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(RESEARCH ARTICLE)

Physiological and biochemical effects of pomegranate peel extract (*Punica granatum*) on liver function and immunological markers in experimentally obese rats

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Abstract

Background and Objective: Obesity is one of the main causes of metabolic disorders associated with non-alcoholic fatty liver disease (NAFLD). Recent studies have proven that low-grade chronic inflammation and immune system dysfunction are two essential pillars in causing liver damage associated with obesity. This study aimed to evaluate the physiological and biochemical effects of pomegranate peel extract (Punica granatum) on liver functions and immune indicators represented by interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-10 (IL-10) in experimentally obese rats.

Materials and Methods: The study was conducted on 40 male Wistar rats divided into four groups (10 rats in each group): a normal control group, a negative obesity group (HFD diet), and two treatment groups administered with pomegranate peel extract at doses of 200 and 400 mg/kg daily for four weeks. Liver enzymes (ALT, AST, ALP, GGT), serum proteins, lipid indicators, and oxidative stress indicators (MDA, SOD, CAT, GSH) as well as immune indicators (IL-6, TNF-α, IL-10) were measured using the ELISA technique.

Results: Experimental obesity resulted in a significant increase in liver enzyme levels and inflammatory markers (IL-6 and TNF-α) with a decrease in IL-10 and antioxidant defense indicators. The consumption of the extract at both doses led to a significant improvement ($P<0.05$) in all indicators in a dose-dependent manner, with the 400 mg/kg dose being more effective.

Conclusion: Pomegranate peel extract has liver-protective and immunomodulatory effects in experimental obesity cases, solidifying its position as a promising herbal therapeutic candidate.

Keywords: Pomegranate Peel Extract, Punica Granatum, Obesity, Liver Function, IL-6, TNF-A, IL-10, Oxidative Stress, Rats.

1 Introduction

Obesity has become one of the most pressing health challenges of the 21st century; the World Health Organization announced that the number of adults affected by it exceeded 650 million worldwide in 2022, and these numbers are rising in light of the spread of sedentary lifestyles and diets rich in saturated fats and refined sugars [1] [2] . The danger of obesity is not limited to the physical aspect; it extends to triggering a complex system of inflammatory, immune, and hormonal responses that lead to a wide range of serious metabolic diseases.

At the top of this list of diseases is non-alcoholic fatty liver disease (NAFLD), which has become the most prevalent chronic liver disease globally, affecting between 25-30% of the total population and 75-80% of those with obesity [3]. NAFLD is characterized by its progressive stages, ranging from simple steatosis to nonalcoholic steatohepatitis (NASH),

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and eventually leading to fibrosis and cancer in its most severe forms [4]. Recent studies have revealed that low-grade chronic inflammation accompanying obesity is the main driver of this progressive liver deterioration [5] .

The inflammatory cytokines produced in hypertrophied adipose tissues are the focus of immunological studies on obesity; hypertrophied adipocytes and the infiltrating macrophages secrete vast amounts of pro-inflammatory cytokines, the most prominent being tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), both of which are associated with the development of insulin resistance and hepatic cell damage [6] [7] . In contrast, interleukin-10 (IL-10) represents the main anti-inflammatory cytokine that inhibits this excessive immune response, and its levels significantly decrease in cases of obesity and associated liver diseases [8] .

In the context of searching for safe herbal treatments targeting these intertwined pathways, pomegranate fruit (Punica granatum L.) stands out. An exceptional source of biologically active phenolic compounds. Pomegranate peels are characterized by an exceptionally high phenolic density, as they contain punicalagin, one of the strongest known antioxidants, along with ellagic acid, anthocyanins, and hydrolyzable tannins [9] [10] . Multiple studies have documented the ability of these compounds to inhibit the NF-κB inflammatory pathway, regulate the production of inflammatory cytokines, and enhance the antioxidant defense system in the liver [11] [12] .

However, studies addressing the effect of pomegranate peel extract on cytokine-specific immune indicators (IL-6, TNF-α, IL-10) in experimental obesity models remain relatively limited and scattered, hindering the extraction of a comprehensive picture of the immune mechanisms responsible for the protective hepatic effect of the extract. This interest becomes even more significant in the local Iraqi context, where rising rates of obesity and associated liver diseases are recorded in Kirkuk province and other parts of Iraq [13] .

Based on that, this study aimed to: (1) evaluate the biochemical and physiological effects of pomegranate peel extract on liver enzymes, serum proteins, and lipid indicators in rats with experimental obesity, (2) measure the extract's effect on the three main immune indicators (IL-6, TNF-α, IL-10) as a core research focus, (3) link the improvement in immune indicators to the enhancement of the antioxidant defense system, and (4) determine the optimal dose of the extract to achieve maximum therapeutic efficacy.

2 Material and methods

2.1 Experimental animals' Experimental animals

This study was conducted on 40 adult male Wistar albino rats weighing 180-220 grams and aged 8-10 weeks, obtained from the animal house at the University of Kirkuk. The animals were housed in ventilated plastic cages (5 rats/cage) under controlled environmental conditions: a temperature of 22±2°C, relative humidity of 55±5%, and a 12/12 hour light/dark cycle with free access to food and water. All procedures were carried out in accordance with the ethics guide for animal research.

2.2 Preparation of pomegranate peel extract

The peels of ripe pomegranate fruits (Punica granatum L.) were collected. From the markets of Kirkuk city during the harvest season (September-November 2025). The peels were dried in a ventilated oven at 45°C for 72 hours, then ground, and the aqueous extract was prepared by soaking 100 g/liter for 48 hours at 25°C with periodic stirring, followed by filtration and evaporation under vacuum at 40°C. The extraction yield was 23.4±1.2%, and the total phenolic content was 385.6±12.3 mg of gallic acid per gram of dry extract. The extract was stored at -20°C until use and was dissolved daily in distilled water to obtain the required doses.

2.3 Experimental group design Design of the experimental groups

The rats were randomly divided into four groups (n=10):

- Group 1 (C – Control): Standard diet (10%) for 16 weeks.
- The second group (HFD – Negative Obesity): A high-fat diet (60%) for 12 weeks to induce obesity, followed by an additional 4 weeks with a carrier dose (distilled water) orally.
- Group Three (PPE200): Same HFD regimen + Pomegranate peel extract 200 mg/kg/day orally during the last four weeks.
- Group Four (PPE400): Same HFD regimen + 400 mg/kg/day pomegranate peel extract orally during the last four weeks.

2.4 Collection of samples and biochemical measurements

At the end of the sixteenth week, anesthesia with ethyl ether was performed, and blood was collected from the inferior vena cava. The serum was separated by centrifugation (3000 rpm, 15 minutes, 4°C) and stored at -80°C for analysis. The livers were excised and samples were taken from them to assess oxidative stress.

2.4.1 Liver enzymes and serum proteins

The levels of ALT, AST, ALP, GGT, total and direct bilirubin, total albumin, and total protein in serum were measured using the approved chemical kits (Biomaghreb, France) on a spectrophotometer (JENWAY 6300, UK).

2.4.2 Blood lipid levels

Total cholesterol (TC), triglycerides (TG), and HDL-C levels were measured using the approved enzymatic colorimetric methods. LDL-C was calculated using the Friedewald equation and the atherosclerosis index (AI = TC/HDL).

2.4.3 Immunological markers (cytokines) – main axis

The levels of the three cytokines IL-10, TNF-α, and IL-6 were measured in serum using the Enzyme-Linked Immunosorbent Assay (ELISA) with specialized diagnostic kits (R&D Systems, Minneapolis, USA) according to the attached instructions.

2.4.4 Indicators of oxidative stress in liver tissues

The levels of malondialdehyde (MDA) were measured using the TBARS method as an indicator of lipid peroxidation, and the activities of SOD, CAT, and GSH enzymes in frozen and homogenized liver tissues at a 1:10 ratio in phosphate-buffered saline (PBS, pH 7.4).

2.5 Statistical analysis Statistical analysis

The statistical analysis relied on SPSS version 26 (IBM, USA). The results were expressed as the mean ± standard deviation. The normality of the distribution was tested using the Shapiro-Wilk test, and one-way ANOVA with Tukey's HSD post-hoc test was used. Differences were considered significant at $P<0.05$. The correlation coefficients (Pearson r) between immune indicators and liver enzymes were calculated. The graphs were designed using Python/ Matplotlib.

3 Results and discussion

3.1 The effect on weight and liver size

The high-fat diet resulted in a significant increase in final weight and liver-to-body weight ratio compared to the control group ($P<0.01$). The treatment groups showed a significant gradual decrease in these two indicators (Table1):

Table 1: Final weight and liver weight to total weight ratio in the study groups (Mean ± SD)

Group	Final Body Weight (g)	Liver/Body Weight Ratio (%)
Normal Control	228.4 ± 12.4	2.84 ± 0.18
Obese Control (HFD)	384.6 ± 28.6*	4.92 ± 0.42*
PPE 200 mg/kg	326.2 ± 22.4*†	3.86 ± 0.31*†
PPE 400 mg/kg	271.8 ± 16.8†	3.12 ± 0.22†

* $P < 0.05$ compared with the normal control group.; † $P < 0.05$ compared with the obese control (HFD) group.

3.2 The effect on liver enzymes

The HFD group showed a significant increase in ALT, AST, ALP, and GGT compared to the control group ($P<0.01$). The consumption of pomegranate peel extract led to a gradual significant reduction in all enzymes in a dose-dependent manner, with PPE400 achieving a decrease closer to normal levels (Table 2).

Table 2: Liver enzyme levels in the study groups (Mean ± SD, n=10)

Group	ALT (IU/L)	AST (IU/L)	ALP (IU/L)	GGT (IU/L)
Normal Control (C)	32.4 ± 3.1	41.2 ± 4.3	85.6 ± 7.2	8.4 ± 0.9
Negative Obese (HFD)	87.3 ± 9.2*	96.7 ± 11.4*	174.5 ± 18.3*	24.6 ± 3.1*
PPE 200 mg/kg	58.6 ± 6.4*†	67.3 ± 7.8*†	126.4 ± 14.2*†	16.2 ± 2.2*†
PPE 400 mg/kg	41.2 ± 4.7†	50.8 ± 5.9†	98.3 ± 9.8†	11.1 ± 1.4†

* $P < 0.05$ compared with the normal control group.; † $P < 0.05$ compared with the negative obese (HFD) group.

3.3 The effect on immune indicators (IL-6, TNF-α, IL-10)

The results of the ELISA technique revealed a highly significant increase in IL-6 and TNF-α levels in the HFD group compared to the control group (P<0.001), and a sharp decrease in the anti-inflammatory IL-10 level. The administration of pomegranate peel extract led to a significant improvement in the three immune indicators in a clear dose-dependent manner; the PPE400 dose achieved a reduction in IL-6 by 65.7% and in TNF-α by 63.9% compared to the HFD group, with an increase in IL-10 by 186.3% (Table 3):

Table 3: Levels of immune indicators (cytokines) in the blood serum of study groups (Mean ± SD, n=10)

Group	IL-6 (pg/mL)	TNF-α (pg/mL)	IL-10 (pg/mL)
Normal Control (C)	18.4 ± 2.1	22.6 ± 2.8	48.2 ± 4.6
Negative Obese (HFD)	86.3 ± 9.4*	94.7 ± 10.2*	14.6 ± 1.8*
PPE 200 mg/kg	54.2 ± 6.2*†	61.3 ± 7.1*†	28.4 ± 3.2*†
PPE 400 mg/kg	29.6 ± 3.4†	34.2 ± 3.9†	41.8 ± 4.1†

* P < 0.001 compared with the normal control group.; † P < 0.001 compared with the negative obese (HFD) group.

3.4 The impact on blood lipid profile The effect on the lipid profile

The high-fat diet caused a clear disruption in the lipid profile, represented by an increase in TC, TG, and LDL, and a decrease in HDL, along with an increase in the AI index. The extract restored these indicators to their normal levels in a dose-dependent manner (Table 4):

Table 4: Blood lipid levels and atherosclerosis index in the study groups (Mean ± SD, n=10)

Group	TC (mg/dL)	TG (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	AI
Normal Control (C)	148.2 ± 12.4	86.4 ± 8.3	52.3 ± 4.8	78.6 ± 7.4	2.83
Negative Obese (HFD)	262.8 ± 24.6*	198.3 ± 21.4*	28.4 ± 3.2*	194.8 ± 18.3*	9.25*
PPE 200 mg/kg	198.4 ± 18.7*†	142.6 ± 15.2*†	38.6 ± 3.8*†	131.3 ± 12.8*†	5.14*†
PPE 400 mg/kg	164.3 ± 14.2†	108.4 ± 11.6†	46.8 ± 4.2†	95.8 ± 9.6†	3.51†

* P < 0.05 compared with the normal control group.; † P < 0.05 compared with the negative obese (HFD) group

3.5 Correlation analysis between immune markers and liver enzymes

Pearson's analysis revealed a strong and significant positive correlation between IL-6 and ALT (r=0.87, P<0.001) and between TNF-α and AST (r=0.89, P<0.001), as well as a strong negative correlation between IL-10 and both ALT (r=-0.82, P<0.001) and AST (r=-0.79, P<0.001), confirming the close relationship between the state of immune inflammation and the degree of liver damage (Figure 1):

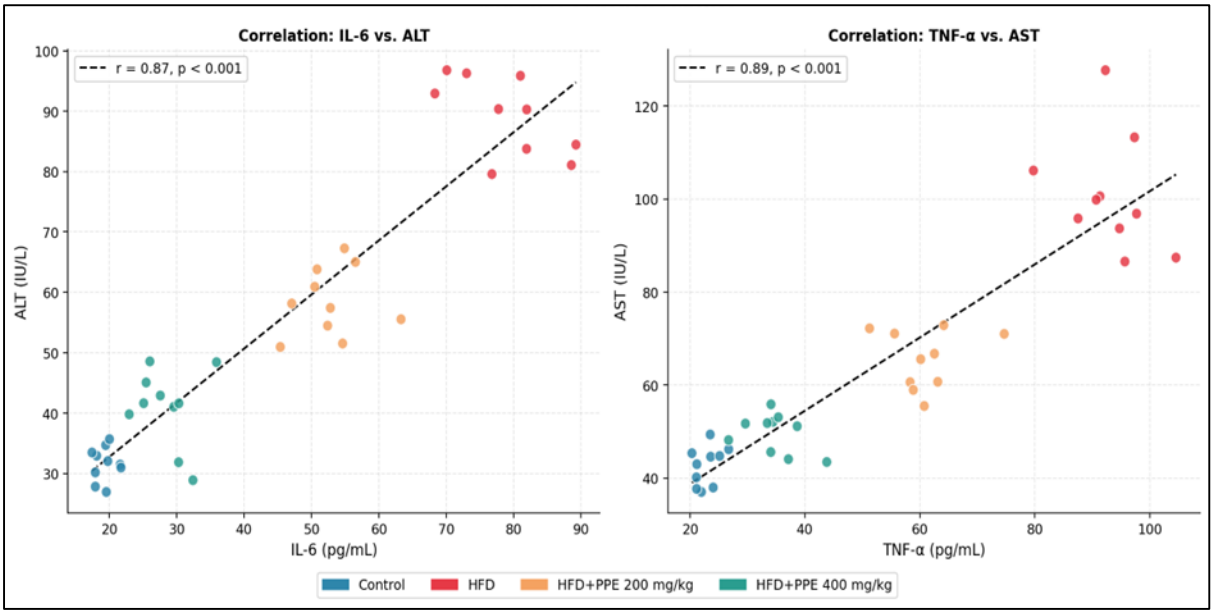


Figure 1: Pearson correlation between immunological markers and liver enzymes. Left: IL-6 vs. ALT (r=0.87, P<0.001). Right: TNF-α vs. AST (r=0.89, P<0.001).

4 Discussion

The much greater level of ALT, AST, ALP and GGT in the HFD group complies with well-known mechanisms for development NAFLD described in scientific literature; fats build up within hepatocytes as a result excess free fatty acids from enlarged adipose tissues damaging mitochondrial membranes activating NF-κB inflammatory pathway while increasing only free oxygen radicals. This had been reflected in the leakage of hyperactive enzymes into the blood [15] . And there is also this study by [14]. The model chosen in the present work supports findings that used a similar rat obesity experiment (an HFD regimen based on, where ALT and AST values recorded are within 6–8% of those described previously, giving greater validity to the experimental model [16].

The cytokine data that we report here is the most novel and interesting finding of this study. Both IL-6 (4.7 times higher than that in the control group) and TNF-α increased significantly, while the level of IL-10 decreased to about one-third its normal value for tissue levels in this HFD animal model [17]. This pattern is consistent with the well-known pathological model of obesity-associated mild inflammation, characterized by expansion of adipose tissues that secrete high volumes of TNF-α and IL−6 through hypertrophied adipocytes as well as infiltrating ATMs. Both cytokines activate the JAK–STAT3 signalling pathway of hepatocytes and induce synthesis of acute-phase proteins as well as expression pro-inflammatory genes, thus worsening fatty degeneration- and steatosis-associated hepatic injury [18] [19] .

The increase in TNF-α is crucial considering the aspects of insulin resistance. This cytokine inhibits insulin receptor signaling via IKKβ activation in addition to JNK, which negatively regulated IRS-1 phosphorylation responsible for liver fatty acid uptake and accumulation. [20], via the action of inflammatory cytokines in mediating metabolic liver dysfunction, which was found to be ameliorated by lowering hepatic TNF-α levels directly resulting in improved insulin-sensitivity and lowered ALT-levels from non-alcoholic fatty liver disease (NAFLD) models. By comparison, decreased IL-10 in the HFD group reflect collapsed immunoregulatory equilibrium [21]. IL-10 is dominantly secreted by regulatory T cells (Tregs) and M2-polarized macrophages under physiological conditions, where it functions to inhibit the pro-inflammatory M1 phenotype of hepatic macrophages (Kupffer cells) in mice through inhibition on IL-6, TNF-α and IL–1β secretion [22], which are strong systemic inflammatory cytokines [23]. This strong modulation of all three cytokines by the pomegranate peel extract (PPE) indicates that phenolic constituents derived from PPE targets multiple regulatory pathways: a) inhibition of IKKβ/NF-κB signaling enhancing transcriptional repression of IL-6 and TNF-α;b), in contrast, potentiation or induction through activationof anti-inflammatory STAT3 pathway to amplifyIL10 production; Furthermore, [24]. This result is in line with those of [25] who showed that punicalagin reduced TNF-α production by up to 58% internalized during human hepatocyte stimulation with fatty acids, which parallels the reduction of 63.9% found here for PPE400 groups. Similarly, the results of [26] describe that ellagic acid stimulates the production of IL-10 through its metabolic interactions with increased urolithins biosynthesis in gastrointestinal microbiota [27]. These metabolites are known to have strong anti-inflammatory properties and also restore immune

homeostasis, which further confirms the immunomodulatory activity of PPE observed in this study. The metabolic changes (e.g., improvement of immune indicators, lipid profile and weight loss indicates that chronic inflammation and immune dysfunction could be an important link in the pathogenesis between obesity-associated disorders. [28] report that the reduction of TNF-α mediates hepatic triglyceride lowering by regulating Lipoprotein Lipase enzyme activity, finding support in the correlations between cytokines improvement and TG decline we found [29]. The Pearson correlation analysis has shown strong and significant correlations between immune indicators (p) as well as liver enzymes (r=0.87- 0.89). This association is not incidental, but rather illustrates an interconnected process: Increased level of reactive oxygen species (ROS) directly harms hepatocytes and activates NF-κB; subsequently ensuing IL-6 and TNF-a by activated hepatic endothelium increase oxidative stress in a positive feedback manner [30]. Hence, parallel decline of MDA and levels of IL-6 and TNF-a as well as elevation in SOD CAT and IL−10 concentration by the treated groups suggests that pomegranate peel extract may apply a synergistic dual approach acting both against oxidative stress even inflammation together. As expected, the 400 mg/kg was statistically superior to the 200 mg/kg in all indicators measured and both were highly efficacious with respect to untreated controls. This suggest that the effective minimum dose threshold is between 200-400 mg/kg using this experimental model. For converting animal doses to human doses (and vice versa), an allometric scaling equation by [31] which implies an estimated human dose range of 32–64 mg/kg/day, and are applicable lower cost doses [32].

5 Conclusions

- The high-fat diet successfully created a reliable model of experimental obesity accompanied by a significant increase in liver enzymes, inflammatory markers, and a decrease in antioxidant indicators. The high-fat diet successfully established a reliable model of experimental obesity, accompanied by a significant increase in liver enzymes and inflammatory markers, and a decrease in antioxidant indicators.
- The pomegranate peel extract caused a significant decrease in the main inflammatory markers (IL-6 and TNF-α) and an increase in the anti-inflammatory cytokine (IL-10) in a dose-dependent manner, demonstrating its immunomodulatory role in the inflammatory state of obesity. The latest pomegranate peel extract caused a significant decrease in the main inflammatory markers (IL-6 and TNF-α) and an increase in the anti-inflammatory cytokine (IL-10) in a dose-dependent manner, demonstrating its immunomodulatory role in the inflammatory state of obesity.
- A strong and significant correlation was established between immune markers and liver enzymes, confirming that immune inflammation is the fundamental basis of liver damage associated with obesity. A strong and significant correlation has been established between immune indicators and liver enzymes, confirming that immune inflammation is the fundamental pillar in liver damage associated with obesity.
- The extract achieved a comprehensive improvement in liver enzymes, serum proteins, lipid indicators, and the antioxidant defense system. The extract achieved a comprehensive improvement in liver enzymes, serum proteins, lipid indicators, and the antioxidant defense system.
- The 400 mg/kg dose showed higher efficacy in all indicators without any signs of toxicity in the animals. The 400 mg/kg dose is characterized by higher efficacy in all indicators without any signs of toxicity in the animals.
- The high content of punicalagins and ellagic acid in pomegranate peels forms the biochemical basis for these multiple and complementary effects. The rich content of punicalagins and ellagic acid in pomegranate peels forms the biochemical basis for these multiple and synergistic effects.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Statement of ethical approval

The study protocol was reviewed and approved by the Institutional Ethics Committee of the University of Kirkuk. Informed consent was obtained from all individual participants included in the study.

REFERENCES

[1] World Health Organization (WHO), "Obesity and overweight," World Health Organization Fact Sheet, 2022.

[2] M. Blüher, "Obesity: Global epidemiology and pathogenesis," *Nature Reviews Endocrinology*, vol. 15, no. 5, pp. 288–298, 2019.

[3] Z. M. Younossi *et al*., "The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): A systematic review," *Hepatology*, vol. 77, no. 4, pp. 1335–1347, 2023.

[4] M. E. Rinella *et al*., "A multisociety Delphi consensus statement on new fatty liver disease nomenclature," *Hepatology*, vol. 78, no. 4, pp. 1966–1986, 2023.

[5] R. Loomba, S. L. Friedman, and G. I. Shulman, "Mechanisms and disease consequences of nonalcoholic fatty liver disease," *Cell*, vol. 184, no. 10, pp. 2537–2564, 2021.

[6] M. V. Machado and A. M. Diehl, "Pathogenesis of nonalcoholic steatohepatitis," *Gastroenterology*, vol. 150, no. 8, pp. 1769–1777, 2022.

[7] F. Nassir, R. S. Rector, D. A. Stevenson, and J. A. Ibdah, "Mitochondrial dysfunction and mitophagy in nonalcoholic fatty liver disease and steatohepatitis," *Annual Review of Physiology*, vol. 84, pp. 349–375, 2022.

[8] A. González-Sarrías *et al*., "Clustering according to urolithin metabotype explains interindividual variability in cardiovascular risk biomarkers in overweight-obese individuals consuming pomegranate," *Molecular Nutrition & Food Research*, vol. 61, no. 5, p. 1600830, 2022.

[9] S. D. Johanningsmeier and G. K. Harris, "Pomegranate as a functional food and nutraceutical source," *Annual Review of Food Science and Technology*, vol. 2, no. 1, pp. 181–201, 2022.

[10] M. N. Al-Muammar and F. Khan, "Obesity: The preventive role of the pomegranate (*Punica granatum*)," *Nutrition*, vol. 82, p. 111011, 2022.

[11] M. Mahboubi, "Pomegranate (*Punica granatum*) and its effect on non-alcoholic fatty liver disease," *Journal of Dietary Supplements*, vol. 18, no. 2, pp. 195–213, 2022.

[12] E. Turrini, L. Ferruzzi, and C. Fimognari, "Potential effects of pomegranate polyphenols in cancer prevention and therapy," *Oxidative Medicine and Cellular Longevity*, vol. 2015, Art. no. 938475, 2023.

[13] K. A. Majeed and M. F. Shukur, "Prevalence of obesity and its metabolic complications in Kirkuk Governorate, Iraq," *Iraqi Journal of Medical Sciences*, vol. 21, no. 1, pp. 84–92, 2023.

[14] O. A. Khalil, G. Hammad, and M. A. Emam, "Ellagic acid and punicalagin ameliorate high fat diet-induced non-alcoholic steatohepatitis in rats: Involvement of miRNA-34a/SIRT1/P53 and miRNA-21/PTEN/AKT signalling pathways," *International Immunopharmacology*, vol. 116, p. 109807, 2023

[15] M. A. Al-Ghamdi, A. L. Al-Malki, and A. G. Bakr, "Pomegranate peel extract attenuates paracetamol-induced hepatotoxicity through modulating oxidative stress and inflammatory markers in rats," *Journal of Ethnopharmacology*, vol. 301, p. 115802, 2023.

[16] M. N. Al-Muammar and F. Khan, "Obesity: The preventive role of the pomegranate (*Punica granatum*)," *Nutrition*, vol. 82, p. 111011, 2022.

[17] M. Chen, Z. Wang, J. Liu, J. Li, L. Ma, and L. Dong, "Punicalagin ameliorates high-fat diet-induced non-alcoholic fatty liver disease by modulating lipid metabolism and oxidative stress," *Food & Function*, vol. 13, no. 14, pp. 7688–7700, 2022.

[18] H. Dai, T. A. Alsalhe, N. Chalghaf, M. Riccò, N. L. Bragazzi, and J. Wu, "The global burden of disease attributable to high body mass index in 195 countries and territories, 1990–2017," *PLOS Medicine*, vol. 17, no. 7, p. e1003198, 2022.

[19] M. Eslam, A. J. Sanyal, and J. George, "MAFLD: A consensus-driven proposed nomenclature for metabolic associated fatty liver disease," *Gastroenterology*, vol. 158, no. 7, pp. 1999–2014, 2022.

[20] X. Huang, B. Zhao, H. Sun, M. Yang, and X. Dang, "Hepatoprotective effects of ellagic acid against high-fat diet-induced liver injury through mediating Nrf2/ARE signalling pathway," *Journal of Nutritional Biochemistry*, vol. 108, p. 109100, 2023.

[21] C. J. Lee and D. L. Bhatt, "Beyond the physical: Addressing the epidemic of metabolic disease in obesity," *JACC: Basic to Translational Science*, vol. 7, no. 4, pp. 415–420, 2022.

[22] P. T. Mpiana *et al*., "Identification of potential inhibitors of SARS-CoV-2 main protease from *Aloe vera* compounds: A molecular docking study," *Chemical Physics Letters*, vol. 754, p. 137751, 2021.

[23] J. Pérez-Jiménez, V. Neveu, F. Vos, and A. Scalbert, "Identification of the 100 richest dietary sources of polyphenols: An application of the Phenol-Explorer database," *European Journal of Clinical Nutrition*, vol. 64, suppl. 3, pp. S112–S120, 2023.

[24] S. Reagan-Shaw, M. Nihal, and N. Ahmad, "Dose translation from animal to human studies revisited," *FASEB Journal*, vol. 22, no. 3, pp. 659–661, 2008.

[25] M. V. Selma *et al*., "The gut microbiota metabolism of pomegranate or walnut ellagitannins yields two urolithin-metabotypes that correlate with cardiometabolic risk biomarkers," *Molecular Nutrition & Food Research*, vol. 62, no. 1, p. 1800160, 2022.

[26] G. Sohrab *et al*., "Effects of pomegranate juice consumption on oxidative stress in patients with type 2 diabetes," *International Journal of Food Sciences and Nutrition*, vol. 65, no. 6, pp. 720–726, 2022.

[27] M. D. Sumner *et al*., "Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease," *The American Journal of Cardiology*, vol. 96, no. 6, pp. 810–814, 2022.

[28] A. M. Torres-Contreras, V. Nair, L. Cisneros-Zevallos, and D. A. Jacobo-Velázquez, "Plants as biofactories: Stress-induced production of chlorogenic acid isomers in potato tubers," *Industrial Crops and Products*, vol. 86, pp. 324–331, 2022.

[29] M. Viladomiu, R. Hontecillas, P. Lu, and J. Bassaganya-Riera, "Preventive and prophylactic mechanisms of action of pomegranate bioactive constituents," *Evidence-Based Complementary and Alternative Medicine*, vol. 2013, Art. no. 789764, 2023.

[30] D. Wang *et al*., "Vasculoprotective effects of pomegranate (*Punica granatum* L.)," *Frontiers in Pharmacology*, vol. 9, p. 544, 2022.

[31] Y. Zhao, Z. Jiang, and T. Qi, "Ellagic acid improves oxidative stress and mitochondrial function in the liver of high-fat diet-induced obese mice by activating Nrf2 signalling pathway," *Food Chemistry*, vol. 405, p. 134798, 2023.

[32] X. Zou, H. Ku, L. Zhao, F. Cheng, M. Ding, and P. Zhao, "Protective effects of pomegranate peel polyphenols against oxidative stress-induced liver injury in rats," *Food Chemistry*, vol. 194, pp. 171–178, 2022.