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Immunomodulatory Effects of Dietary Cashew in Obese Rats with Cisplatin-Induced Immunosuppression

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ABSTRACT:

Background: Immune homeostasis is closely associated with nutritional and metabolic status. Obesity can disrupt this balance by promoting chronic low-grade inflammation and immunometabolic dysregulation, while cisplatin exposure may further impair immune and hematological function through oxidative stress and systemic toxicity. Cashew (Anacardium occidentale L.) kernels contain essential nutrients and bioactive compounds with potential antioxidant and anti-inflammatory properties.

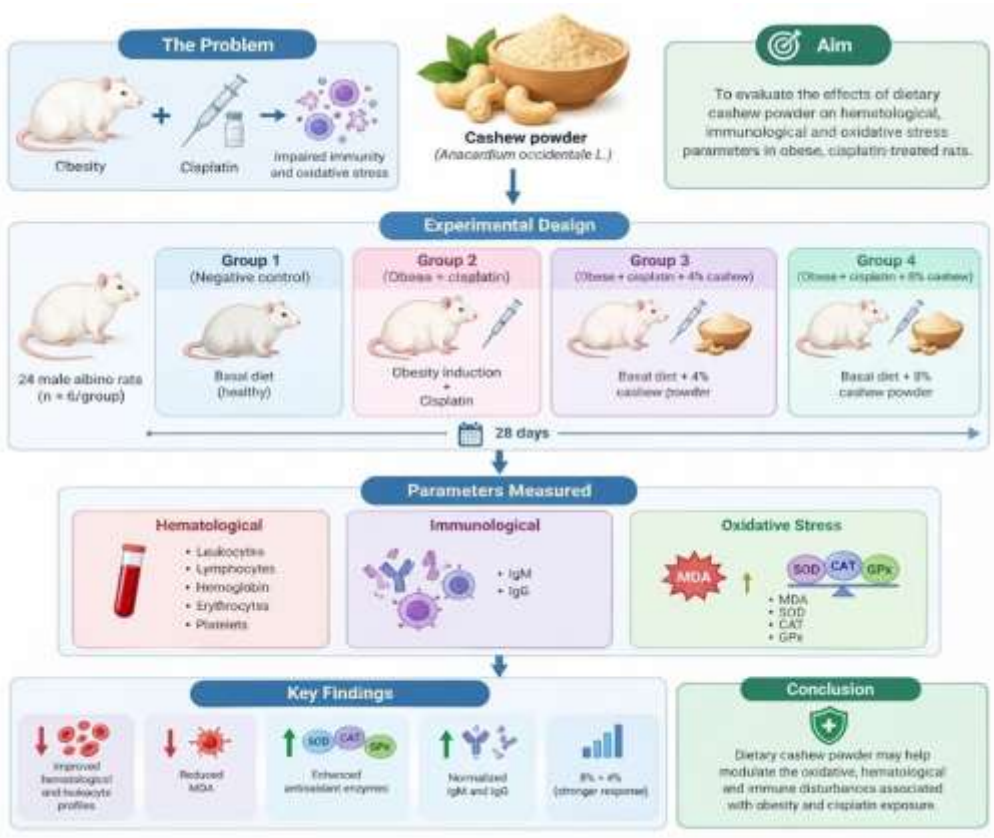
Objective: This study investigated the effects of dietary cashew powder supplementation on hematological, immunological, and oxidative stress-related parameters in obese rats subjected to cisplatin exposure.

Methods: Twenty-four adult male albino rats were randomly assigned to four groups (n = 6). The negative-control group received a basal diet, whereas the remaining groups were subjected to obesity induction and cisplatin administration. Obese cisplatin-treated rats received either a basal diet alone or a diet supplemented with 4% or 8% cashew powder for 28 days. Hematological indices, serum IgM and IgG, and oxidative stress biomarkers, including malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), were evaluated.

Results: Cisplatin-treated obese rats showed reductions in leukocyte, lymphocyte, hemoglobin, erythrocyte, and platelet parameters, accompanied by increased MDA and decreased SOD, CAT, and GPx activities. Serum IgM and IgG concentrations were also altered. Cashew supplementation was associated with improvement in hematological and leukocyte profiles, reduction of MDA, and enhancement of antioxidant enzyme activities. The 8% supplementation level generally produced a greater response than the 4% level.

Conclusion: Dietary cashew powder may contribute to the modulation of oxidative, hematological, and immune-related disturbances associated with obesity and cisplatin exposure. Further mechanistic studies are warranted to clarify its potential nutritional and protective effects

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Graphical Abstract. Modulatory effects of dietary cashew powder on immune, hematological, and oxidative responses in obese cisplatin-treated rats.

1. INTRODUCTION

The immune system is a highly integrated biological network that depends on adequate nutritional and metabolic support to maintain cellular function, tissue homeostasis, and effective host defense. Both innate and adaptive immune responses require coordinated energy production, macronutrient availability, micronutrients, and metabolic signaling. Consequently, disturbances in nutritional or metabolic status can influence immune-cell development, activation, differentiation, and effector function. The emerging field of immunometabolism has highlighted the close relationship between cellular metabolism and immune regulation, demonstrating that metabolic signals can substantially shape immune responses under both physiological and pathological conditions (Calder, 2022; Dunbar et al., 2023; Medina-Urrutia et al., 2024). Immune dysfunction is frequently accompanied by alterations in oxidative balance. Reactive oxygen species (ROS) are physiologically involved in cellular signaling and antimicrobial defense; however, excessive ROS generation or inadequate antioxidant protection can result in oxidative stress and damage to cellular lipids, proteins, and nucleic acids. Oxidative stress can also interfere with immune-cell signaling and function, thereby establishing an interaction between redox imbalance, inflammation, and immune dysregulation. For this reason, assessment of both immune-related and oxidative biomarkers can provide complementary information regarding the systemic response to a nutritional or pharmacological intervention. Cisplatin is a widely used platinum-based chemotherapeutic agent with established antineoplastic activity. Its therapeutic effects are primarily associated with DNA damage, but its administration may also produce systemic toxicity involving oxidative stress, inflammation, mitochondrial dysfunction, and tissue injury (Al-Mars et al., 2024; Hesari et al., 2024). Importantly, cisplatin has been experimentally associated with immunotoxic effects in laboratory animals. A previously established rat model demonstrated that intraperitoneal cisplatin administration at 3.5 mg/kg body weight once every 3 days for two consecutive weeks produced measurable alterations in total and differential leukocyte counts, phagocytic activity, serum proteins, γ-globulin concentration, antibody responses, and splenic morphology (Khalaf et al., 2019). This model provides a useful experimental framework for investigating nutritional strategies that may modulate immune and oxidative responses under

conditions of induced immunosuppression. Nutrition represents an important modifiable factor capable of influencing immune and redox homeostasis. Diets containing adequate protein, unsaturated fatty acids, vitamins, minerals, and bioactive phytochemicals can contribute to the maintenance of normal immune-cell activity and antioxidant defense (Calder, 2022; Abd Elmeged et al., 2020; Dunbar et al., 2023). Increasing interest has consequently focused on nutrient-dense plant foods and nuts as potential sources of compounds that may influence inflammatory and oxidative pathways. Such approaches are particularly relevant because nutritional components can affect immune function through multiple interconnected mechanisms rather than through a single biological pathway. Cashew (*Anacardium occidentale* L.) is a nutrient-dense tree nut containing protein, unsaturated fatty acids, dietary fiber, minerals, vitamins, and other biologically active constituents. The nutritional composition of cashew kernels can vary according to geographical origin and other production-related factors, but cashew generally represents a concentrated source of nutrients relevant to metabolic and physiological functions (Rico et al., 2016). Beyond its nutritional composition, cashew contains phenolic and other bioactive compounds that have attracted interest because of their potential antioxidant and anti-inflammatory activities. Experimental evidence suggests that cashew consumption may influence pathways involved in oxidative and inflammatory regulation. Fusco et al. (2020) reported that *A. occidentale* consumption modulated oxidative stress through effects involving the Nrf2/HO-1 antioxidant pathway and NF-ʁB-related inflammatory signaling. Other experimental research has likewise described antioxidant and anti-inflammatory effects associated with cashew nuts in inflammatory models. These findings provide a biological rationale for investigating cashew as a dietary intervention under conditions characterized by oxidative and immune imbalance. Recent human evidence has further increased interest in cashew as a component of dietary strategies for individuals with obesity. In a randomized clinical trial involving adolescents with obesity, 12 weeks of cashew consumption was associated with reductions in waist circumference and thiobarbituric acid reactive substances (TBARS), although effects were not uniform across all anthropometric and oxidative outcomes (Nunes de Oliveira et al., 2025). A separate randomized controlled trial investigated the effects of 30 g/day of roasted cashew nuts for 12 weeks on copper, zinc, and superoxide dismutase (SOD)-related biomarkers in adolescents with obesity, further supporting investigation of the relationship between cashew intake, micronutrient status, and antioxidant defense (Dias et al., 2025).The relationship between immunity and obesity is bidirectional and increasingly understood within the framework of immunometabolism. Adipose tissue is not merely an energy-storage organ but also an active endocrine and immunological tissue containing substantial populations of macrophages, lymphocytes, and other immune cells. Excessive adipose tissue accumulation can alter communication between adipocytes and immune cells and promote a chronic low-grade inflammatory environment. This altered immunometabolic state may subsequently influence systemic immune regulation and metabolic homeostasis (Medina-Urrutia et al., 2024; Jiang et al., 2025). Recent reviews have further emphasized that obesity is associated with broad immune dysregulation involving innate and adaptive immune pathways and that metabolic and inflammatory processes are closely interconnected (Alzahrani et al., 2022; Daryabor et al., 2019).

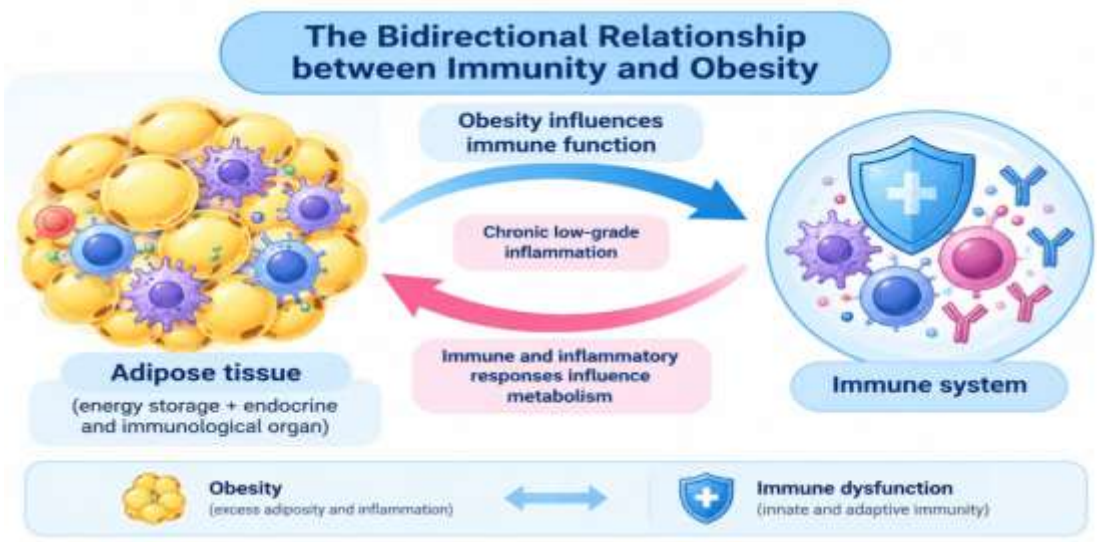


Figure 1. Bidirectional relationship between obesity and immune function: the role of adipose tissue in immunometabolic regulation.

Experimental obesity induced by high-fat feeding is widely used to investigate the interaction between excess adiposity, metabolic disturbances, inflammation, oxidative stress, and immune function in laboratory rodents. Although experimental protocols vary in dietary composition, feeding duration, animal characteristics, and criteria used to establish obesity, high-fat diet models provide a useful platform for evaluating dietary interventions under obesity-associated metabolic stress (Sadie-Van Gijsen & Kotzé-Hörstmann, 2023; Tibaes et al., 2024). The coexistence of obesity and induced immunosuppression is therefore of particular experimental interest. Obesity can alter immune and inflammatory homeostasis, while cisplatin-induced immunotoxicity introduces an additional challenge to systemic immune and oxidative balance (Mahzari et al., 2024). Studying these conditions together provides an opportunity to examine whether a nutrient-dense dietary intervention can influence multiple interconnected biological responses. Evaluation of hematological indices, serum proteins, immunoglobulins, lipid peroxidation, and antioxidant enzyme activities can provide a multidimensional assessment of these responses. The use of hematological and immunological parameters is particularly relevant in experimental cisplatin-induced immunotoxicity, where alterations in leukocyte profiles, serum proteins, phagocytic activity, and humoral immune responses have been documented (Khalaf et al., 2019). Despite the growing evidence concerning the nutritional and biological properties of cashew, limited experimental information is available regarding the effects of different dietary levels of cashew powder on integrated immune, biochemical, hematological, and oxidative responses in obese animals subjected to cisplatin-induced immunosuppression. In particular, comparative evaluation of different dietary inclusion levels may help clarify whether the magnitude of the response varies according to the amount of cashew incorporated into the diet.Therefore, the present study was designed to investigate the effects of dietary cashew powder at two inclusion levels (4% and 8%) on biochemical, hematological, immunological, and oxidative stress parameters in obese rats with cisplatin-induced immunosuppression. Body weight, red blood cell count, differential leukocyte counts, serum total protein, albumin, globulin, IgG, IgM, MDA, SOD, CAT, and GPx were evaluated. The study aimed to determine whether dietary cashew supplementation could modulate immune-related and oxidative responses in this combined experimental model and to examine whether these responses differed between the two dietary inclusion levels (Mashnafi et al., 2024).

2. MATERIALS AND METHODS

2.1. Experimental Animals

Twenty-four adult male albino rats, weighing approximately 150 ± 10 g, were used in the present experimental study. The animals were housed at the Animal House of the Faculty of Home Economics, Menoufia University, Menoufia, Egypt, under controlled laboratory conditions with a 12-h light/12-h dark cycle and free access to drinking water. Before initiation of the experimental procedures, the animals were allowed to acclimatize to the laboratory environment. The experimental procedures and reporting of animal-related information were conducted with consideration of the principles outlined in the ARRIVE 2.0 guidelines for animal research (Percie du Sert et al., 2020).

2.2. Ethical Approval

All experimental procedures involving animals were reviewed and approved by the Institutional Research Ethics Committee of Al-Baha University, Saudi Arabia (Approval No. 47119677; approved on 17 May 2026). The experimental procedures were conducted at the Animal House of the Faculty of Home Economics, Menoufia University, Menoufia, Egypt. All animals were handled according to the approved experimental protocol and applicable principles governing the humane care and use of laboratory animals.

2.3. Experimental Materials and Reagents

The principal materials used in the study included cashew kernels, cisplatin, and the dietary ingredients required for preparation of the basal and high-fat diets. The basal diet consisted of casein, corn oil, mineral and vitamin mixtures, fiber, sucrose, choline chloride, and corn starch. Appropriate reagents and commercially available diagnostic kits were used for the determination of hematological, biochemical, immunological, and oxidative stress parameters.

2.4. Preparation of Cashew Powder

Cashew kernels were carefully inspected before use, and damaged kernels and foreign materials were removed. The selected kernels were subsequently ground to obtain a homogeneous fine powder suitable for dietary incorporation.The prepared cashew powder was incorporated into the experimental diets at two inclusion levels, 4% and 8% (w/w), according to the

experimental design.

2.5. Preparation of the Basal Diet

The basal diet was formulated to provide 14% protein, 5% corn oil, 3.5% mineral mixture, 1% vitamin mixture, 5% fiber, 10% sucrose, and 0.25% choline chloride, with corn starch used as the remaining component to bring the formulation to 100%. Accordingly, the calculated proportion of corn starch was 61.25%. The diet was prepared according to the general principles of purified rodent diets described by Reeves et al. (1993), with modifications appropriate to the present experimental design. The AIN-93 report established standardized purified diets for laboratory rodents and emphasized the importance of defined nutrient composition for controlled nutritional experimentation (Reeves et al., 1993).

2.6. Induction of Experimental Obesity

Experimental obesity was induced in three of the four experimental groups, namely the positive-control group and the two cashew-supplemented groups. The negative-control group remained healthy and non-obese and did not undergo obesity induction. Before initiation of the 28-day experimental treatment period, rats assigned to the obese groups were fed a high-fat diet (HFD) according to the dietary composition and preparation protocol adopted in the experimental protocol. The HFD was provided for the established obesity-induction period to promote the development of the obese phenotype. The development of obesity was assessed by monitoring changes in body weight during the induction period and according to the predefined criteria established in the experimental protocol. High-fat diet feeding is widely used as a preclinical approach for inducing obesity-associated metabolic alterations and for investigating nutritional interventions targeting body weight and metabolic health (Sadie-Van Gijsen & Kotzé-Hörstmann, 2023). Following successful induction of obesity, the animals assigned to the obese groups proceeded to the subsequent experimental phase, whereas the negative-control animals remained non-obese and continued to receive the basal diet.

2.7. Induction of Cisplatin-Induced Immunosuppression

Following obesity induction, immunosuppression was induced in the obese experimental groups by intraperitoneal administration of cisplatin at a dose of 3.5 mg/kg body weight once every 3 days for two consecutive weeks. This dosing regimen was selected based on a previously established rat model of cisplatin-induced immunotoxicity. Khalaf et al. (2019) reported that intraperitoneal administration of cisplatin at 3.5 mg/kg body weight once every 3 days for successive 2 weeks produced measurable alterations in immune-related parameters, including serum proteins, leukocyte profiles, and humoral immune responses. Accordingly, this regimen was adopted for the induction of immunosuppression in the present study (Khalaf et al., 2019). The negative-control group did not receive cisplatin and remained untreated with respect to immunosuppression.

2.8. Experimental Design

After completion of the obesity-induction phase, the animals were divided into four experimental groups, with six rats per group (n = 6):

Group 1 – Negative control: Healthy, non-obese rats were maintained on the basal diet and received neither the high-fat diet nor cisplatin.

Group 2 – Positive control: Rats underwent experimental obesity through high-fat feeding and subsequently received cisplatin to induce immunosuppression. They were maintained on the basal diet without cashew supplementation.

Group 3 – 4% cashew: Obese rats with cisplatin-induced immunosuppression received the basal diet supplemented with 4% ground cashew powder.

Group 4 – 8% cashew: Obese rats with cisplatin-induced immunosuppression received the basal diet supplemented with 8% ground cashew powder.

The experimental treatment period lasted 28 days. The experimental sequence consisted of obesity induction followed by cisplatin administration in the obese groups and dietary intervention with either 4% or 8% cashew powder according to the assigned experimental group.

2.9. Body-Weight Assessment

Body weight was recorded at baseline and monitored throughout the experimental protocol. Changes in body weight were used to assess the development of obesity and the subsequent body-weight response to the experimental dietary treatments. Body-weight monitoring is a fundamental outcome in rodent models of diet-induced obesity because it provides an important measure of the development and progression of the obese phenotype and the response to dietary interventions (Sadie-Van Gijsen & Kotzé-Hörstmann, 2023).

2.10. Blood Collection and Serum Preparation

At the end of the 28-day experimental period, blood samples were collected from the animals according to the approved experimental procedures. Blood samples intended for serum analyses were allowed to clot and were subsequently centrifuged for serum separation.The separated serum was carefully collected and used for the determination of biochemical, immunological, and oxidative stress biomarkers.

2.11. Hematological Analysis

Hematological parameters were evaluated to assess changes in erythrocyte and leukocyte profiles associated with the experimental conditions and dietary intervention. The parameters assessed included red blood cell (RBC) count and differential leukocyte counts, including lymphocytes, neutrophils, monocytes, eosinophils, and basophils. Hematological analyses were performed according to standard procedures described by Ochei and Kolhatkar (2008).

2.12. Determination of Serum Biochemical Parameters

Serum total protein, albumin, and globulin concentrations were determined to evaluate alterations in serum protein status. Serum total protein was determined according to the procedures described by Burtis et al. (1999). Serum albumin was determined according to Young (1995). Serum globulin concentration was calculated from the difference between total protein and albumin concentrations.

2.13. Determination of Serum Immunoglobulins

Serum immunoglobulin G (IgG) and immunoglobulin M (IgM) concentrations were determined according to the procedures described by Zilva and Pannall (1984). IgG and IgM were evaluated as indicators of humoral immune status and to assess the potential effects of dietary cashew supplementation on antibody-related immune responses in obese rats subjected to cisplatin-induced immunosuppression.

2.14. Determination of Oxidative Stress and Antioxidant Biomarkers

Oxidative status was assessed by measuring malondialdehyde (MDA) concentration and the activities of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). MDA concentration was determined as an indicator of lipid peroxidation according to the method described by Draper and Hadley (1990). The determination of MDA provides an established approach for assessing lipid peroxidation and oxidative damage in biological samples (Draper & Hadley, 1990). SOD activity was determined according to the method described by Spitz and Oberley (1989), which provides an assay for evaluating SOD activity in mammalian tissue preparations (Spitz & Oberley, 1989).

CAT activity was determined according to the method of Aebi (1984), based on the measurement of hydrogen peroxide decomposition by catalase (Aebi, 1984). GPx activity was determined according to the method described by Moin (1986), which provides a method for determining glutathione peroxidase activity in erythrocytes (Moin, 1986). The combined determination of MDA and antioxidant enzyme activities was used to characterize oxidative status and endogenous antioxidant defense in the experimental groups.

2.15. Statistical Analysis

The data were expressed as mean ± standard error of the mean (SEM). Statistical analyses were performed using IBM SPSS Statistics, version 25. The distribution of the data was assessed for normality before inferential analysis. Differences among the four experimental groups were evaluated using one-way analysis of variance (ANOVA). Statistical significance was considered at $p < 0.05$. The statistical procedures were conducted according to the general principles described by Snedecor and Cochran (1989).

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3. RESULTS

Effect of dietary cashew powder supplementation on body-weight parameters in obese rats with cisplatin-induced immunosuppression

Figure 2 illustrates the effect of dietary cashew powder supplementation on body-weight parameters in obese rats subjected to cisplatin-induced immunosuppression. The obese groups exhibited higher initial body weights than the healthy, non-obese control group. Following the experimental treatment, the positive control group showed a lower percentage of body-weight gain compared with the healthy control group. Dietary supplementation with cashew powder was associated with an increase in final body weight and body-weight gain compared with the positive control group. This effect was more pronounced in rats receiving 8% cashew powder than in those receiving 4% supplementation. The 8% cashew powder group showed the highest final body weight and body-weight gain among the obese, cisplatin-treated groups, approaching the values observed in the healthy control group. Statistical differences among the experimental groups are indicated by different superscript letters ($P < 0.05$).

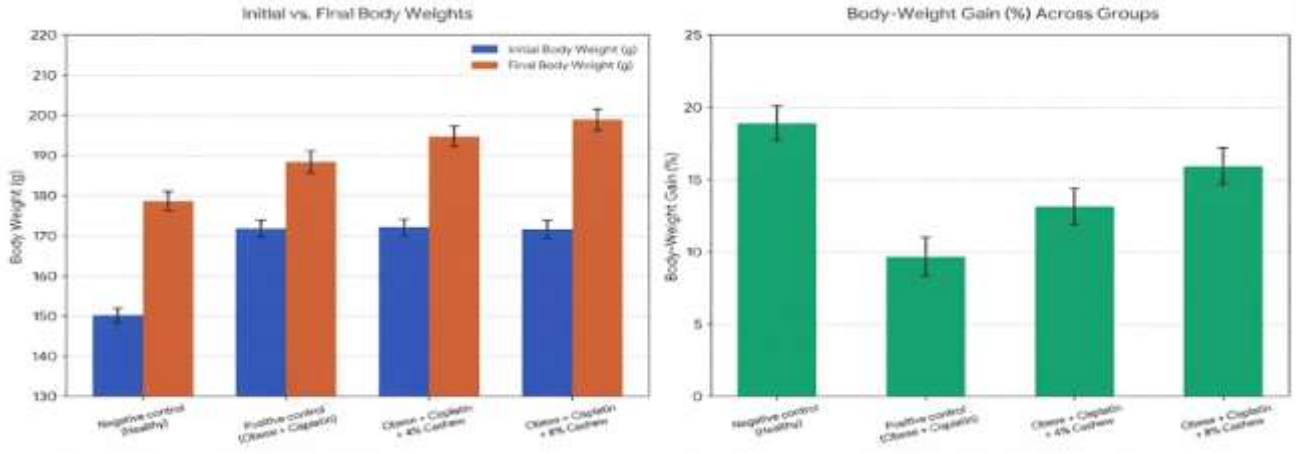


Figure 2. Effect of dietary cashew powder supplementation on body weight in obese rats subjected to cisplatin-induced immunosuppression.

Effect of Dietary Cashew Powder Supplementation on Serum Immunoglobulin Levels

Data Figure 3 presents the serum concentrations of IgM and IgG in the different experimental groups. Compared with the healthy non-obese control group, cisplatin-treated obese rats exhibited higher serum IgM and IgG concentrations. Dietary supplementation with cashew powder modified this response, with both IgM and IgG levels declining relative to the cisplatin-treated group. The 4% cashew-supplemented group showed lower immunoglobulin concentrations than the 8% group, whereas both supplemented groups remained above the levels recorded in the healthy control animals. The differences observed among the experimental groups were statistically significant, as indicated by the different superscript letters ($P < 0.05$).

These data indicate that dietary cashew powder supplementation was associated with a reduction in the elevated serum IgM and IgG concentrations observed following cisplatin treatment, with the magnitude of the response varying according to the supplementation level.

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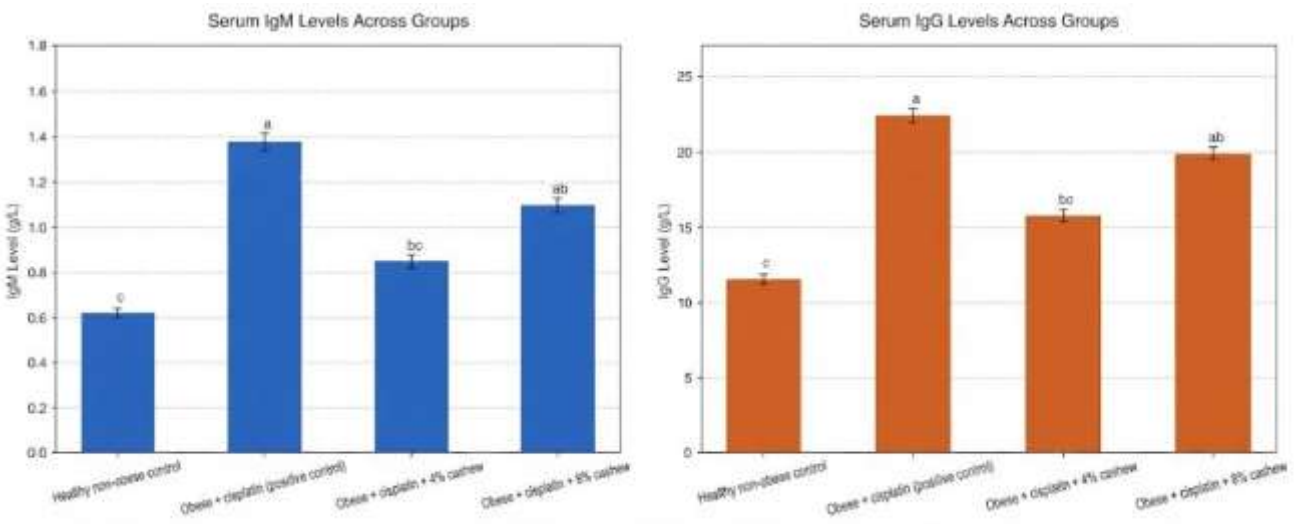


Figure 3. Changes in Serum IgM and IgG Levels Following Dietary Cashew Powder Supplementation

Effects of Dietary Cashew Powder Supplementation on Leukocyte Profiles in Cisplatin-Treated Obese Rats.

Figure 4 shows the changes in total leukocyte count and differential leukocyte counts among the experimental groups. The healthy non-obese rats had the highest total leukocyte count, whereas the obese rats treated with cisplatin showed a pronounced reduction in total leukocytes. This reduction was accompanied by marked decreases in lymphocyte and neutrophil counts, indicating substantial alterations in the circulating leukocyte profile following cisplatin treatment. Cashew powder supplementation was associated with a progressive increase in the total leukocyte count compared with the cisplatin-treated group. The increase was more evident in rats receiving 8% cashew powder, in which the total leukocyte count reached 10.15 × 10^3/μL, compared with 7.85 × 10^3/μL in the 4% supplementation group and 6.12 × 10^3/μL in the cisplatin group. Although the 8% group did not reach the value recorded in the healthy control animals, its leukocyte count was considerably closer to the control level. A similar pattern was observed for lymphocytes. The cisplatin-treated group exhibited the lowest lymphocyte count (1.28 × 10^3/μL), whereas supplementation with 4% and 8% cashew powder increased the lymphocyte count to 2.95 and 4.10 × 10^3/μL, respectively. The value observed with 8% supplementation was therefore closer to that of the healthy control group (5.25 × 10^3/μL). Neutrophil counts also differed among the groups. The healthy control group recorded the highest value (5.82 × 10^3/μL), while the cisplatin-treated group showed a lower count (3.85 × 10^3/μL). The 4% cashew group showed a comparable value (3.75 × 10^3/μL), whereas the 8% group exhibited a higher neutrophil count (4.77 × 10^3/μL).

In contrast, monocyte counts showed relatively small differences among the experimental groups, ranging from 0.68 to 0.78 × 10^3/μL. This suggests that monocytes were less affected than the other leukocyte populations measured in this study. Eosinophil and basophil counts were lower in the cisplatin-treated group than in the healthy control group. Following cashew powder supplementation, both parameters showed a tendency toward higher values, with the 8% group displaying eosinophil and basophil counts close to those of the healthy control group.

The statistical analysis further demonstrated significant differences among the experimental groups for parameters carrying different superscript letters within the same column ($P < 0.05$). Taken together, the findings show that cisplatin treatment was accompanied by substantial changes in the leukocyte profile, particularly in total leukocytes and lymphocytes. Dietary cashew powder supplementation was associated with a partial normalization of these parameters, and the changes were generally more pronounced at the 8% supplementation level than at 4%.

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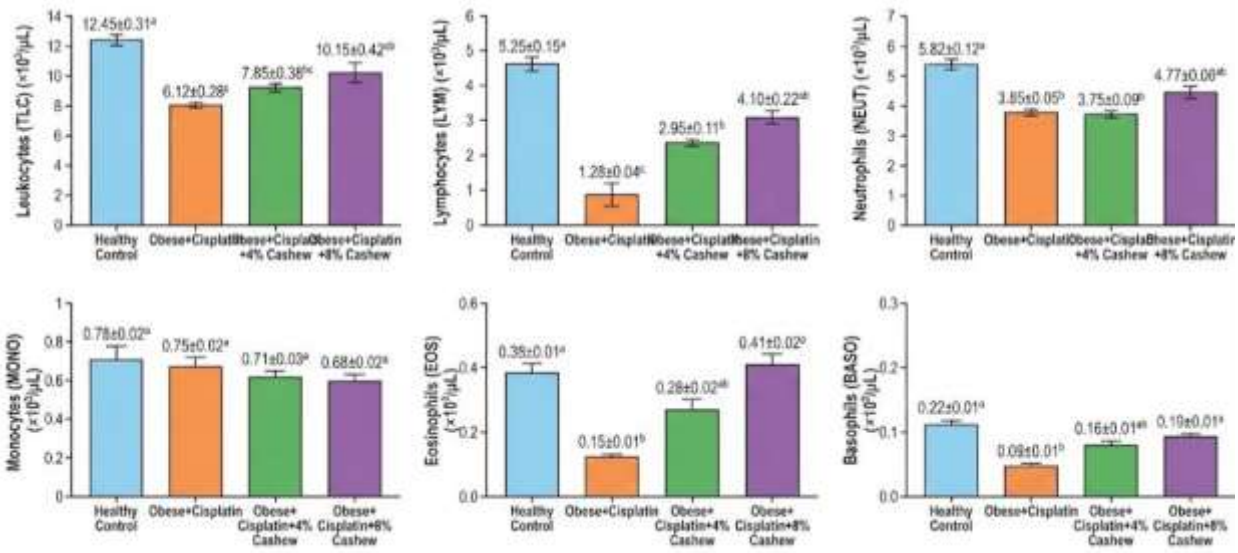


Figure 4. Effects of Dietary Cashew Powder Supplementation on Leukocyte Profiles in Cisplatin-Treated Obese Rats.

Effects of Dietary Cashew Powder Supplementation on Oxidative Stress and Antioxidant Biomarkers in Obese Rats Treated with Cisplatin

Figure 5 shows the changes in malondialdehyde (MDA) and the antioxidant enzymes superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) among the experimental groups. The obese rats treated with cisplatin exhibited a marked increase in MDA concentration compared with the healthy non-obese control group, reaching 265.18 ± 1.65 nmol/mL versus 98.42 ± 0.75 nmol/mL, respectively. This increase was accompanied by substantial reductions in SOD, CAT, and GPx activities, suggesting an altered oxidative balance in the cisplatin-treated animals.

Dietary supplementation with cashew powder was associated with a reduction in MDA levels compared with the cisplatin-treated group. MDA decreased to 218.30 ± 1.12 nmol/mL in the 4% cashew group and to 185.60 ± 1.85 nmol/mL in the 8% group. The greater reduction observed with the 8% supplementation level indicates a stronger shift toward the MDA concentration recorded in the healthy control animals.

A different pattern was observed for the antioxidant enzymes. SOD activity increased from 0.48 ± 0.01 U/mL in the cisplatin group to 0.71 ± 0.02 and 0.89 ± 0.01 U/mL following supplementation with 4% and 8% cashew powder, respectively. CAT activity showed a similar increase, rising from 6.92 ± 0.12 U/mL in the cisplatin-treated group to 11.20 ± 0.25 U/mL with 4% supplementation and 14.45 ± 0.29 U/mL with 8% supplementation. Likewise, GPx activity increased from 44.20 ± 0.65 µmol/mL in the cisplatin group to 53.80 ± 0.82 µmol/mL and 59.45 ± 0.55 µmol/mL in the 4% and 8% cashew groups, respectively.

Although the antioxidant enzyme activities in the supplemented groups did not consistently reach the levels observed in the healthy control animals, the overall pattern showed partial recovery following cashew powder supplementation. The changes were generally more pronounced at the 8% supplementation level than at 4%. Different superscript letters indicate statistically significant differences among groups within the same parameter ($P < 0.05$). Overall, the findings demonstrate a clear alteration in oxidative stress-related biomarkers following cisplatin treatment, characterized by elevated MDA and reduced antioxidant enzyme activities. Cashew powder supplementation was associated with lower MDA concentrations and higher SOD, CAT, and GPx activities, indicating an improvement in the measured oxidative stress and antioxidant parameters..

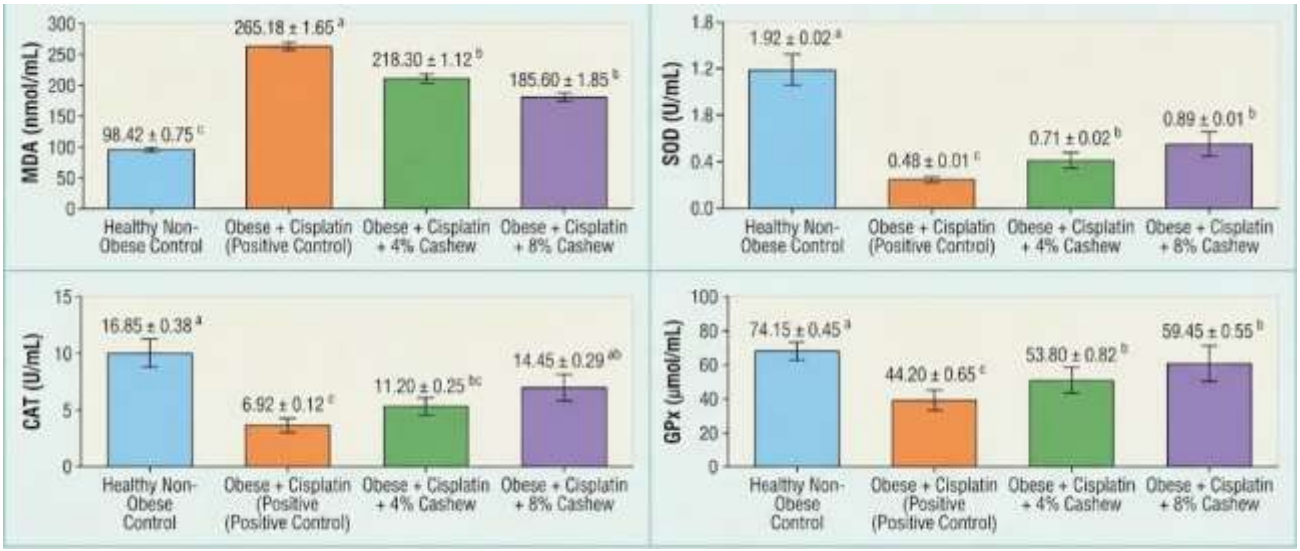


Figure 5. Effects of Dietary Cashew Powder Supplementation on Oxidative Stress and Antioxidant Biomarkers in Obese Rats Treated with Cisplatin

Hematological Responses to Dietary Cashew Powder Supplementation

Figure 6 presents the effects of dietary cashew powder supplementation on selected hematological parameters, including hemoglobin concentration, red blood cell count, and platelet count, in obese rats treated with cisplatin. The healthy non-obese control group exhibited the highest values for all three hematological parameters, with hemoglobin, RBC count, and platelet count reaching 14.25 ± 0.12 g/dL, 5.12 ± 0.08 $\times 10^6$ cells/µL, and 215.4 ± 5.80 $\times 10^3$ cells/µL, respectively.

In contrast, the obese rats receiving cisplatin showed a pronounced reduction in the measured hematological parameters. Hemoglobin concentration decreased to 8.12 ± 0.14 g/dL, while the RBC count declined to 2.35 ± 0.06 $\times 10^6$ cells/µL. Similarly, the platelet count was reduced to 122.5 ± 2.15 $\times 10^3$ cells/µL. These values represented the lowest levels among the experimental groups and were significantly different from those of the healthy control group, as indicated by the different superscript letters ($P < 0.05$). Dietary supplementation with cashew powder was associated with an improvement in the hematological profile of the cisplatin-treated obese rats. In the group receiving 4% cashew powder, hemoglobin concentration increased to 10.85 ± 0.35 g/dL, accompanied by an increase in RBC count to 3.10 ± 0.05 $\times 10^6$ cells/µL. The platelet count also increased to 158.2 ± 1.85 $\times 10^3$ cells/µL compared with the corresponding values recorded in the cisplatin-treated group.

A more pronounced response was observed in rats supplemented with 8% cashew powder. Hemoglobin concentration increased to 12.15 ± 0.18 g/dL, whereas the RBC count reached 3.75 ± 0.06 $\times 10^6$ cells/µL. The platelet count also increased to 184.6 ± 2.20 $\times 10^3$ cells/µL. Although the values obtained following 8% supplementation remained below those of the healthy control group, they were considerably closer to the control values than those observed in the cisplatin-treated group.

Overall, the hematological findings showed a consistent pattern in which cisplatin treatment was associated with lower hemoglobin, RBC, and platelet values, whereas dietary cashew powder supplementation was associated with a partial recovery of these parameters. The response was generally more pronounced at the 8% supplementation level than at 4%, suggesting a concentration-related pattern within the experimental conditions. Statistically significant differences among groups are indicated by different superscript letters within each parameter column ($P < 0.05$).

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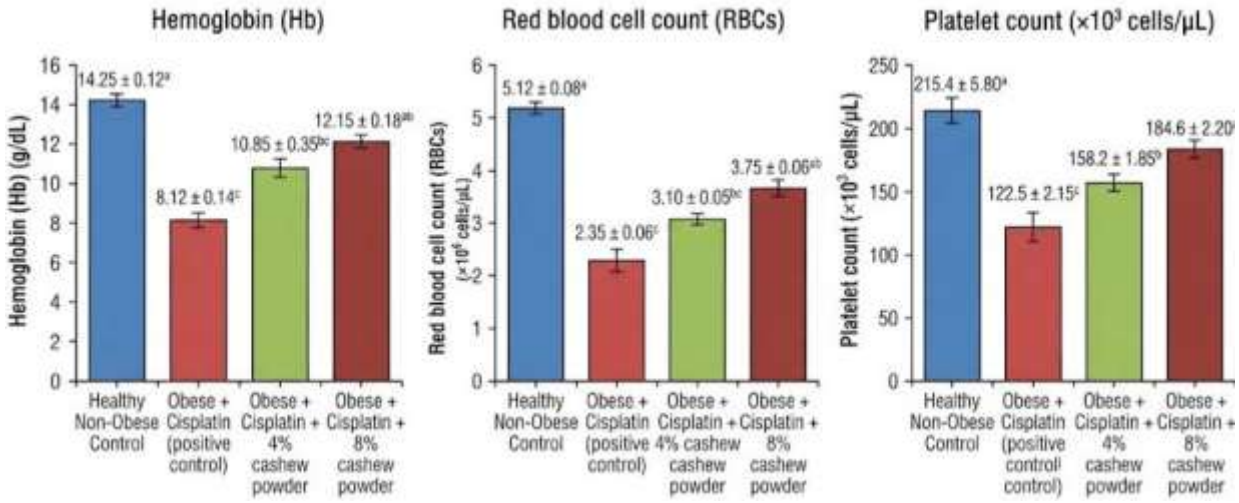


Figure 6. Effects of Dietary Cashew Powder Supplementation on Hematological Parameters in Cisplatin-Treated Obese Rats

4. DISCUSSION

The The present study evaluated the effects of dietary cashew powder at 4% and 8% on body weight, hematological and immune parameters, and oxidative stress in obese rats exposed to cisplatin. Obesity is increasingly recognized as an immunometabolic disorder characterized by complex interactions between adipose tissue, immune cells, and metabolic pathways. Excess adiposity can alter immune-cell function and inflammatory signaling, thereby contributing to systemic immune dysregulation (Medina-Urrutia et al., 2024; Bradley et al., 2024). Cisplatin, although widely used as a chemotherapeutic agent, can induce systemic toxicity through multiple mechanisms, including oxidative stress, inflammation, DNA damage, apoptosis, mitochondrial dysfunction, and hematological toxicity (Elmorsy et al., 2024).

4.1 Body-weight changes

The obese groups had higher initial body weights than the healthy control group, supporting the effectiveness of the high-fat diet in inducing an obesity-associated phenotype. However, cisplatin-treated rats showed the lowest body-weight gain. This reduction may be associated with the systemic toxicity of cisplatin, which can affect metabolic homeostasis, tissue integrity, and normal physiological functions (Elmorsy et al., 2024). In the present study, cashew supplementation increased final body weight and body-weight gain compared with the cisplatin-treated group, with a greater response observed at the 8% inclusion level. Cashew provides protein, unsaturated fatty acids, minerals, dietary fiber, and bioactive compounds that may contribute to nutritional and metabolic homeostasis (Rico et al., 2016: Abbas et al., 2024). However, body weight alone cannot distinguish changes in lean mass from changes in fat mass. Therefore, the increase in body weight observed following cashew supplementation should not be interpreted as direct evidence of improved body composition or reduced adiposity. Future studies incorporating fat mass, lean mass, and body-composition measurements would provide a more comprehensive interpretation of these changes.

4.2 Immunoglobulin responses

Cisplatin-treated obese rats showed higher serum IgM and IgG concentrations than the healthy control group. This increase should not necessarily be interpreted as enhanced immune competence because circulating immunoglobulin concentrations alone do not provide a complete assessment of immune function. Obesity is associated with alterations in both innate and adaptive immunity, accompanied by persistent inflammatory and metabolic signaling that may influence immune-cell activity and humoral responses (Shaikh et al., 2024; Mohammed Nouret al., 2025). In the present study, cashew supplementation reduced both IgM and IgG concentrations compared with the cisplatin-treated group, with values tending toward those observed in the healthy control group. This pattern may indicate partial normalization of the altered humoral profile. Nevertheless, because antigen-specific antibody responses, B-cell populations, and functional antibody activity were not evaluated, the biological significance of the changes in circulating IgM and IgG remains uncertain. Therefore, these findings

should be interpreted as changes in humoral biomarkers rather than direct evidence of improved or impaired immune competence.

4.3 Leukocyte profile

Cisplatin treatment markedly reduced total leukocyte, lymphocyte, neutrophil, eosinophil, and basophil counts. These findings are compatible with the hematological toxicity and myelosuppressive effects that may accompany platinum-based chemotherapy (Elmorsy et al., 2024; Zheng et al., 2024). The reduction in lymphocyte numbers is particularly relevant because lymphocytes represent major cellular components of adaptive immunity. Cashew supplementation increased total leukocyte and lymphocyte counts compared with the cisplatin-treated group, with a more pronounced response observed at the 8% dietary inclusion level. Previous experimental evidence has demonstrated antioxidant and anti-inflammatory activities associated with *Anacardium occidentale*, providing a possible biological basis for the observed changes (Fusco et al., 2020; Silva Júnior ; Adam et al., 2026). However, inflammatory cytokines, bone-marrow cellularity, and immune-cell phenotypes were not assessed in the present study. Consequently, the mechanisms responsible for the improvement in leukocyte counts cannot be established from the current findings alone.

4.4 Hematological parameters

Cisplatin exposure resulted in marked reductions in hemoglobin, red blood cell count, and platelet count. These findings are consistent with the recognized hematological toxicity associated with platinum-based chemotherapy, which may involve anemia, leukopenia, neutropenia, and thrombocytopenia (Aljehaniet al., 2026; Zheng et al., 2024). Oxidative stress, impaired hematopoietic function, and direct or indirect effects on bone-marrow cells may contribute to these abnormalities; however, bone-marrow parameters were not evaluated in the present study. Cashew supplementation was associated with improvements in hemoglobin, red blood cell, and platelet values, particularly at the 8% inclusion level, where values approached those of the healthy control group. The nutritional composition and antioxidant properties of cashew may contribute to the maintenance of cellular integrity and physiological homeostasis (Rico et al., 2016; Silva Júnior et al., 2025). Nevertheless, additional investigations involving bone-marrow histology, erythropoietic markers, iron status, and platelet production are required to determine whether these hematological improvements reflect direct effects on hematopoiesis or secondary effects related to the overall nutritional and oxidative status of the animals.

4.5 Oxidative stress and antioxidant defense

One of the most consistent findings of the present study was the marked increase in malondialdehyde (MDA), accompanied by reductions in superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) activities in cisplatin-treated rats. This pattern is consistent with increased lipid peroxidation and impaired antioxidant defense and supports the recognized contribution of oxidative stress to cisplatin-induced toxicity (Elmorsy et al., 2024). Cashew supplementation produced an opposite pattern, characterized by lower MDA concentrations and higher SOD, CAT, and GPx activities. The response was generally more pronounced in the 8% group. These findings are supported by experimental evidence concerning the antioxidant properties of cashew. Fusco et al. (2020) reported that *Anacardium occidentale* consumption modulated oxidative stress through pathways involving Nrf2/HO-1 and NF-κB signaling. More recently, Silva Júnior et al. (2025), in a systematic review of experimental studies in rats, reported that cashew consumption was generally associated with reductions in oxidative stress and improvements in antioxidant enzyme activity. Therefore, the present findings are consistent with previous experimental evidence suggesting that cashew-derived nutrients and bioactive compounds may contribute to antioxidant defense. Nevertheless, because molecular markers of antioxidant signaling were not measured in the present study, the involvement of specific pathways such as Nrf2/HO-1 cannot be confirmed.

4.6 Integrated interpretation

The simultaneous improvement in oxidative, leukocyte, and hematological parameters suggests that the effects observed following cashew supplementation may involve interconnected biological processes. Obesity creates an immunometabolic environment characterized by altered adipose-tissue signaling, chr onic low-grade inflammation, and changes in immune-cell function, whereas cisplatin introduces additional oxidative and hematological stress (Alkhudhayri et al., 2026; Bradley et al., 2024; Elmorsy et al., 2024). The reduction in oxidative stress observed following cashew supplementation may have contributed to the maintenance of cellular integrity and hematological homeostasis; however, this interpretation remains mechanistic and cannot be established definitively from the measured variables alone. The 8% cashew supplementation level

generally produced greater changes than the 4% level across several measured parameters, including body-weight gain, leukocyte counts, hematological indices, and oxidative-stress biomarkers. This pattern suggests that the amount of cashew incorporated into the diet may influence the magnitude of the observed response (Ali et al., 2026) . However, because only two dietary inclusion levels were evaluated and no broader dose range was investigated, the present findings should be considered an indication of a possible dose-related effect rather than definitive evidence of a dose-response relationship. Overall, the present findings suggest that dietary cashew supplementation was associated with partial improvement in oxidative-stress biomarkers, leukocyte counts, hematological parameters, and the altered immunoglobulin profile in obese rats exposed to cisplatin. Among these outcomes, the antioxidant response was particularly consistent, as reflected by the reduction in MDA and the increases in SOD, CAT, and GPx activities. The findings provide experimental evidence supporting further investigation of cashew as a nutritional intervention under conditions characterized by combined metabolic, oxidative, and immune disturbances. However, additional studies incorporating inflammatory cytokines, bone-marrow histology, immune-cell phenotyping, body-composition measurements, antigen-specific immune responses, and molecular markers such as Nrf2/HO-1 and NF-κB are needed to determine the mechanisms underlying these effects.

5. CONCLUSION

In conclusion, the present study demonstrated that obesity combined with cisplatin exposure was associated with marked alterations in hematological, immunological, and oxidative stress-related parameters in rats. These alterations included reductions in leukocyte, erythrocyte, hemoglobin, and platelet indices, together with increased lipid peroxidation and reduced antioxidant enzyme activities. Changes in serum IgM and IgG concentrations further indicated an altered humoral immune profile under the experimental conditions. Dietary supplementation with cashew powder was associated with partial improvement of these abnormalities. Both 4% and 8% cashew supplementation reduced MDA levels and increased SOD, CAT, and GPx activities, while also improving several hematological and leukocyte parameters. Cashew supplementation additionally shifted the elevated IgM and IgG concentrations toward the values observed in the healthy control group. In general, the 8% supplementation level produced a more pronounced response than the 4% level, particularly for oxidative and hematological parameters.These findings suggest that cashew powder may have a potential nutritional role in modulating oxidative and immune-related disturbances associated with obesity and cisplatin exposure. The observed effects may be related, at least in part, to the antioxidant and bioactive components of cashew. However, the present findings should be considered preliminary because the underlying molecular mechanisms and functional immune responses were not directly investigated. Further studies incorporating inflammatory cytokines, immune-cell phenotyping, bone marrow assessment, body-composition analysis, and molecular markers of antioxidant and inflammatory signaling are warranted to clarify the mechanisms involved and to determine the optimal dietary level of cashew supplementation.

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