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Effects of Hydro-Methanolic Extract of Macadamia Nuts on Haematological Parameters in Male Wistar Rats

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ABSTRACT

Background: To evaluate the effects of the hydro-methanolic extract of *Macadamia integrifolia* nuts on haematological parameters in male Wistar rats.

Methods: The study employed an experimental, controlled laboratory study using a dose–dependent treatment model. The study was conducted in an animal house of the Department of Human Physiology, Rivers State University, Nigeria. Twenty-four male Wistar rats were randomly assigned into four groups (n=6 per group): control, low dose (250 mg/kg), medium dose (500 mg/kg), and high dose (1000 mg/kg) of hydro-methanolic *Macadamia integrifolia* nuts extract. The extract was administered daily for 28 days. Wistar rats received daily administration of hydro-methanolic extract of Macadamia integrifolia nuts for 28 days. Standard haematological parameters were analysed using established laboratory methods. Data were expressed as mean ± SEM, and statistical significance was set at $P < 0.05$.

Results: Significant dose-dependent alterations were observed in erythrocyte indices. The low-dose group showed marked reductions in packed cell volume (33.0 ± 0.6% vs 45.3 ± 1.5%), haemoglobin (11.0 ± 0.2 g/dL vs 15.1 ± 0.5 g/dL), and red blood cell count (5.0 ± 0.3 $\times 10^6$/µL vs 6.7 ± 0.1 $\times 10^6$/µL) compared with control ($P < 0.05$). The medium dose partially attenuated these reductions. In contrast, the high dose restored packed cell volume (44.3 ± 1.5%), haemoglobin (14.97 ± 0.7 g/dL), and red blood cell count (6.02 ± 0.1 $\times 10^6$/µL) to values comparable with control. Mean corpuscular haemoglobin increased significantly at low and medium doses, while mean corpuscular haemoglobin concentration remained unchanged across groups. Mean corpuscular volume decreased at low and medium doses but increased at the high dose. White blood cell count was significantly elevated at the high dose (13.57 ± 1.1 $\times 10^3$/µL) relative to control (10.8 ± 1.0 $\times 10^3$/µL; $P < 0.05$), whereas platelet count and differential leukocyte percentages showed no significant differences.

Conclusion: Hydro-methanolic *Macadamia integrifolia* nuts extract exerted biphasic, dose-dependent effects on haematological parameters, with low doses associated with erythrocyte suppression and higher doses restoring erythroid indices and increasing total leukocyte count.

KEYWORDS: Macadamia integrifolia; haematology; erythrocytes; leukocytes; dose–response.

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1. INTRODUCTIONS

Haematological parameters are fundamental indicators of physiological integrity and are widely applied in clinical and experimental medicine to evaluate oxygen transport capacity, immune competence, inflammatory status, and haemostatic balance. Alterations in red blood cell indices, white blood cell counts, and platelet parameters often reflect underlying metabolic disturbances, nutritional imbalances, oxidative stress, or systemic inflammation (Camaschella, 2019; Park & Chang, 2025). Because the haematopoietic system responds dynamically to environmental and nutritional influences, blood indices serve as sensitive biomarkers for evaluating the biological effects and safety profile of dietary bioactives and plant-derived compounds (Kaushansky, 2015).

Nutrition plays a critical role in the regulation of haematopoiesis. Adequate availability of iron, folate, vitamin

B12, and essential fatty acids is required for effective erythropoiesis, while dietary bioactive compounds can modulate leukopoiesis and thrombopoiesis through antioxidant and anti-inflammatory pathways (Calder, 2020; Camaschella, 2019). Oxidative stress contributes to erythrocyte membrane lipid peroxidation, haemoglobin oxidation, and reduced red cell lifespan, thereby promoting anaemia and related haematological abnormalities (Pretorius et al., 2016). Chronic low-grade inflammation similarly alters leukocyte distribution and activation, influencing immune regulation and cardiometabolic risk (Furman et al., 2019). Consequently, plant-based foods rich in antioxidant and anti-inflammatory constituents have attracted increasing attention for their potential to support haematological and immune homeostasis.

Tree nuts are nutrient-dense foods consistently associated with cardiometabolic benefits. Contemporary meta-analyses report that regular nut consumption is linked to improved lipid profiles, reduced systemic inflammation, and lower cardiovascular disease risk (Aune et al., 2016; Schwingshackl et al., 2017). These protective effects are largely attributed to their high content of unsaturated fatty acids, fibre, plant sterols, tocopherols, and polyphenolic compounds (Batubo, 2023). Emerging evidence also suggests that nut-derived bioactives may modulate oxidative stress pathways and immune cell signalling, mechanisms closely connected to haematological stability (Lorenzon Dos Santos et al., 2020). However, the specific effects of individual nut species on haematological indices remain insufficiently explored.

Macadamia integrifolia (Macadamia nuts) are distinguished by their high monounsaturated fatty acid content, particularly oleic and palmitoleic acids, alongside appreciable levels of phenolic antioxidants and vitamin E compounds. Monounsaturated fatty acids have been shown to exert anti-inflammatory effects, potentially influencing leukocyte activation and cytokine production (Hung et al., 2023). In parallel, phenolic antioxidants may mitigate oxidative damage to erythrocyte membranes and support red cell stability (Gulcin, 2025). Given that oxidative stress and inflammation are key modulators of haematopoietic function, these bioactive constituents provide plausible biological pathways through which macadamia-derived compounds could affect haematological parameters.

Despite the established cardiometabolic relevance of macadamia nuts, research has predominantly focused on lipid metabolism and glycaemic control, with limited attention to haematological outcomes. Yet, an evaluation of blood indices is essential when exploring the physiological effects of bioactive plant extracts, as both beneficial modulation and potential haematotoxicity must be considered. Changes in erythrocyte indices may reflect alterations in oxygen-carrying capacity, while variations in leukocyte and platelet counts can signal shifts in immune regulation or inflammatory tone. Therefore, understanding the haematological impact of macadamia-derived bioactives contributes to a more complete appraisal of their systemic effects. Therefore, this study investigated the effects of the hydro-methanolic extract of *Macadamia integrifolia* nuts on haematological parameters in male Wistar rats.

2. MATERIALS AND METHODS

2.1 Study Design

This study used a controlled experimental design using albino Wistar rats to evaluate the effects of hydro-methanolic *Macadamia integrifolia* nut extracts on haematological indices. Randomisation was used to allocate animals into treatment groups, thereby reducing bias and strengthening internal validity.

2.2 Study Area

The study was conducted at the Animal House and Physiology Laboratory, Department of Human Physiology, Rivers State University, Port Harcourt, Nigeria.

2.3 Experimental Animals

Twenty-four adult Wistar rats aged weighing 140-160 grams were procured from a registered breeder in Port Harcourt, Nigeria. Animals were housed in ventilated polypropylene cages under controlled conditions (temperature 25 ± 2 °C, relative humidity 50–60%, 12-h light/dark cycle) and provided standard rat chow and water ad libitum (Kilkenny et al., 2010). Rats were acclimatised for two weeks before experimentation. All procedures adhered to the NIH Guide for the Care and Use of Laboratory Animals (National Institutes of Health, 2011).

2.4 Plant Material and Extract Preparation

Fresh nuts of *Macadamia integrifolia* were collected from Jos, Plateau State, Nigeria, authenticated by a taxonomist in the Department of Plant Science and Biotechnology, Rivers State University, and deposited as voucher specimen RSUPbH0259. 4.3 kg of *Macadamia integrifolia* nuts were dried, and the pulverised nut paste was macerated in methanol (1:5 w/v) at room temperature for 72 h with intermittent agitation. The filtrate was concentrated at 40–45 °C in a water bath to yield a semi-solid methanolic extract, which was stored at 4°C in amber bottles (Azwanida, 2015; Handa et al., 2008).

2.5 Experimental Design and Grouping

Twenty-four male Wistar rats weighing between 140–160 grams were used in this study. The rats were randomly assigned to four groups (eight rats per group):

1. Group 1 (Control): Wistar rats fed with a standard diet and water without treatment.
2. Low-dose group: Wistar rats treated with 250 mg/kg/day of hydromethanolic extract of *Macadamia integrifolia* nut extract.
3. Medium-dose group: Wistar rats treated with 500 mg/kg/day of hydromethanolic extract of *Macadamia integrifolia* nut extract.
4. High-dose group: Wistar rats treated with 1000 mg/kg/day of hydromethanolic extract of *Macadamia integrifolia* nut extract.

Treatments were administered orally by gavage once daily for 28 consecutive days, in accordance with OECD Test No. 423 for the acute oral toxicity study (OECD, 2002).

2.6 Sample Collection and Handling

At the end of treatment, rats were fasted overnight and anaesthetised with chloroform. Blood was collected via cardiac puncture: 2 mL into EDTA tubes for haematological parameters determination.

2.7 Determination of Haematological Parameters

Haematological parameters were measured using an automated haematology analyser (Sysmex KX-21N, Japan), according to the manufacturer's protocol. Indices included RBC, WBC, Hb, PCV, platelet count, and leukocyte differentials (lymphocytes, neutrophils, monocytes, eosinophils, basophils).

2.8 Statistical Analysis

Data were expressed as mean ± SD. Normality was assessed using the Shapiro–Wilk test; homogeneity of variance was assessed using Levene's test. Parametric data were analysed by one-way ANOVA followed by Tukey's post hoc test; non-parametric alternatives were applied where assumptions were violated. Statistical significance was set at $p < 0.05$. Analyses were performed using R version 4.3.3 (R Core Team, 2024).

3. RESULTS

The results of the 28-day treatment with the hydro-methanol extract of *Macadamia Nuts* on haematological parameters in Wistar rats are presented in **Table 1**. Packed cell volume (PCV) was significantly reduced in the low-dose group (33.00 ± 0.58%) compared with controls (45.33 ± 1.45%, p<0.01). Medium-dose rats showed partial recovery (38.00 ± 1.00%), while high-dose rats had values comparable to controls (44.33 ± 1.45%). Haemoglobin concentration (Hb) followed a similar pattern: controls recorded 15.10 ± 0.49 g/dL, low-dose rats 11.00 ± 0.17 g/dL (P<0.01), medium-dose rats 13.00 ± 0.40 g/dL, and high-dose rats 14.97 ± 0.69 g/dL. Red blood cell (RBC) counts were significantly lower in the low-dose group (5.00 ± 0.27 ×10⁶/µL) compared with controls (6.69 ± 0.11 ×10⁶/µL, p<0.01). Medium-dose rats had 5.80 ± 0.20 ×10⁶/µL, whereas high-dose rats had 6.02 ± 0.13 ×10⁶/µL, values close to control levels.

Additionally, red cell indices demonstrated dose-dependent changes. Mean corpuscular volume (MCV) was significantly reduced in the low-dose group (64.30 ± 0.79 fL) compared with controls (70.63 ± 1.96 fL, P<0.01), indicating microcytosis. Medium-dose rats had intermediate MCV values (68.00 ± 1.20 fL), whereas high-dose rats showed a significantly increased MCV (78.47 ± 4.88 fL; $P < 0.01$), consistent with macrocytosis. Mean corpuscular haemoglobin (MCH) was higher in the low-dose group (21.50 ± 0.51 pg) compared with controls (19.57 ± 0.19 pg, P<0.05), while medium-dose rats recorded 20.50 ± 0.40 pg and high-dose rats 19.80 ± 0.30 pg. Mean corpuscular haemoglobin concentration (MCHC) did not differ significantly between groups (control: 34.00 ± 0.50 g/dL; low dose: 33.00 ± 0.40 g/dL; medium dose: 33.50 ± 0.45 g/dL; high dose: 34.20 ± 0.55 g/dL).

Furthermore, white blood cell (WBC) counts were significantly elevated in the high-dose group (13.57 ± 1.05 ×10³/µL) compared with controls (10.77 ± 1.03 ×10³/µL, P<0.05). Low- and medium-dose groups showed no significant differences (9.50 ± 0.90 and 11.20 ± 1.10 ×10³/µL, respectively). At the same time, leukocyte differentials (neutrophils, lymphocytes, monocytes, eosinophils, basophils) showed no significant between-group variation, with values remaining within normal ranges. Finally, platelet counts did not differ significantly across groups (control: 250 ± 15 ×10³/µL; low dose: 245 ± 12 ×10³/µL; medium dose: 248 ± 14 ×10³/µL; high dose: 252 ± 13 ×10³/µL).

Table 1. Haematological parameters of Wistar rats after 28 days of treatment with hydro-methanolic *Macadamia integrifolia* nuts extract

Parameter (n=6)	Control	Low dose (250 mg/kg)	Medium dose (500 mg/kg)	High dose (1000 mg/kg)
PCV (%)	45.3 ± 1.5[a]	33.0 ± 0.6[b]	38.0 ± 1.0[c]	44.3 ± 1.5[a]
Hb (g/dL)	15.1 ± 0.5[a]	11.0 ± 0.2[b]	13.0 ± 0.4[c]	14.97 ± 0.7[a]
RBC (×10⁶/µL)	6.7 ± 0.1[a]	5.0 ± 0.3[b]	5.8 ± 0.2[c]	6.02 ± 0.1[a]
MCHC (g/dL)	34.0 ± 0.5[a]	33.0 ± 0.4[a]	33.5 ± 0.5[a]	34.2 ± 0.6[a]
MCH (pg)	19.6 ± 0.2[a]	21.5 ± 0.5[b]	20.5 ± 0.4[c]	19.8 ± 0.3[a]
MCV (fL)	70.6 ± 2.0[a]	64.3 ± 0.8[b]	68.0 ± 1.2[c]	78.5 ± 1.3
WBC (×10³/µL)	10.8 ± 1.0[a]	9.5 ± 0.9[a]	11.20 ± 1.1[a]	13.57 ± 1.1[b]
Platelets (×10³/µL)	250.0 ± 15.0[a]	245.0 ± 12.0[a]	248.0 ± 14.0[a]	252 ± 13.0[a]
Neutrophils (%)	35.0 ± 2.0[a]	34.5 ± 1.8[a]	36.0 ± 2.1[a]	35.5 ± 2.0[a]
Lymphocytes (%)	55.0 ± 3.0[a]	54.0 ± 2.5[a]	56.0 ± 2.8[a]	55.5 ± 2.7[a]
Monocytes (%)	6.0 ± 0.8[a]	6.2 ± 0.7[a]	6.1 ± 0.9[a]	6.3 ± 0.8[a]
Eosinophils (%)	4.0 ± 0.5[a]	4.3 ± 0.6[a]	4.2 ± 0.5[a]	4.1 ± 0.6[a]

Values are expressed as mean ± SEM. Different superscripts (a, b, ab) within a column indicate statistically significant differences between groups (P < 0.05). PCV: packed cell volume; Hb: haemoglobin; RBC: red blood cell count; WBC: white blood cell count; PLT: platelet count; MCHC: mean corpuscular haemoglobin concentration; MCH: mean corpuscular haemoglobin; MCV: mean corpuscular volume.

4. DISCUSSION

The present study demonstrates a dose-dependent modulation of haematological parameters following 28 days of administration of hydro-methanolic extract of *Macadamia integrifolia* nuts in male Wistar rats. The significant reductions in packed cell volume (PCV), haemoglobin (Hb), and red blood cell (RBC) count at 250 mg/kg suggest an anaemia-like effect at low dose. Reductions in these indices are classical indicators of impaired erythropoiesis or increased erythrocyte destruction (Park & Chang, 2025). The concomitant decrease in mean corpuscular volume (MCV) at the low dose may reflect a microcytic trend, often associated with disturbances in iron metabolism or haem synthesis (Camaschella, 2019). Although iron parameters were not assessed, phytochemicals such as polyphenols and tannins, present in many plant extracts, can reduce mineral bioavailability by chelation, potentially influencing haemoglobin synthesis when administered at certain concentrations (Delimont et al., 2017).

Interestingly, the medium dose (500 mg/kg) partially restored RBC indices, while the high dose (1000 mg/kg) normalised PCV, Hb, and RBC values to levels comparable with control. This pattern suggests a biphasic or hormetic response, where low doses may exert inhibitory effects and higher doses confer adaptive or protective benefits (Calabrese & Kozumbo, 2021). Macadamia nuts are rich in monounsaturated fatty acids (MUFA), tocopherols, and antioxidant polyphenols, which have been shown to reduce oxidative stress and enhance cellular membrane stability (Glenn et al., 2023). Oxidative stress is a key contributor to erythrocyte membrane damage and reduced red cell lifespan (Batubo et al., 2023; Obeagu et al., 2024). Therefore, the normalisation observed at higher doses may reflect antioxidant-mediated preservation of erythrocyte integrity and improved bone marrow responsiveness.

The stability of mean corpuscular haemoglobin concentration (MCHC) across groups indicates that intracellular haemoglobin concentration remained largely unaffected, suggesting that the extract did not significantly impair haemoglobin incorporation into erythrocytes. The elevated MCV at the highest dose may indicate enhanced erythrocyte maturation or improved membrane fluidity, potentially linked to improved lipid incorporation into cell membranes, a known effect of MUFA-rich dietary components (Capece et al., 2024). In this study, low-dose treatment induced anaemia-like changes, with reduced packed cell volume (PCV), haemoglobin (Hb), and red blood cell (RBC) counts. In contrast, high-dose treatment restored these values and significantly elevated white blood cell (WBC) counts, suggesting immune stimulation. The increase in WBC counts is consistent with the findings of El-Hawary et al. (2022), who reported immunomodulatory effects of macadamia extracts in rats (Batubo et al., 2023; Seham El-Hawary, 2022). The red cell indices further support this dichotomy: low-dose treatment induced microcytosis, whereas high-dose treatment promoted macrocytosis, possibly reflecting adaptive erythropoietic responses (Batubo et al., 2023). These findings suggest that macadamia nuts extracts may exert dose-dependent effects on haematological effects, with low doses impairing erythropoiesis and high doses enhancing immune function.

Furthermore, white blood cell (WBC) counts were significantly elevated only at the highest dose, while differential counts remained unchanged. This isolated leukocytosis without shifts in neutrophil or lymphocyte proportions suggests immunostimulatory modulation rather than inflammatory pathology (Rosales, 2018). Plant-derived bioactive compounds, particularly phenolic constituents, have been reported to enhance immune surveillance and modulate leukocyte activity without provoking systemic inflammation (Ganesan & Xu, 2017). Leukocyte differential counts revealed no significant changes in neutrophil, lymphocyte, eosinophil, or monocyte proportions across groups. However, total WBC counts were significantly elevated in the high-dose group. This indicates that macadamia extract stimulates leukocyte proliferation without altering distribution, complementing prior evidence of its immunomodulatory potential (El-Hawary et al., 2022). Such immune stimulation may contribute to the protective effects observed in lipid and cardiovascular parameters (Batubo et al., 2023).

Platelet counts were unaffected across all treatment groups, indicating preserved thrombopoiesis and haemostatic stability. This finding supports the haematological safety of the extract, as alterations in platelet count are often early indicators of marrow suppression or toxicological stress (Kaushansky, 2015). Overall, the findings demonstrate a dose-dependent dual effect of hydro-methanolic Macadamia integrifolia extract on erythrocytic parameters, characterised by suppression at low dose and restoration at higher dose. The observed hormetic pattern underscores the importance of dose optimisation in nutraceutical applications. While higher doses appear haematologically safe and potentially protective, lower doses may transiently impair erythrocytic indices. Further studies evaluating iron status, oxidative stress biomarkers, and erythropoietin dynamics are warranted to elucidate the precise mechanistic pathways underlying these observations.

5. CONCLUSION

Administration of hydro-methanolic extract of Macadamia integrifolia nuts for 28 days produced dose-dependent alterations in haematological indices in male Wistar rats. The low dose was associated with significant reductions in packed cell volume, haemoglobin concentration, and red blood cell count, suggesting a transient suppressive effect on erythrocytic parameters. In contrast, medium and high doses progressively restored these indices, with values at the

highest dose comparable to control, indicating possible haematoprotective or erythropoietic support at higher concentrations. White blood cell counts increased modestly at the highest dose without significant shifts in differential counts, while platelet parameters remained stable across all groups, suggesting preserved immune balance and haemostatic function. Overall, the findings indicate a biphasic haematological response, underscoring the importance of dose optimisation in the therapeutic or nutraceutical application of macadamia nut extracts. Further mechanistic studies are warranted to clarify the pathways underlying the observed erythrocytic modulation.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

AUTHORS' CONTRIBUTIONS

Edith Reuben designed the research methodology and performed the experiments, analysed the data, and drafted the first manuscript. Nimisoere P Batubo and Boma H Opusunju reviewed the manuscript. Bright Ichechi Owhorji provided critical and analytical feedback. Edith Reuben, Nimisoere P Batubo, Boma H Opusunju and Bright Ichechi Owhorji revised the manuscript. All authors approved the final manuscript.

ETHICS APPROVAL

All experimental procedures received approval from the Research Ethics Committee at the University of Port Harcourt (Approval No: UPH/CERMAD/REC/MM90/216). Animal handling and protocols adhered to the NIH Guide for the Care and Use of Laboratory Animals (8th edition). The study also followed the ARRIVE 2.0 guidelines for reporting animal research. Measures were taken to minimise animal suffering, reduce the number of animals used, and refine procedures in line with the 3Rs principles (Replacement, Reduction, and Refinement) (National Institutes of Health, 2011).

REFERENCES

I. Aune, D., Keum, N., Giovannucci, E., Fadnes, L. T., Boffetta, P., Greenwood, D. C., Tonstad, S., Vatten, L. J., Riboli, E., & Norat, T. (2016). Nut consumption and risk of cardiovascular disease, total cancer, all-cause and cause-specific mortality: a systematic review and dose-response meta-analysis of prospective studies. *BMC Med*, *14*(1), 207. https://doi.org/10.1186/s12916-016-0730-3

II. Batubo, N. P., Ogbu, O. S., & Victor, D. D. (2023). Hematological, histopathological and oxidative stress responses to n-hexane extract of Terminalia catappa nuts in leukemia-induced Wistar rats. *International Journal of Research in Medical Sciences*, *12*(1), 61-69.https://doi.org/10.18203/2320-6012.ijrms20233978

III. Batubo, N. P., Ogbu, O. S., & Victor, D. D.;. (2023). Chemical profiles and proximate analysis of n-hexane extract of Terminalia catappa kernel from Nigeria. *International Journal of Research in Medical Sciences*, *12*(1), 17-25. https://doi.org/10.18203/2320-6012.ijrms20233971

IV. Calabrese, E. J., & Kozumbo, W. J. (2021). The hormetic dose-response mechanism: Nrf2 activation. *Pharmacol Res*, *167*, 105526. https://doi.org/10.1016/j.phrs.2021.105526

V. Calder, P. C. (2020). Nutrition, immunity and COVID-19. *BMJ Nutr Prev Health*, *3*(1), 74-92. https://doi.org/10.1136/bmjnph-2020-000085

VI. Camaschella, C. (2019). Iron deficiency. *Blood*, *133*(1), 30-39. https://doi.org/10.1182/blood-2018-05-815944

VII. Capece, U., Gugliandolo, S., Morciano, C., Avolio, A., Splendore, A., Di Giuseppe, G., Ciccarelli, G., Soldovieri, L., Brunetti, M., Mezza, T., Pontecorvi, A., Giaccari, A., & Cinti, F. (2024). Erythrocyte Membrane Fluidity and Omega-3 Fatty Acid Intake: Current Outlook and Perspectives for a Novel, Nutritionally Modifiable Cardiovascular Risk Factor. *Nutrients*, *16*(24). https://doi.org/10.3390/nu16244318

VIII. Delimont, N. M., Haub, M. D., & Lindshield, B. L. (2017). The Impact of Tannin Consumption on Iron Bioavailability and Status: A Narrative Review. *Curr Dev Nutr*, *1*(2), 1-12. https://doi.org/10.3945/cdn.116.000042

IX. Furman, D., Campisi, J., Verdin, E., Carrera-Bastos, P., Targ, S., Franceschi, C., Ferrucci, L., Gilroy, D. W., Fasano, A., Miller, G. W., Miller, A. H., Mantovani, A., Weyand, C. M., Barzilai, N., Goronzy, J. J., Rando, T. A., Effros, R. B., Lucia, A., Kleinstreuer, N., & Slavich, G. M. (2019). Chronic inflammation in the etiology of disease across the life span. *Nat Med*, *25*(12), 1822-1832. https://doi.org/10.1038/s41591-019-0675-0

X. Ganesan, K., & Xu, B. (2017). Polyphenol-Rich Dry Common Beans (Phaseolus vulgaris L.) and Their Health Benefits. *Int J Mol Sci*, *18*(11). https://doi.org/10.3390/ijms18112331

XI. Glenn, A. J., Aune, D., Freisling, H., Mohammadifard, N., Kendall, C. W. C., Salas-Salvado, J., Jenkins, D. J. A., Hu, F. B., & Sievenpiper, J. L. (2023). Nuts and Cardiovascular

Disease Outcomes: A Review of the Evidence and Future Directions. *Nutrients*, *15*(4). https://doi.org/10.3390/nu15040911

XII. Gulcin, I. (2025). Antioxidants: a comprehensive review. *Arch Toxicol*, *99*(5), 1893-1997. https://doi.org/10.1007/s00204-025-03997-2

XIII. Hung, H. C., Tsai, S. F., Chou, H. W., Tsai, M. J., Hsu, P. L., & Kuo, Y. M. (2023). Dietary fatty acids differentially affect secretion of pro-inflammatory cytokines in human THP-1 monocytes. *Sci Rep*, *13*(1), 5511. https://doi.org/10.1038/s41598-023-32710-5

XIV. Kaushansky, K. (2015). Thrombopoiesis. *Semin Hematol*, *52*(1), 4-11. https://doi.org/10.1053/j.seminhematol.2014.10.003

XV. Lorenzon Dos Santos, J., Quadros, A. S., Weschenfelder, C., Garofallo, S. B., & Marcadenti, A. (2020). Oxidative Stress Biomarkers, Nut-Related Antioxidants, and Cardiovascular Disease. *Nutrients*, *12*(3). https://doi.org/10.3390/nu12030682

XVI. National Institutes of Health. (2011). National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals. In *Guide for the Care and Use of Laboratory Animals* (8th ed.). https://doi.org/10.17226/12910

XVII. Obeagu, E. I., Igwe, M. C., & Obeagu, G. U. (2024). Oxidative stress's impact on red blood cells: Unveiling implications for health and disease. *Medicine (Baltimore)*, *103*(9), e37360. https://doi.org/10.1097/MD.0000000000037360

XVIII. OECD. (2002). *Test No. 423: Acute Oral toxicity - Acute Toxic Class Method, OECD Guidelines for the Testing of Chemicals*. P. OECD Publishing.

XIX. Park, M., & Chang, Y. H. (2025). Clinical Significance of Red Blood Cell Indices. In V. Rajashekaraiah (Ed.), *Red Blood Cells - Functions and Significance*. IntechOpen. https://doi.org/10.5772/intechopen.1008323

XX. Pretorius, E., Olumuyiwa-Akeredolu, O. O., Mbotwe, S., & Bester, J. (2016). Erythrocytes and their role as health indicator: Using structure in a patient-orientated precision medicine approach. *Blood Rev*, *30*(4), 263-274. https://doi.org/10.1016/j.blre.2016.01.001

XXI. R Core Team. (2024). *_R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing*. In (Version 4.4.2) Vienna, Austria. https://www.R-project.org/.

XXII. Rosales, C. (2018). Neutrophil: A Cell with Many Roles in Inflammation or Several Cell Types? *Front Physiol*, *9*, 113. https://doi.org/10.3389/fphys.2018.00113

XXIII. Schwingshackl, L., Schwedhelm, C., Hoffmann, G., Knuppel, S., Iqbal, K., Andriolo, V., Bechthold, A., Schlesinger, S., & Boeing, H. (2017). Food Groups and Risk of Hypertension: A Systematic Review and Dose-Response Meta-Analysis of Prospective Studies. *Adv Nutr*, *8*(6), 793-803. https://doi.org/10.3945/an.117.017178

XXIV. Seham El-Hawary, M. A., Engy A. Mahrous, . (2022). Extracts of different organs of Macadamia integrifolia ameliorate oxidative damage in a D-galactose accelerated ageing model in rats. . *Biointerface Research in Applied Chemistry*, *12*(5), 7125-7135. https://doi.org/https://doi.org/10.33263/BRIAC125.71257135