepatocellular injury, as elevated enzyme levels typically reflect membrane leakage and impaired liver function. Treatment with sesame seeds resulted in a noticeable improvement in liver enzyme profiles. In G3 (2% sesame), AST decreased to 55.80 ± 5.70 µ/ml, ALT to 18.50 ± 2.10 µ/ml, and ALP to 41.20 ± 3.90 µ/ml compared with the positive control group, indicating partial restoration of liver function. A further improvement was observed in G4 (6% sesame), where AST

decreased to 52.40 ± 6.30 µ/ml, ALT to 17.20 ± 1.80 µ/ml, and ALP to 39.80 ± 4.20 µ/ml, showing a stronger hepatoprotective effect.

The most pronounced improvement was recorded in G5 (8% sesame), which showed AST levels of 49.60 ± 5.10 µ/ml, ALT of 16.40 ± 2.40 µ/ml, and ALP of 38.50 ± 3.50 µ/ml. Although these values did not fully return to the levels of the negative control group, they demonstrated a clear and consistent reduction compared with the positive control group. Overall, the findings indicate that sesame seed supplementation exerts a hepatoprotective effect, as evidenced by the progressive reduction in liver enzyme levels (AST, ALT, and ALP) in a dose-dependent manner, suggesting improved liver function and reduced hepatic injury.

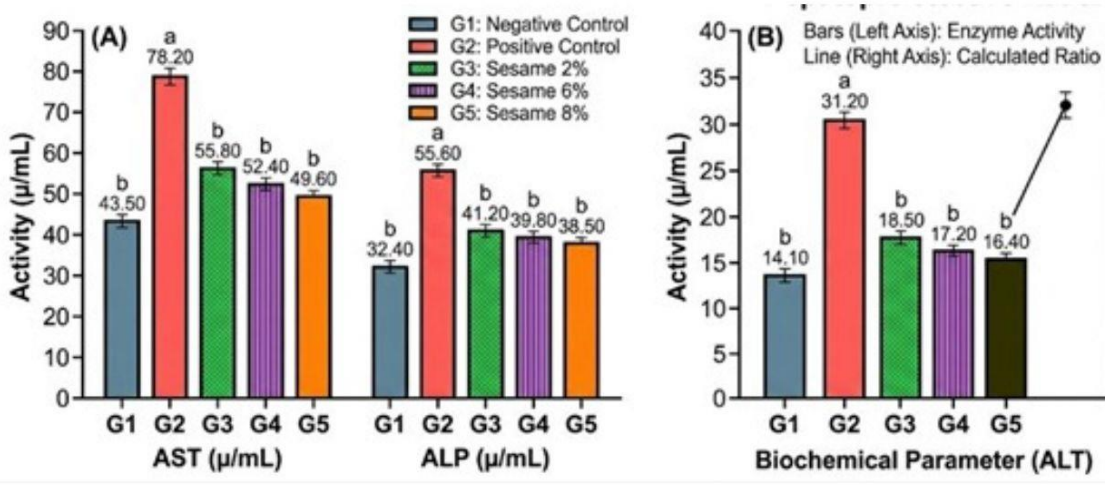

Figure 5. Effect of sesame seeds supplementation on liver function enzymes (AST, ALT, and ALP) and the calculated hepatoprotective index in experimental rats. Different superscript letters (a, b, c, etc.) indicate statistically significant differences among the experimental groups at $p < 0.05$, whereas groups sharing the same superscript letter are not significantly different.

Figure (6) illustrates the effect of different concentrations of sesame seeds on kidney function parameters, namely serum creatinine and uric acid levels, in experimental rats. The results showed that the negative control group (G1) exhibited normal kidney function, with creatinine recorded at 0.82 ± 0.05 mg/dl and uric acid at 1.95 ± 0.32 mg/dl, indicating normal renal filtration and excretory function. In contrast, the positive control group (G2) demonstrated a significant impairment in kidney function, as evidenced by a marked increase in creatinine to 2.15 ± 0.18 mg/dl and uric acid to 4.85 ± 0.95 mg/dl. These elevated levels reflect reduced renal efficiency and possible renal stress or dysfunction. Administration of sesame seeds led to an overall improvement in kidney function parameters. In G3 (2% sesame), creatinine decreased to 1.15 ± 0.08 mg/dl, while uric acid decreased to 2.65 ± 0.72 mg/dl compared with the positive control group, indicating partial renal recovery. A more noticeable improvement was observed in G4 (6% sesame), where creatinine further decreased to 0.98 ± 0.10 mg/dl and uric acid to 2.50 ± 0.65 mg/dl, suggesting enhanced nephroprotective activity. The most effective response was recorded in G5 (8% sesame), which showed creatinine levels of 0.79 ± 0.09 mg/dl and uric acid levels of 2.25 ± 0.55 mg/dl. These values approached those of the negative control group, indicating a strong protective effect of sesame supplementation on renal function.

Overall, the findings suggest that sesame seeds exert a dose-dependent nephroprotective effect, as evidenced by the gradual normalization of creatinine and uric acid levels, likely reflecting improved kidney function and reduced renal stress

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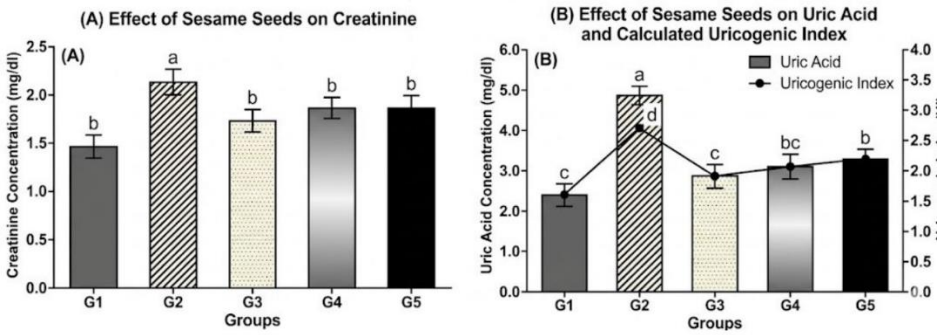

Figure 6. Effect of dietary sesame seeds supplementation on kidney function parameters (Creatinine and Uric acid) in experimental rats. Different superscript letters (a, b, c, etc.) indicate statistically significant differences among the experimental groups at $p < 0.05$, whereas groups sharing the same superscript letter are not significantly different.

Figure (7) illustrates the effect of different concentrations of sesame seeds on hematological parameters in experimental rats, including red blood cell count (RBC), white blood cell count (WBC), platelet count (PLT), hemoglobin concentration (Hb), and packed cell volume (PCV). The results showed that the negative control group (G1) exhibited normal hematological values, with RBC count of 7.01 ± 0.25 $\times 10^6$/ml, WBC count of 8.80 ± 0.15 $\times 10^3$/ml, platelet count of 402.15 ± 6.20 $\times 10^3$/ml, hemoglobin level of 16.85 ± 0.40 g/dL, and PCV of 61.20 ± 2.10%. These values reflect normal blood profile and adequate hematopoietic function. In contrast, the positive control group (G2) demonstrated a marked deterioration in hematological indices, with significant reductions in RBC (3.15 ± 0.18 $\times 10^6$/ml), WBC (4.15 ± 0.38 $\times 10^3$/ml), PLT (245.50 ± 7.15 $\times 10^3$/ml), Hb (8.95 ± 0.60 g/dL), and PCV (29.40 ± 1.95%). These findings indicate anemia, immune suppression, and overall impairment of blood formation. Administration of sesame seeds resulted in a noticeable improvement in hematological parameters. In G3 (2% sesame), RBC increased to 5.12 ± 0.40 $\times 10^6$/ml, WBC to 6.30 ± 0.45 $\times 10^3$/ml, PLT to 322.80 ± 8.10 $\times 10^3$/ml, Hb to 14.15 ± 0.50 g/dL, and PCV to 48.60 ± 3.10%, compared with the positive control group. A further improvement was observed in G4 (6% sesame), where RBC reached 4.25 ± 0.38 $\times 10^6$/ml, WBC 5.10 ± 0.35 $\times 10^3$/ml, PLT 288.20 ± 6.40 $\times 10^3$/ml, Hb 12.75 ± 0.65 g/dL, and PCV 39.15 ± 2.05%, indicating partial recovery of hematological status.

The most pronounced improvement was recorded in G5 (8% sesame), which showed RBC of 5.95 ± 0.20 $\times 10^6$/ml, WBC of 7.95 ± 0.15 $\times 10^3$/ml, PLT of 358.60 ± 6.10 $\times 10^3$/ml, hemoglobin level of 15.35 ± 0.30 g/dL, and PCV of 54.80 ± 1.85%. These values approached those of the negative control group, indicating a strong restorative effect on blood parameters.

Overall, the findings suggest that sesame seed supplementation exerts a beneficial hematopoietic effect, improving red and white blood cell indices, platelet count, hemoglobin concentration, and packed cell volume in a dose-dependent manner, and thereby supporting blood health and bone marrow function.

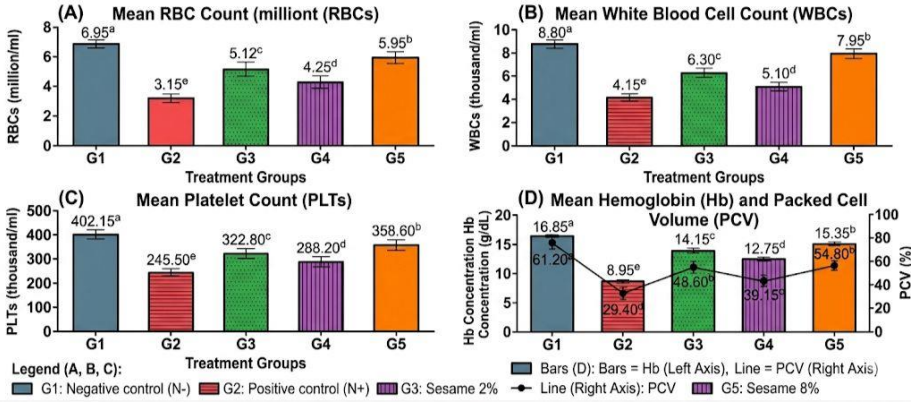

Figure 7. Effect of different sesame seed concentrations on hematological parameters in experimental rats. Different superscript letters (a, b, c, etc.) indicate statistically significant differences among the experimental groups at $p < 0.05$, whereas groups sharing the same superscript letter are not significantly different.

The results presented in figure 8 illustrate the effect of different concentrations of sesame seeds on immunological parameters, specifically IgM and IgG in experimental rats.

The negative control group (G1) exhibited the highest immune status, with IgM recorded at 97.80 ± 2.15 mg/dl and IgG at 868.45 ± 5.20 mg/dl, indicating a strong and normal humoral immune response under physiological conditions.

In contrast, the positive control group (G2) showed a severe suppression of immune function, as evidenced by a marked reduction in IgM to 35.20 ± 2.40 mg/dl and IgG to 355.90 ± 4.80 mg/dl. These results reflect significant impairment of antibody-mediated immunity.

Supplementation with sesame seeds led to a clear improvement in immunoglobulin levels. In G3 (2% sesame), IgM increased to 72.10 ± 2.90 mg/dl, while IgG rose to 745.20 ± 4.50 mg/dl, indicating partial restoration of immune function compared with the positive control group.

A more variable response was observed in G4 (6% sesame), where IgM reached 46.50 ± 1.95 mg/dl and IgG increased to 625.30 ± 4.30 mg/dl, showing moderate immunological improvement but still below the levels of the lower-dose group.

The most pronounced enhancement was observed in G5 (8% sesame), which recorded IgM levels of 76.90 ± 2.50 mg/dl and IgG levels of 785.60 ± 6.10 mg/dl. These values approached those of the negative control group, suggesting a strong immunostimulatory effect of sesame seed supplementation at higher concentrations.

Overall, the findings indicate that sesame seeds exert a beneficial modulatory effect on humoral immunity, as reflected by improved IgM and IgG levels in a dose-dependent manner, highlighting their potential role in enhancing immune function and antibody production

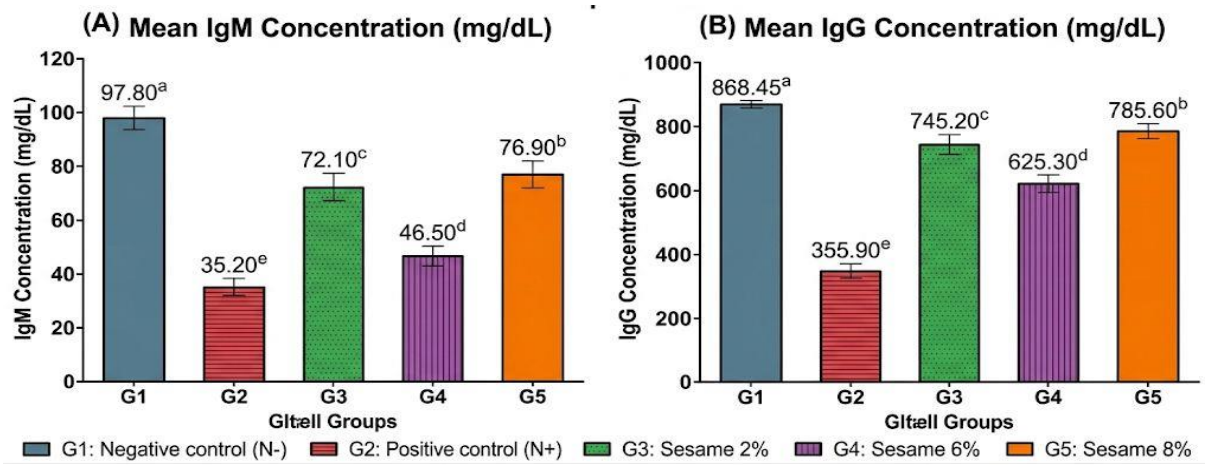

Figure 8. Effect of different concentrations of sesame seeds on IgM and IgG levels in experimental rats. Different superscript letters (a, b, c, etc.) indicate statistically significant differences among the experimental groups at $p < 0.05$, whereas groups sharing the same superscript letter are not significantly different.

Figure (9) illustrates the effect of different concentrations of sesame seeds on oxidative stress biomarkers, namely Total Antioxidant Status and Total Oxidant Status in experimental rats. The results showed that the negative control group (G1) exhibited a balanced oxidative status, with a relatively high Total Antioxidant Status of 1.62 ± 0.18 mmol Trolox equivalent per liter, accompanied by a low Total Oxidant Status of 3.95 ± 0.42 µmol hydrogen peroxide equivalent per liter. This reflects a normal physiological redox balance. In contrast, the positive control group (G2) demonstrated a severe oxidative imbalance, characterized by a marked reduction in Total Antioxidant Status to 0.75 ± 0.07 mmol Trolox equivalent per liter, along with a pronounced elevation in Total Oxidant Status to 10.25 ± 0.55 µmol hydrogen peroxide equivalent per liter. These findings indicate a state of intense oxidative stress. Treatment with sesame seeds resulted in a gradual improvement in oxidative stress markers. In G3 (2% sesame), Total Antioxidant Status increased to 1.22 ± 0.09 mmol Trolox equivalent per liter, while Total Oxidant Status decreased to 8.15 ± 0.40 µmol hydrogen peroxide equivalent per liter compared with the positive control group. A more noticeable improvement was observed in G4 (6% sesame), where Total Antioxidant Status further increased to 1.15 ±

0.05 mmol Trolox equivalent per liter, and Total Oxidant Status decreased to 7.30 ± 0.35 µmol hydrogen peroxide equivalent per liter. The most pronounced improvement was recorded in G5 (8% sesame), which showed a Total Antioxidant Status of 1.58 ± 0.06 mmol Trolox equivalent per liter, approaching the level of the negative control group, while Total Oxidant Status decreased significantly to 5.25 ± 0.38 µmol hydrogen peroxide equivalent per liter.

Overall, the findings indicate that sesame seed supplementation exerts a protective antioxidant effect by enhancing Total Antioxidant Status and reducing Total Oxidant Status in a dose-dependent manner, thereby improving the overall oxidative balance in experimental rats.

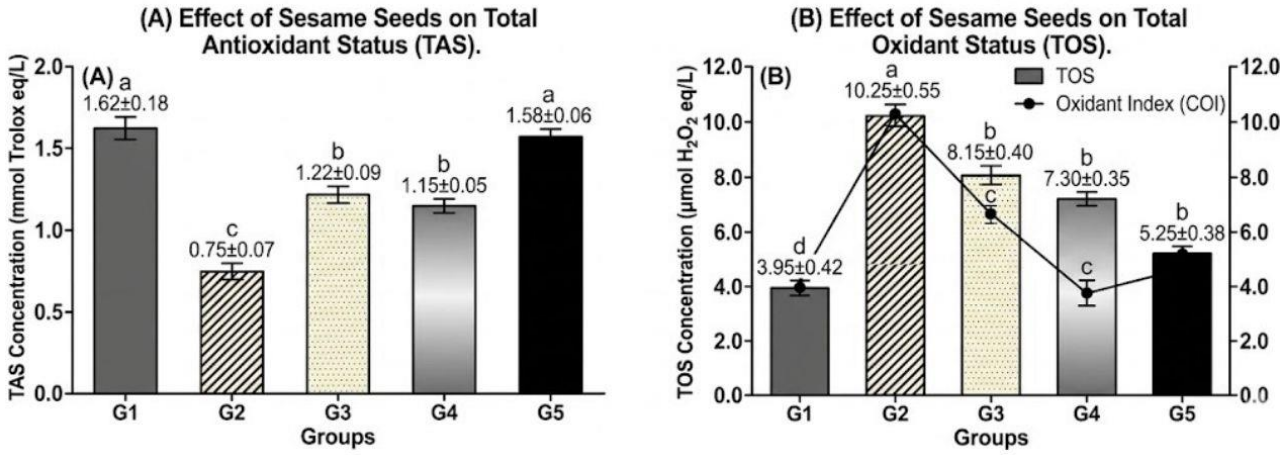

Figure 9. Effect of dietary sesame seeds supplementation on Total Antioxidant Status (TAS) and Total Oxidant Status (TOS) in experimental rats. Different superscript letters (a, b, c, etc.) indicate statistically significant differences among the experimental groups at $p < 0.05$, whereas groups sharing the same superscript letter are not significantly different.

Figure 10 illustrates the effect of different concentrations of sesame seeds on the inflammatory biomarker TNF-α in experimental rats. The results demonstrated that the negative control group (G1) exhibited the lowest physiological level of TNF-α, recorded at 0.88 ± 0.03 ng/L, indicating a normal inflammatory state and absence of immune activation.

In contrast, the positive control group (G2) showed a marked elevation in TNF-α level, reaching 4.12 ± 0.09 ng/L. This significant increase reflects a strong inflammatory response and confirms the presence of induced inflammation in the experimental model. Treatment with sesame seeds resulted in a clear reduction in TNF-α levels compared with the positive control group. In G3 (2% sesame), TNF-α decreased to 2.95 ± 0.05 ng/L, indicating a partial anti-inflammatory effect.

A further reduction was observed in G4 (6% sesame), where TNF-α reached 3.55 ± 0.06 ng/L; although lower than the positive control, it remained higher than the 2% sesame group, suggesting a moderate anti-inflammatory response.

The most pronounced improvement was recorded in G5 (8% sesame), where TNF-α decreased significantly to 1.65 ± 0.04 ng/L, approaching the level of the negative control group. This indicates a strong anti-inflammatory effect at the highest sesame concentration. Overall, the findings suggest that sesame seed supplementation exerts a dose-dependent anti-inflammatory effect, as evidenced by the reduction in TNF-α levels, highlighting its potential role in modulating inflammatory responses in experimental rats.

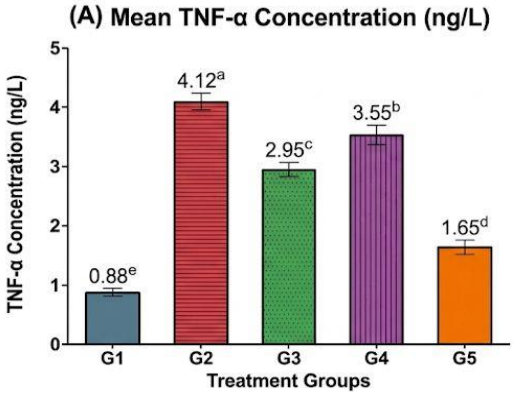

Figure 10. Combined Effect of Different Concentrations of Sesame Seeds on Inflammatory Biomarker TNF-α Levels in Experimental Rats. Different superscript letters (a, b, c, etc.) indicate statistically significant differences among the experimental groups at $p < 0.05$, whereas groups sharing the same superscript letter are not significantly different.

5. DISCUSSION

The present study demonstrated that dietary supplementation with sesame seeds (*Sesamum indicum* L.) effectively attenuated oxidative stress-induced biochemical and immunological disturbances in experimental rats. The protective effects were evident through improvements in oxidative balance, lipid metabolism, liver and kidney function, hematological parameters, inflammatory status, and humoral immunity. Notably, these beneficial effects were dose-dependent, with the 8% sesame supplementation group exhibiting the most pronounced restoration toward normal physiological conditions. The phytochemical analysis revealed that sesame seeds contained considerable amounts of total phenolic and flavonoid compounds, which are recognized as major contributors to antioxidant activity. Phenolic compounds possess strong free radical scavenging properties and are capable of interrupting lipid peroxidation chain reactions, thereby protecting cellular structures from oxidative damage. The antioxidant potential of sesame lignans, particularly sesamin and sesamolin, has been widely documented in recent literature (Wei et al., 2022; Dossou et al., 2023).

Carbon tetrachloride-induced oxidative stress resulted in marked dyslipidemia characterized by elevated serum total cholesterol, triglycerides, LDL-c, and VLDL-c levels, accompanied by reduced HDL-c concentrations. These alterations are consistent with the established mechanism of CCl_4 toxicity, whereby reactive oxygen species generated during hepatic metabolism promote lipid peroxidation and disrupt lipid homeostasis (Weber et al., 2003).

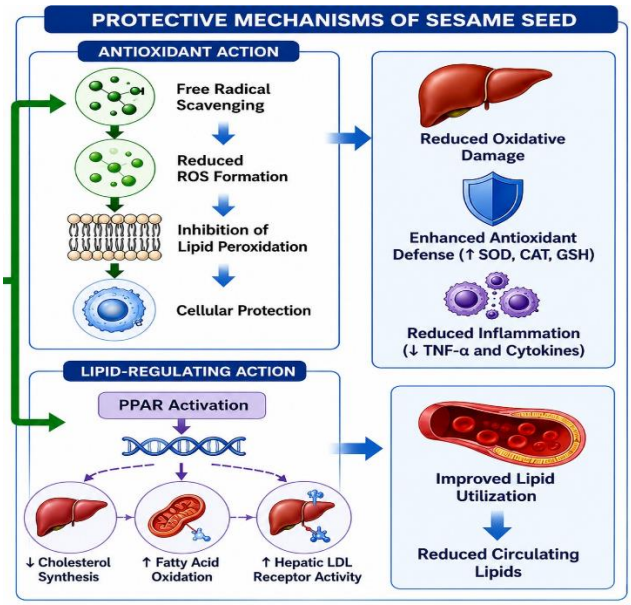

Figure 11. Protective Mechanisms of Sesame Seed: Antioxidant and Lipid-Regulating Effects.

Dietary sesame supplementation significantly improved all lipid profile parameters, particularly at the 8% inclusion level. This hypolipidemic effect may be attributed to sesame lignans and unsaturated fatty acids, which have been shown to regulate lipid metabolism through multiple mechanisms, including inhibition of cholesterol synthesis, enhancement of fatty acid oxidation, and modulation of hepatic lipid regulatory pathways (Mashnafi et al., 2025; Dossou et al., 2023).Overall, the observed protective effects are consistent with the broader biological activities of sesame bioactive compounds, which include antioxidant, anti-inflammatory, and metabolic regulatory properties mediated through redox-sensitive signaling pathways such as Nrf2 activation and NF-ϰB suppression (Wei et al., 2022; Sies, 2017). Furthermore, sesamin has been reported to modulate peroxisome proliferator-activated receptor (PPAR) signaling pathways, thereby improving lipid utilization and reducing circulating lipid concentrations (Abbas et al., 2025). The elevated serum activities of AST, ALT, and ALP observed in the positive control group indicate hepatocellular injury and increased membrane permeability resulting from oxidative damage. Carbon tetrachloride undergoes metabolic activation by cytochrome P450 enzymes to generate trichloromethyl radicals, which initiate extensive lipid peroxidation within hepatocyte membranes (Aljehani et al., 2026). Sesame supplementation significantly reduced liver enzyme activities, suggesting preservation of hepatic cellular integrity. These findings support previous studies reporting hepatoprotective effects of sesame lignans through enhancement of endogenous antioxidant defense systems and suppression of oxidative injury (Majdalawieh & Carr, 2017). The reduction in liver enzyme leakage may also reflect stabilization of cellular membranes by sesame-derived polyunsaturated fatty acids and antioxidant compounds.

Kidney function parameters showed a similar pattern of improvement following sesame supplementation. The elevated serum creatinine and uric acid levels induced by oxidative stress reflect impaired renal filtration and structural injury within kidney tissues. Oxidative stress is strongly associated with renal inflammation, endothelial dysfunction, and damage to both glomerular and tubular cells. Recent evidence indicates that sesame bioactive compounds, particularly lignans such as sesamin and sesamolin, possess strong antioxidant properties that help protect renal tissues by reducing oxidative damage and enhancing cellular defense mechanisms (Dossou et al., 2023; Oboulbiga et al., 2023). In addition, sesamol has been reported to exert potent anti-inflammatory and immunomodulatory effects, which may further contribute to renal protection under oxidative conditions (Majdalawieh et al., 2023). Activation of antioxidant defense pathways, including Nrf2 signaling, also appears to play an important role in improving cellular resistance to oxidative injury (Hassanein et al., 2024). Overall, these findings support the potential of sesame seeds as a natural dietary approach to help preserve kidney function under oxidative stress conditions.

The hematological results showed marked reductions in red blood cell count, hemoglobin concentration, packed cell volume, white blood cells, and platelets following carbon tetrachloride exposure. These changes are most likely related to oxidative damage to blood cell membranes, suppression of bone marrow activity, and increased destruction of circulating cells. Because erythrocyte membranes are rich in polyunsaturated fatty acids, they are particularly vulnerable to oxidative injury, which can lead to hemolysis and reduced oxygen-carrying capacity. Sesame seeds are nutritionally rich and contain essential minerals such as iron, zinc, copper, and selenium, all of which are important for normal hematopoiesis and immune function (Oboulbiga et al., 2023). Moreover, variation in lignan content among sesame varieties may influence their antioxidant capacity and protective effects on blood parameters (Kim et al., 2024). Supplementation with sesame therefore appears to improve hematological indices by reducing oxidative stress and supporting blood cell formation. A significant improvement was also observed in humoral immune responses. Oxidative stress significantly reduced serum IgM and IgG levels, indicating impaired B-cell activity and antibody production. Excess reactive oxygen species can interfere with immune cell signaling and reduce lymphocyte proliferation, ultimately weakening adaptive immunity. Sesame lignans have been reported to exhibit immunomodulatory effects that support lymphocyte function and help restore immune balance (Majdalawieh et al., 2023). In addition, improved redox status through enhanced antioxidant defenses may further support normal antibody synthesis and secretion. Finally, oxidative stress induced a clear disturbance in antioxidant status, characterized by decreased total antioxidant capacity and increased total oxidant levels. Sesame supplementation helped restore this balance in a dose-dependent manner. This effect can be attributed to both direct free radical scavenging activity and indirect activation of endogenous antioxidant enzymes. Sesame lignans have been shown to activate the Nrf2 signaling pathway, which enhances the expression of antioxidant enzymes and improves cellular resistance to oxidative damage (Hassanein et al., 2024). Variability in lignan content among sesame varieties may also contribute to differences in antioxidant effectiveness (Kim et al., 2024), highlighting the importance of bioactive composition in determining biological activity. Inflammation represents another critical consequence of oxidative stress, and the elevated TNF-α levels observed in the positive control group confirm the induction of a strong inflammatory response. Reactive oxygen species activate redox-sensitive transcription factors such as nuclear factor-kappa B (NF-ϰB), resulting in

increased production of pro-inflammatory cytokines including TNF-α, IL-1β,and IL-6 (Mahzari,& Saad 2024). Dietary sesame supplementation significantly reduced TNF-α concentrations, with the greatest reduction observed in the 8% supplementation group. This anti-inflammatory effect may be attributed to the ability of sesame lignans to inhibit NF-ϰB activation and suppress cytokine production (Majdalawieh et al., 2020). The simultaneous reduction in oxidative stress and inflammatory signaling highlights the interconnected nature of redox regulation and immune homeostasis. The dose-dependent pattern observed throughout the study suggests that increasing dietary sesame inclusion enhances the availability of bioactive compounds responsible for antioxidant and immunomodulatory activities. The superior efficacy of the 8% supplementation level may reflect a greater accumulation of lignans, phenolic compounds, and essential nutrients capable of exerting synergistic biological effects. Such synergy likely contributes to the simultaneous improvement in metabolic, inflammatory, antioxidant, and immunological parameters observed in the present investigation.

Collectively, the findings indicate that sesame seeds provide substantial protection against oxidative stress-induced tissue injury and immune dysfunction through multiple complementary mechanisms. These include free radical scavenging activity, enhancement of endogenous antioxidant defenses, modulation of inflammatory signaling pathways, stabilization of cellular membranes, improvement of lipid metabolism, and restoration of immune competence. Therefore, sesame seeds represent a promising functional food with potential applications in the prevention and management of disorders associated with oxidative stress and immune imbalance

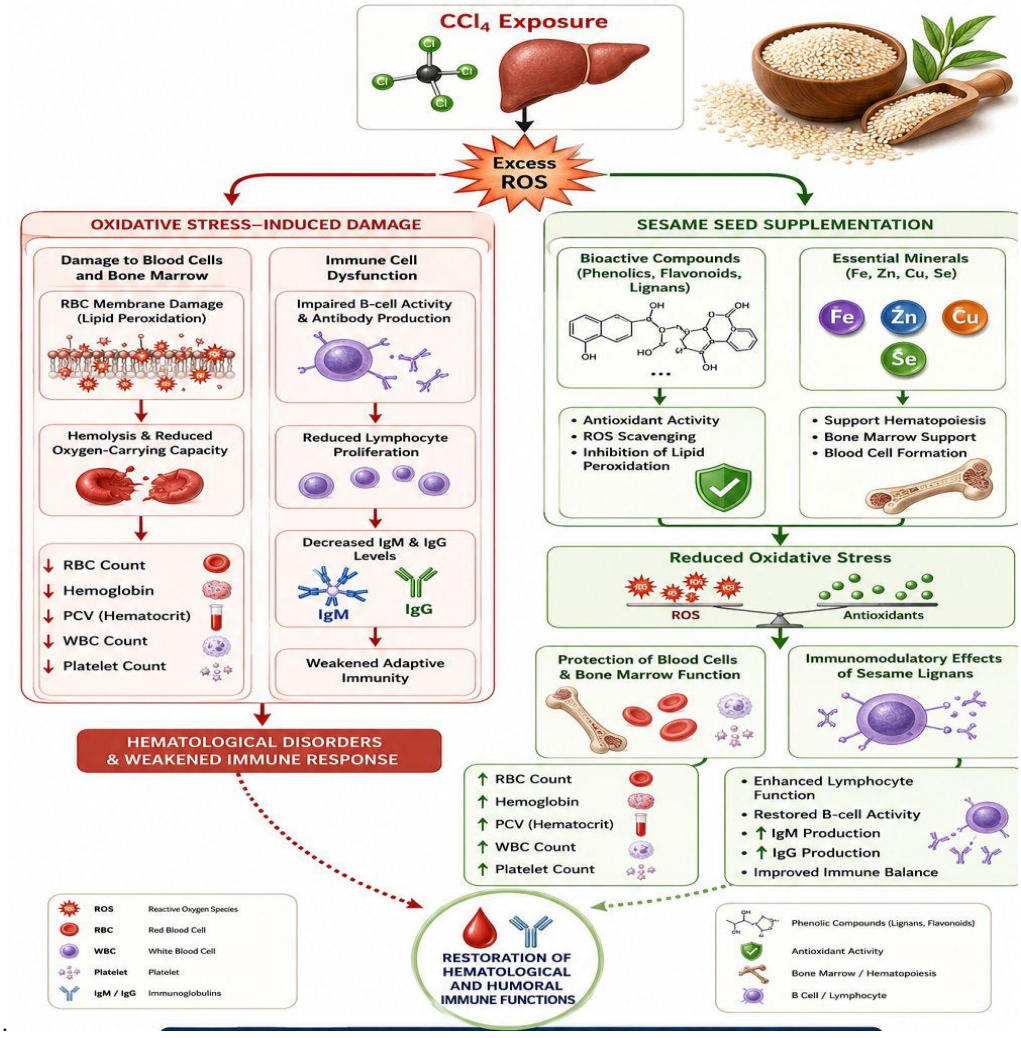

Figure 12. Proposed Mechanism Underlying the Protective Effects of Sesame Seed Supplementation on Hematological and Humoral Immune Functions in CCl_4-Induced Oxidative Stress.

6. CONCLUSION

The present study demonstrates that dietary sesame seed (*Sesamum indicum* L.) supplementation effectively alleviates CCl_4-induced oxidative stress and its associated biochemical, hematological, and immunological disturbances in experimental rats. Sesame supplementation improved antioxidant status, reduced inflammatory responses, restored liver and kidney function, enhanced hematological parameters, and strengthened humoral immunity in a dose-dependent manner. Among the tested levels, the 8% sesame diet showed the greatest protective effect, producing values closest to those of the healthy control group. These findings suggest that sesame seeds possess significant antioxidant, anti-inflammatory, and immunomodulatory properties and may serve as a promising functional food for mitigating oxidative stress–related disorders and supporting immune homeostasis. Further molecular and clinical studies are recommended to confirm these beneficial effects and elucidate the underlying mechanisms.

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