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RESEARCH ARTICLE

Physiological effects of aqueous pomegranate peel extract on hematological, liver and lipid profiles in moderately obese men

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Abstract

This study evaluates the therapeutic potential of Pomegranate Peel Extract (PPE) in 104 individuals over a 12-week period. A total of 66 moderately obese participants (groups 4, 5 and 6) received 2000 mg of PPE, while 38 healthy individuals (groups 1, 2 and 3) received 1500 mg, with and without adherence to a healthy diet. Hematological indices [Red Blood Cell (RBC) and White Blood Cell (WBC) count, platelet (PLT), haemoglobin (HGB) levels and hematocrit (HCT) percentages], biochemical markers [glucose, lipid profiles - Total Cholesterol (TC), triglycerides (TG) and Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL)] and liver enzymes - Aspartate aminotransferase (AST), Alanine Aminotransferase (ALT before and after the study period. Additionally, body mass index (BMI), systolic and diastolic blood pressure recorded. Results showed significant increases in HGB, PLT, WBC and HDL levels particularly in moderately obese individuals who consume PPE alongside a healthy diet (group 6). This group also exhibited notable reductions in glucose, TC, TG, LDL, ALT, AST, BMI, systolic and diastolic blood pressure. These results suggest that PPE may serve as a promising natural intervention for managing obesity and improving metabolic health due to its anti-glycemic, hepatoprotective, cardio-protective, weight management and metabolic regulation effects. However, further clinical studies are required to determine optimal dosages and long-term effects across diverse populations.

Keywords

cardiometabolic protection; hematological and biochemical parameters; metabolic health; obesity management; Pomegranate Peel Extract (PPE)

Introduction

Obesity is a long-term complex condition marked by an abnormal accumulation of body fat that can detrimentally impact health (1). It results from a disparity between calorie intake and energy expenditure, typically influenced by interplay combination of genetic, lifestyle and environmental factors (2). This condition is associated with various health complications, including type 2 diabetes, cardiovascular disorders and respiratory issues. These complications ultimately diminish quality of life and heighten the risk of early mortality. (3).

On a societal scale obesity presents substantial public health challenges, placing considerable pressure on healthcare systems worldwide due to the expenses involved in managing obesity related conditions (4). Obesity is a major contributor to the rising rates of non-communicable diseases globally with its prevalence continuing to increase and affecting millions across various age groups and socio-economic groups (5). Additionally, obesity's links to

psychological issues such as depression and diminished self-esteem, underscore its significant impact on mental health as well (6).

Managing obesity frequently requires a multifaceted approach, including lifestyle adjustments, dietary changes, enhanced physical activity and in some instances, medical treatments such as pharmacotherapy or bariatric surgery (7). Behavioural therapy and support networks also play an essential role in helping individuals attain long-term weight loss and enhance overall health (8). Recently, studies on natural compounds-such as those present in pomegranates have indicated promising potential in aiding weight control and alleviating obesity-related complications (9).

Punica granatum L, commonly known as pomegranate, is a nutrient-rich fruit originally from the Mediterranean region but now cultivated worldwide, where it grows as a small tree or shrub (10). Pomegranates are loaded with bioactive compounds, including major phenolics, tannins and flavonoids (11-12). Edible parts like seeds, peels and juice are widely used in products such as beverages and jams, while pomegranate peels can also be repurposed as animal feed (11-15). This versatile plant has multiple useful parts including peels, seeds, oils, roots, trunk, leaves, flowers and rinds, each offering potential applications (16).

Recently, research has focused on extracting bioactive compounds from pomegranate peel, leading to the development of various extraction methods to maximize the benefits of these compounds from both peels and seeds (17). Pomegranate peels, in particular have demonstrated significant pharmaceutical potential offering benefits like anti-proliferative, anti-inflammatory and anti-cancer effects (18-20). Additionally, pomegranates show documented anti-obesity properties (21). Studies on liver health reveal that pomegranate fruit extract (PGF) can reduce liver weight, triglyceride levels and lipid droplet formation while enhancing fatty acid oxidation and alleviating obesity-related fatty liver disease (22).

Multiple bioactive compounds from pomegranate peels were identified by employing various solvents, including water, ethanol, acetone, chloroform and petroleum ether. Among these, the ethanol and aqueous extracts of the peel were found to contain the highest concentrations of active compounds. The aqueous extract included a wide range of components, such as carbohydrates, tannins, saponins, flavonoids, alkaloids, quinones, cardiac glycosides, terpenoids, phenols, coumarins and steroids (23).

The compounds in pomegranate peel and their anti-obesity effects have prompted interest in examining the impact of aqueous PPE on obese individuals. This study aims to assess the physiological effects of aqueous PPE on blood parameters, liver enzymes, lipids level, Body Mass Index (BMI) and blood pressure, both with and without dietary interventions along with regular health monitoring to determine the extent of improvements in these biomarkers in moderate obese men.

Materials and Methods

Study participants

This research was a randomized open-label trial with two unparallel groups conducted from February 2023 to January 2024. The study was registered in the Department of Pharmacology, College of Pharmacy, University of Thi Qar [IQR20230781N13]. The research sample was 104 person (38 healthy people who did not suffer from any health problems and 66 people who suffered from moderate obesity. Individuals with severe cardiac conditions or a history of previous heart attacks were excluded). Tables 1 and 2 show the details of the initial data for the two groups.

The healthy group was divided into 3 groups and the obese group into 31 groups as well, as shown in the Fig. 1.

From observing the figure above, it is noted that there are 6 groups in the current study:

- G1 (healthy individual who received 1500 mg PPE without adherence to a healthy diet) = 15
- G2 (healthy individual who did not received PPE but adherence to a healthy diet) = 13
- G3 (healthy individual who received 1500 mg PPE and adherence to a healthy diet) = 10
- G4 (moderately obese participants who received 2000 mg of PPE without adherence to a healthy diet) = 26
- G5 (moderately obese participants who did not receive PPE but adherence to a healthy diet) = 28
- G6 (moderately obese participants who received 2000 mg of PPE and adherence to a healthy diet) = 12

All participants were informed about the study's purpose, underwent clinical examinations to confirm their health status and provided consent to be included as part of the study sample.

The health status of all participants in the study was monitored at Um Al-Baneen Center in Nasiriyah / Thi- Qar every two weeks throughout the 12-week study period.

Pomegranate Peel Extract preparation

A total of 350 kg of pomegranate peels were collected from the market in Nasiriyah City, thoroughly washed by water to remove impurities and dried in an oven at 40-50 °C to preserve their bioactive compounds. Once dried the peels were ground into a fine powder, which was then used for extraction. To prepare the aqueous extract, 100 g of pomegranate peel powder was mixed with 1 L of distilled water in a conical flask and placed on a shaker at room temperature for 24 hrs to ensure the release of bioactive compounds. The mixture was kept in the dark to prevent degradation of light-sensitive compounds. After extraction the liquid was separated from the solid residue using Whatman No. 2 filter paper, with repeated filtration to ensure purity. To concentrate on the extract, the solvent was evaporated using a water bath at 40-50 °C, maintaining continuous stirring until the extract became viscous and thick. For powder formation, the concentrated extract was further dried by spreading it onto a parchment-lined tray and placing it in an oven at a low temperature (40-50 °C) until all moisture was removed.

Table 1. Parameters level in all persons of study sample before starting study period

Parameters	Reference or normal range	healthy group (n=38)	Study group (n=66)
RBCs (10^6 cells / mL^3)	4.9 -5.4	4.8 ± 0.22	4.99 ± 0.3
PLT (platelet / µl)	150-400	255.91 ± 40.68	289.74 ± 45.97
HGB (g/ 100 mL)	14-16	13.67 ± 0.94	14.42 ± 1.08
HCT (%)	43-45	41.47 ± 1.06	43.86 ± 1.27
WBCs (10^3 cells / mL^3)	5-7	6.28 ± 0.32	7.12 ±0.23
Glucose level (mg/dL)	70-120	122.54 ± 3.2	148.23 ± 10.5
AST(IU/L)	0-38	33.34 ± 3.2	34.81 ±2.87
ALT(IU/L)	0-40	35.9 ± 2.32	44.63 ±2.68
Total cholesterol (TC) (mg/dL)	< 200	180.34 ±11.56	215.08 ±15.75
Triglycerides (TG) (mg/dL)	40-160	101.93 ±9.94	154.33 ±13.34
High Density Lipoprotein (HDL) (mg/dL)	> 40	34.27 ± 4.34	30.93 ±4.92
Low Density Lipoprotein(LDL) (mg/dL)	<160	128.3 ± 7.28	154.9 ±13.32
Systolic blood pressure (mmHg)	120-130	128.5 ± 3	137.5 ± 5
Diastolic blood pressure (mmHg)	70-80	81.4 ± 4	91.2 ± 5

Table 2. Age, height, weight and BMI in all persons of study sample before starting study period

Parameters	healthy group (n=38)	Study group (n=66)
Age (year)	33.31 ± 3.22	35.79 ± 3.56
Height (10^2 cm)	1.85 ± 0.04	1.73 ± 0.05
Weight (kg)	81.59 ± 3.34	116.92 ± 8.53
BMI	23.96 ± 1.73	39.26 ± 3.8

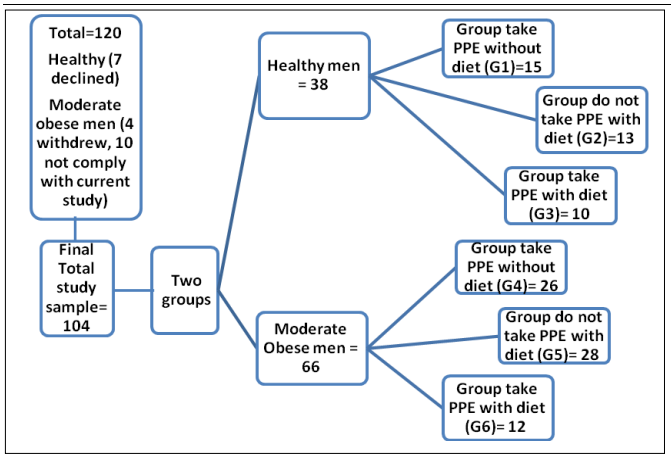

Fig. 1. Research sample division.

The dried material was then ground into a uniform, fine powder, ensuring purity and consistency. The extraction process was conducted at the Medical Drugs Laboratory, College of Pharmacy, University of Thi-Qar by using equipments – oven, water bath, rotary evaporator and analytical balance- while the final capsule formulation (500 mg per capsule) was carried out in the Industrial Laboratory at the same institution by using equipment's - powder blender, hot air oven and capsule filling machine. The biochemical composition of PP was analyzed in the Organic Chemistry Laboratory. The major components of PP powder are as follows: crude protein (3 %), carbohydrates (94 %), crude fiber (8.2%) and moisture (6.1 %).

Dose and study design

In this study, the dosage of the pomegranate peel supplement was determined based on previous research findings (24, 25). The dose conversion formula considers the body weight ratio between humans and the tested animal models to ensure a safe dosage for humans without causing any complications. Additionally, prior research has indicated no adverse effects associated with this dosage. For these reasons, the dose given in this study was 1500 mg per day for healthy individuals and 2000 mg per day for moderately obese individuals, depending on the body weight of the research sample. Each capsule contained 500 mg of PPE. The dosage was administered, three times a day to groups 1, 3, 4 and 6. Healthy participants (group 1 and 3) were given the capsule 3 times a day (1 at breakfast, 1 at lunch, 1 at dinner), while moderately obese participants (group 4 and 6) were also given it 3 times a day (1 at breakfast, 2 at lunch, 1 at dinner). The capsules were administered over a 12-week period.

The diet for the groups (2 - 6) was defined by a high protein intake, moderate carbohydrate levels and low-fat content (55 % protein, 30 % carbohydrates and 15 % fat) (26). Thus each meal (breakfast, lunch and dinner) individually provided 500 kcal.

Data and laboratory analysis

Data was collected at baseline and after 12 weeks to assess changes in health parameters such as weight, height, age, BMI and blood pressure. A 5 mL blood sample was drawn at the beginning and after the end of the study period and used to analyze the complete blood count, glucose level, liver enzymes- Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and lipids profile level.

Statical analysis

All results are expressed as mean ± S.D. The data was analyzed using t-tests and ANOVA in SPSS program. A p-value of less than 0.05 was considered statistically significant.

Results

Table 3 presents the results that reflect various hematological measurements before and after the study period across six different groups. Significant changes in various parameters were observed after the study. Across all the groups, significant increases were observed in RBCs, hemoglobin (HGB) and hematocrit (HCT) after the study period. Regarding platelets (PLT), no significant changes were observed in any group. However, White Blood Cell (WBC) counts exhibited a significant increase in groups 1, 4 and 6. Overall, the results highlighted notable improvements in RBC, HGB, HCT and WBC levels

across specific groups, indicating positive hematological responses to the interventions. Across all groups, significant increases were observed in RBCs, HGB and HCT after the study period, with WBCs showing notable increases particularly in groups 4 and 6 which were taken PPE.

Table 4 presents glucose levels, liver enzymes and lipids profile before and after the study period. After analyzing the results, several variables showed significant changes across the groups. Glucose levels showed a significant reduction in all groups after the study period. AST levels decreased significantly in groups 1 and 6, while ALT levels experienced a notable reduction in groups 1, 3, 5 and 6. Similarly Total Cholesterol (TC) showed significant reductions in groups 1, 3, 4, 5 and 6. Triglycerides (TG) also decreased significantly in groups 1, 4, 5 and 6, while HDL levels increased significantly in groups 2, 3 and 4. Lastly, LDL levels demonstrated significant reductions in groups 1, 2, 4, 5 and 6.

Table 5 shows the average weight, BMI and blood pressure of the six study groups. After the study period, all groups demonstrated significant changes in various parameters. For body weight (W), all groups exhibited a significant reduction compared to baseline measurements. Regarding BMI, similar trends of significant decreases were observed in all groups, indicating effective weight management interventions across the study. In systolic blood pressure, every group showed significant reductions in post-intervention, suggesting improvements in cardiovascular health. A comparable significant decrease was also observed in diastolic blood pressure across all groups, further supporting the positive effects of the intervention on blood pressure regulation. These findings underline the overall effectiveness of the study's intervention in reducing weight, BMI and blood pressure parameters in all study groups.

After the study period, the results in table 6 showed various changes in blood parameters across the groups. For RBCs , all groups showed a consistent range of values with no significant differences between them, indicating that the intervention did not have a major impact on RBC count. Regarding PLT, group 4 and group 5 showed a significant increase compared to other groups, suggesting a potential effect of the intervention on platelet count in these groups. For HGB, group 3 and group 6 displayed a notable increase compared to the baseline, but these differences were not as pronounced across other groups. As for HCT, groups (3, 4 and 6) showed improvements, but group 4 achieving the highest levels, indicating a positive influence of the intervention on blood volume and oxygen-carrying capacity. Finally, WBCs showed a significant increase in group 6 compared to the other groups, suggesting a possible immune system response. In group 4 and group 5 also demonstrated increased WBC counts, although to a lesser extent than group 6.

Table 7 presents the biochemical parameter changes across study groups, revealing varying impacts of the

Table 3. RBCs, PLT, HGB and WBCs account in all persons of study sample before and after study period

Para. / Groups study		RBCs (10^6 cells / ml^3)	PLT (platelet / µl)	HGB (g/ 100 ml)	HCT (%)	WBCs (10^3 cells / ml^3)
G1 (n=15)	B. R.	4.84 ±0.21	255.9 ±40.67	13.66 ±0.93	41.47 ±1.06	6.27 ±0.32
	A. R.	5.5 ±0.37*	260.65 ±7.39	14.86 ±1.4*	44.15 ±4.04	6.83 ±0.74
G2 (n=13)	B. R.	4.83 ±0.21	255.42 ±40.37	13.58 ±0.95	41.54 ±1.05	6.25 ±0.31
	A. R.	5.48 ±0.37*	259.92 ±7.48	14.23 ±1.08	42.93 ±3.04	6.34 ±0.72
G3 (n=10)	B. R.	4.83 ±0.19	258.59 ±39.92	13.61 ±0.96	41.06 ±0.96	6.26 ±0.31
	A. R.	5.46 ±0.48*	262.54 ±7.87	15.38 ±1.43	46.35 ±4.09*	6.85 ±0.71
G4 (n=26)	B. R.	4.96 ±0.29	288.68 ±46.29	14.42 ±1.07	43.73 ±1.15	7.1 ±0.21
	A. R.	5.61 ±0.33*	290.5 ±9.35	15.5 ±1.36	46.47 ±4.11	7.63 ±0.64*
G5 (n=28)	B. R.	5.02 ±0.34	290.65 ±46.91	14.42 ±1.08	43.86 ±1.32	7.09 ±0.24
	A. R.	5.45 ±0.35*	289.89 ±5.58	14.8 ±1.73	44.16 ±5.04	7.36 ±0.73
G6 (n=12)	B. R.	5.01 ±0.25	292.2 ±47.82	14.28 ±1.12	43.92 ±1.44	7.24 ±0.24
	A. R.	5.55 ±0.32*	292.55 ±11.06	15.65 ±1.16	46.88 ±3.52	8.2 ±0.88

Data are expressed as mean ± SD; G= group; n= the number of individuals; B.R. =before research period; A.R.= after research period; para.= parameters; PLT=Platelet ; HGB= Hemoglobin ; HCT= Hematocrit . *Represents significant at *P*<0.05.

Table 4. Liver enzymes and lipids profile levels in all persons of study sample before and after study period

Para. / Groups study		GLU (mg/dL)	AST (IU/L)	ALT (IU/L)	TC (mg/dL)	TG (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
G1 (n=15)	B. R.	122.13 ±2.92	33.53 ±2.58	35.47 ±2.2	181.73 ±11.44	101.53 ±9.22	34.6 ±6.98	128.93 ±6.61
	A. R.	118.22 ±3.37*	31.33 ±2.63*	33.34 ±2.23*	164.33 ±10.68*	86.49 ±6.96*	35.96 ±5.55	114.14 ±8.17*
G2 (n=13)	B. R.	122.08 ±2.98	33.38 ±2.75	35.31 ±2.25	183.92 ±10.64	101.23 ±9.44	33.92 ±7.01	129.23 ±7.07
	A. R.	119.5 ±4.44*	32.05 ±2.59	34.22 ±2.12	170.89 ±8.36	89.18 ±6.87	37.29 ±5.16	115.82 ±9.04*
G3 (n=10)	B. R.	122.4 ±3.06	33.7 ±2.45	35.3 ±2.4	181.5 ±10.39	103.2 ±9.72	32.6 ±7.42	127.6 ±7.31
	A. R.	117.55 ±3.46	30.53 ±1.64	32.61 ±2.78*	160.94 ±8.98*	82.74 ±10.49	35.92 ±7.28*	112.78 ±10.17
G4 (n=26)	B. R.	149.23 ±10.67	34.88 ±2.73	44.62 ±2.29	216.46 ±15.59	153.15 ±13.11	30.96 ±4.181	153.85 ±12.89
	A. R.	135.87 ±8.06*	32.62 ±2.35	42.92 ±2.62	189.2 ±13.76*	132.16 ±10.5*	33.73 ±4.36*	125.61 ±7.63*
G5 (n=28)	B. R.	148.64 ±10.62	34.43 ±2.6	44.68 ±2.32	214.82 ±15.21	154.21 ±13.21	31.46 ±4.25	155.14 ±13.34
	A. R.	138.51 ±7.68*	33.4 ±1.49	40.61 ±2.46*	192.23 ±13.59*	134.85 ±11.4*	33.71 ±5.01	127.4 ±7.32*
G6 (n=12)	B. R.	148.5 ±10.93	34.58 ±2.67	44.5 ±2.39	215.42 ±15.8	151.92 ±13.17	30.25 ±4.12	153.0 ±13.29
	A. R.	130.63 ±7.93*	31.92 ±2.39*	39.36 ±1.61*	185.36 ±8.29*	129.45 ±9.88*	32.51 ±5.94	122.26 ±6.51*

Data are expressed as mean ± SD; G= group; n= the number of individuals; B.R. =before research period; A.R.= after research period; para.=parameters; GLU= Glucose; AST=Aspartate aminotransferase ; ALT= Alanine transaminase ; TC= Total Cholesterol; TG= Triglyceride; HDL= High Density Lipoprotein; LDL= Low Density Lipoprotein .

*Represents significant at *P*<0.05.

Table 5. Weight, BMI, Systolic and Diastolic blood pressure in all persons of study sample before and after study period

Para. / Groups study		W (kg)	BMI (kg/m²)	SBP (mmHg)	DBP (mmHg)
G1 (n=15)	B. R.	81.59 ±3.33	23.96 ±1.73	129.49 ± 3.18	82.06 ±3.11
	A. R.	79.23 ±3.38*	23.26 ±1.67*	126.68 ±2.89*	78.86 ±3.22*
G2 (n=13)	B. R.	80.96 ±3.01	23.51 ±1.35	129.01 ±3.03	81.85 ±3.2
	A. R.	77.86 ±2.8*	22.6 ±1.15*	127.17 ±2.43*	79.16 ±4.05
G3 (n=10)	B. R.	80.65 ±2.93	23.26 ±1.39	129.61 ±3.19	81.64 ±3.49
	A. R.	76.85 ±2.82*	22.16 ±1.25*	125.32 ±2.8*	78.01 ±3.94
G4 (n=26)	B. R.	117.35 ±7.91	39.52 ±3.54	137.68 ±1.77	91.27 ±3.07
	A. R.	109.46 ±7.21*	36.82 ±2.75*	132.17 ±2.68*	87.43 ±2.56*
G5 (n=28)	B. R.	117.84 ±7.8	39.51 ±4.17	137.86 ±1.75	91.17 ±2.98
	A. R.	107.76 ±7.64*	36.14 ±3.97*	134.42 ±3.04*	88.73 ±3.64*
G6 (n=12)	B. R.	115.3 ±9.77	38.72 ±2.2	137.5 ±1.64	91.27 ±3.18
	A. R.	104.8 ±8.34*	35.27 ±2.92*	131.32 ±2.7*	85.29 ±2.82*

Data are expressed as mean ± SD; G= group; n= the number of individuals; B.R. =before research period; A.R.= after research period; para.=parameters; W=weight ; BMI= Body Mass Index ; SBP= Systolic Blood Pressure; DBP=Diastolic Blood Pressure *Represents significant at *P*<0.05.

intervention. Glucose (GLU) levels showed minimal significant changes across most groups, with group 6 exhibiting a slight decrease compared to baseline, though no consistent pattern was observed. AST levels remained largely stable with group 4 and group 5 showing slight increases, though not statistically significant compared to other groups. ALT levels increased significantly in group 4 and 5, suggesting potential alterations in liver function due to the intervention. TC levels rose significantly in groups 4 and 5 compared to baseline, indicating changes in lipid metabolism, while group 1 and 3 displayed smaller increases. TG also showed a marked increase in groups (4, 5 and 6), further supporting alterations in fat metabolism due to the intervention. HDL levels remained stable across all groups, with no significant changes observed, implying that the intervention had a minimal effect on HDL levels. Finally, LDL levels increased significantly in groups 4, 5 and 6. Overall, the results highlighted the most substantial effects on lipid metabolism in group 4 and group 5, with increased cholesterol and triglyceride levels.

Table 8 presents significant changes in various physical parameters across study groups. Weight (W) decreased in groups 1, 2 and 3 but the changes were not statistically significant compared to baseline. However, groups 4, 5 and 6 exhibited a significant decrease in weight compared to their baseline values, with group 6 showing the greatest reduction. BMI significantly decreased in groups 4, 5 and 6 compared to baseline, suggesting a beneficial impact of the intervention on weight management. Systolic blood pressure decreased across all groups, with groups 4, 5 and 6 showing significant decreases compared to baseline values, while groups 1, 2 and 3 showed minimal changes. Diastolic blood pressure significantly decreased in groups 4, 5 and 6 after the intervention, whereas groups 1, 2 and 3 showed only minor changes. These findings suggest that the intervention had a stronger effect on reducing SBP, DBP, BMI and weight in groups 4, 5 and 6 indicating potential cardiovascular and metabolic benefits.

Discussion

The results of the current study, which aimed to examine the effect of 2000 mg aqueous PPE on moderately obese individuals, revealed that pomegranate peel has a beneficial

Table 6. Compare mean of RBCs, PLT, HGB and WBCs account between all groups of study after study period

Para. / Groups study	RBCs (10^6 cells / mL^3)	PLT (platelet / µL)	HGB (g/ 100 mL)	HCT (%)	WBCs (10^3 cells / mL^3)
G1 (n=15)	5.5 ±0.37a	260.65 ±7.39a	14.86 ±1.4a	44.15 ±4.04a	6.83 ±0.74a
G2 (n=13)	5.48 ±0.37a	259.92 ±7.48a	14.23 ±1.08a	42.93 ±3.04a	6.34 ±0.72a
G3 (n=10)	5.46 ±0.48a	262.54 ±7.87a	15.38 ±1.43a	46.35 ±4.09a	6.85 ±0.71a
G4 (n=26)	5.61 ±0.33a	290.5 ±9.35b	15.5 ±1.36ab	46.47 ±4.11a	7.63 ±0.64bc
G5 (n=28)	5.45 ±0.35a	289.89 ±5.58b	14.8 ±1.73a	44.16 ±5.04a	7.36 ±0.73c
G6 (n=12)	5.55 ±0.32a	292.55 ±11.06b	15.65 ±1.16ab	46.88 ±3.52a	8.2 ±0.88bcd

Data are expressed as mean ± SD; G= group; n= the number of individuals; PLT=Platelet ; HGB= Hemoglobin ; HCT= Hematocrit .Difference in letters a, b, c, d, e, f represents significant at P<0.05

Table 7. Compare means of liver enzymes and lipids profile levels between all groups of study after study period

Para. / Groups study	GLU (mg/dL)	AST (IU/L)	ALT (IU/L)	TC (mg/dL)	TG (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
G1 (n=15)	118.22 ±3.37a	31.33 ±2.63ac	33.34 ±2.23a	164.33 ±10.68a	86.49 ±6.96a	35.96 ±5.55a	114.14 ±8.17ad
G2 (n=13)	119.5 ±4.44a	32.05 ±2.59a	34.22 ±2.12a	170.89 ±8.36a	89.18 ±6.87a	37.29 ±5.16a	115.82 ±9.04a
G3 (n=10)	117.55 ±3.46a	30.53 ±1.64ac	32.61 ±2.78a	160.94 ±8.98ac	82.74 ±10.49a	35.92 ±7.28a	112.78 ±10.17ad
G4 n=26)	135.87 ±8.06b	32.62 ±2.35a	42.92 ±2.62b	189.2 ±13.76b	132.16 ±10.5b	33.73 ±4.36b	125.61 ±7.63bc
G5 (n=28)	138.51 ±7.68b	33.4 ±1.49b	40.61 ±2.46b	192.23 ±13.59b	134.85 ±11.4b	33.71 ±5.01b	127.4 ±7.32bc
G6 (n=12)	130.63 ±7.93c	31.92 ±2.39a	39.36 ±1.61b	185.36 ±8.29b	129.45 ±9.88b	32.51 ±5.94a	122.26 ±6.51b

Data are expressed as mean ± SD; G= group; n= the number of individuals; GLU= Glucose; AST=Aspartate aminotransferase ; ALT=Alanine transaminase ; TC= Total Cholesterol; TG= Triglyceride; HDL= High Density Lipoprotein; LDL= Low Density Lipoprotein .Difference in letters a, b, c, d, e, f represents significant at P<0.05

Table 8. Compare means of weight, BMI, systolic and diastolic blood pressure between all groups of study after study period

Para. / Groups study	W (kg)	BMI (kg/m²)	SBP (mmHg)	DBP (mmHg)
G1 (n=15)	79.23 ±3.38a	23.26 ±1.67a	126.68 ±2.89a	78.86 ±3.22a
G2 (n=13)	77.86 ±2.8a	22.6 ±1.15a	127.17 ±2.43a	79.16 ±4.05a
G3 (n=10)	76.85 ±2.82a	22.16 ±1.25a	125.32 ±2.8a	78.01 ±3.94a
G4 (n=26)	109.46 ±7.21b	36.82 ±2.75b	132.17 ±2.68bc	87.43 ±2.56bcd
G5 (n=28)	107.76 ±7.64b	36.14 ±3.97b	134.42 ±3.04b	88.73 ±3.64bc
G6 (n=12)	104.8 ±8.34b	35.27 ±2.92b	131.32 ±2.7bc	85.29 ±2.82bd

Data are expressed as mean ± SD; G= group; n= the number of individuals; W=weight ; BMI= Body Mass Index ; SBP= Systolic Blood Pressure; DBP=Diastolic Blood Pressure; Difference in letters a, b, c, d, e, f represents significant at P<0.05

impact on hematological and biochemical markers associated with glucose, liver enzymes and blood lipid profiles. Additionally, it was found to improve weight, BMI and blood pressure.

The hematological improvements observed in RBCs, HGB and HCT indicate that PPE positively influences blood health. These changes may stem from the antioxidant properties of PPE, which reduce systemic inflammation and protect blood cells from oxidative damage (27). Furthermore, the increase in PLT and WBCs suggests an overall enhancement in immune function, possibly driven by the anti -inflammatory effects of PPE (28, 29).

The results showed a decrease in blood sugar levels in moderate obese individuals, especially those who followed a diet and consumed PPE, compared to healthy individuals. This finding differs from the findings of previous study (30). Differences in fasting blood glucose results between this study and others could arise from variations in participants' health conditions, such as diabetes, long-term metformin therapy and the absence of dietary guidelines in other studies. In contrast, our study included specific dietary recommendations and calorie restriction, which might have influenced the outcomes. Animal studies present mixed findings on the effect of pomegranate peel on serum glucose levels. While some studies have demonstrated significant reductions in glucose levels in diabetic rats (31-33), others, like a study on rats with induced diabetes, found no significant changes in weight or glucose levels (34). These discrepancies could be attributed to differences in intervention doses, sample characteristics and study designs.

Hypoglycemic effect of PPE, as observed in the current study's results, may be attributed to the presence of polyphenols in pomegranate peel, such as ellagic acid and punicalagin. Notably, these compounds are known to enhance carbohydrate metabolism and insulin sensitivity by inhibiting alpha-glucosidase and alpha-amylase enzymes (35, 36).

The observed decrease in liver enzyme levels suggests a hepatoprotective effect of PPE in moderately obese individuals. This result is supported by multiple studies (37, 38). The reductions in ALT and AST suggest that PPE may have hepatoprotective effects. These findings are supported by previous study (38), which revealed that PPE reduces liver inflammation and oxidative stress in animal models of metabolic syndrome. The hepatoprotective properties of PPE can be linked to its ability to neutralize reactive oxygen species and inhibit lipid peroxidation in liver tissues (37-40).

The lipid profile improvements in this study, marked by reductions in TC, TG and LDL, along with modest increases in HDL. A study (41) demonstrated that PPE reduce LDL oxidation and improve lipid metabolism in hyperlipidemic patients. Similarly pomegranate polyphenols modulate lipid profiles by reducing oxidative stress and enhancing cholesterol clearance mechanisms (42). Animal studies provide additional insights into the lipid-lowering effects of pomegranate peel. For instance, PPE has been shown to inhibit key enzymes involved in lipid metabolism, such as pancreatic lipase, HMG-CoA reductase and ACAT, resulting in decreased cholesterol and triglyceride levels (43). Furthermore, polyphenolic compounds like ellagic acid, punicalagin and gallic acid in pomegranate peel have been demonstrated to activate PPAR receptors, enhancing cholesterol metabolism and reducing cardiovascular risk factors (44). Catechins in the peel also inhibit intestinal fat absorption and lipid biosynthesis (45). These mechanisms likely underlie the significant lipid profile improvements observed in this study.

The observed reductions in body weight and BMI across the groups highlight the potential of PPE as a natural intervention for weight management. This effect may be attributed to the polyphenolic compounds in pomegranate peel, which have been reported to enhance fat metabolism and suppress adipogenesis (46). Furthermore, pomegranate polyphenols may regulate appetite and energy expenditure through their interaction with metabolic pathways (47). These findings were agreed with previous works who reported a significant decrease in waist circumference among participants receiving pomegranate peel supplementation (31). But in study (48) found no significant changes in BMI among osteoarthritis patients after consuming PPE. Animal studies further support this study findings regarding weight management. For instance, a study involving rats on a high-fat diet revealed that those consuming cake with 15 % pomegranate peel powder experienced less weight gain compared to controls (49). This consistent with evidence suggesting that pomegranate peel exhibits stronger appetite-suppressing effects under high-fat diet conditions. Similarly, a study demonstrated a significant reduction in leptin levels in overweight rats supplemented with pomegranate peel powder (50). In this study, there was a somewhat positive effect of taking pomegranate peel supplements on the appetite of individuals, which was observed in the first and fourth groups, as these two groups did not follow the diet specified in the study, but there was an improvement in the weights of individuals and the body mass index. This may be attributed to animal studies that linked the appetite-suppressing effects of pomegranate peel with its effect on leptin regulation.

The improvements in systolic and diastolic blood pressure observed in this study agree with previous findings

supporting the cardioprotective properties of PPE. Notably, while a study observed a significant trend just in systolic blood pressure reduction (48), significant decreases in both systolic and diastolic pressures (31). These beneficial effects are primarily attributed to PPE's high antioxidant content, which enhances nitric oxide bioavailability and promotes vascular relaxation (51). Additionally, the anti-inflammatory properties of pomegranate extracts have been shown to reduce arterial stiffness and improve endothelial function, both of which are essential for maintaining healthy blood pressure levels (52) and were not measured in the current study. The reason of antihypertensive effects of pomegranate peel can be largely attributed to its polyphenols, which inhibit angiotensin-converting enzyme activity and enhance vasodilation through nitric oxide pathways (52, 53).

Conclusion

Overall, these findings in the current study suggest that PPE represents a promising natural approach for managing obesity and its related complications by supporting hematological health, improving lipid and liver function, facilitating weight loss and promoting cardiovascular health. However, the study has some limitations, including the small sample size and the lack of long-term follow-up to assess the sustainability of the effects. Further research is needed to confirm these findings. Future studies should consider employing randomized controlled trials with larger sample sizes and extended follow-up periods to validate the efficacy of PPE in managing obesity and its associated risks.

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Authors' contributions

ZAQ was responsible for the collection, preparation and packaging of the aqueous extract of pomegranate peel. AHA conducted the chemical analysis of the pomegranate peel extract powder. ALM, WSA and NSF interviewed the study volunteers, distributed the research information forms, obtained informed consent and assessed their health status at Umm Al-Banin Health Center. NSF and ALM performed the blood sample analysis and biochemical assessments. The study design, statistical analysis and manuscript organization were carried out by WSA. All researchers reviewed and approved the final version of the manuscript.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflict of interests to declare

Ethical issues: The study was registered at college of pharmacy/ University of Thi-qar [IQR20230781N13] and informed consent was obtained from all participants.

References

1. World Health Organization. "Obesity and Overweight." WHO. 2024. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
2. Gadde KM, Martin CK, Berthoud HR, Heymsfield SB. Obesity: Pathophysiology and management. Journal of the American College of Cardiology. 2018;71(1):69–84. https://doi.org/10.1016/j.jacc.2017.11.011
3. Pi-Sunyer FX. Health implications of obesity. The American Journal of Clinical Nutrition. 1991;53(6 Suppl):1595S–1603S. https://doi.org/10.1093/ajcn/53.6.1595S
4. Wang YC, McPherson K, Marsh T, Gortmaker SL, Brown M. Health and economic burden of the projected obesity trends in the USA and the UK. Lancet (London, England). 2011;378(9793):815–25. https://doi.org/10.1016/S0140-6736(11)60814-3
5. Ng M, Fleming T, Robinson M, Thomson , Graetz N, Margono C et al. Global, regional and national prevalence of overweight and obesity in children and adults during 1980-2013: A systematic analysis for the Global burden of disease study 2013. Lancet (London, England). 2014;384(9945):766–81. https://doi.org/10.1016/S0140-6736(14)60460-8
6. de Wit L, Luppino F, van Straten A, Penninx B, Zitman F, Cuijpers, P. Depression and obesity: A meta-analysis of community-based studies. Psychiatry Research. 2010;178(2):230-35. https://doi.org/10.1016/j.psychres.2009.04.015
7. Bray GA. A Guide to obesity and the metabolic syndrome: Origins and Treatment (1st ed.). CRC Press. 2011. https://doi.org/10.1201/b10790
8. Wadden TA, Webb VL, Moran CH, Bailer BA. Lifestyle modification for obesity: New developments in diet, physical activity and behavior therapy. Circulation. 2012;125(9):1157–70. https://doi.org/10.1161/CIRCULATIONAHA.111.039453
9. Bahari H, Pourreza S, Goudarzi K, Mirmohammadali SN, Asbaghi, Kolbadi K, et al. The effects of pomegranate consumption on obesity indices in adults: A systematic review and meta-analysis. Food Science and Nutrition. 2024;12:641–60. https://doi.org/10.1002/fsn3.3739
10. Puneeth HR, Chandra SSP. A review on potential therapeutic properties of Pomegranate (*Punica granatum* L.). Plant Science Today. 2020;7(1):9–16. https://doi.org/10.14719/pst.2020.7.1.619
11. Boussaa F, Zaouay F, Burlo-Carbonell F, Noguera-Artiaga L, Carbonell-Barrachina A, Melgarejo P, et al. Growing location affects physical properties, bioactive compounds and antioxidant activity of pomegranate fruit (*Punica granatum* L. var. Gabsi). International Journal of Fruit Science. 2020;20(sup2):508–23. https://doi.org/10.1080/15538362.2020.1741058
12. Ko K, Dadmohammadi Y, Abbaspourrad A. Nutritional and bioactive components of pomegranate waste used in food and cosmetic applications: A review. Foods. 2021;10(3):657. https://doi.org/10.3390/foods10030657
13. Mphahlele RR, Fawole OA, Makunga NP, et al. Effect of drying on the bioactive compounds, antioxidant, antibacterial antityrosinase activities of pomegranate peel. BMC Complement Altern Med. 2016;16:143. https://doi.org/10.1186/s12906-016-1132-y
14. Malviya S, Arvind Jha A, Hettiarachchy N. Antioxidant and antibacterial potential of pomegranate peel extracts. Journal of Food Science and Technology. 2014;51(12):4132–37. https://doi.org/10.1007/s13197-013-0956-4
15. Rajha HN, Abi-Khattar AM, El Kantar S, Boussetta N, Lebovka N,

Maroun R G, et al. Comparison of aqueous extraction efficiency and biological activities of polyphenols from pomegranate peels assisted by infrared, ultrasound, pulsed electric fields and high-voltage electrical discharges. Innovative Food Science & Emerging Technologies. 2019;58:102212. https://doi.org/10.1016/j.ifset.2019.102212

16. Atabik A, Muqtada MR, Suhadi Irnawati, Rohman A. Pomegranate (*Punica granatum* L.) fruits in the quranic hermeneutics and scientific perspectives. Food Research. 2022;6(5):1–13. https://doi.org/10.26656/fr.2017.6(5).504
17. Jurenka JS. Therapeutic applications of pomegranate (*Punica granatum* L.): A review. Alternative medicine review. A Journal of Clinical Therapeutic. 2008;13(2):128–44.
18. Wong TL, Strandberg KR, Croley CR, Fraser SE, Nagulapalli Venkata KC, et al. Pomegranate bioactive constituents target multiple oncogenic and oncosuppressive signaling for cancer prevention and intervention. Seminars in Cancer Biology. 2021;73:265–93. https://doi.org/10.1016/j.semcancer.2021.01.006
19. Esther Lydia D, Khusro A, Immanuel P, Esmail GA, Al-Dhabi NA, Arasu MV. Photo-activated synthesis and characterization of gold nanoparticles from *Punica granatum* L. seed oil: An assessment on antioxidant and anticancer properties for functional yoghurt nutraceuticals. Journal of Photochemistry and Photobiology. Biology. 2020;206:111868. Advance online publication. https://doi.org/10.1016/j.jphotobiol.2020.111868
20. Rafiqul Islam ATM, Ferdousi J, Shahinozzaman M. Previously published ethno-pharmacological reports reveal the potentiality of plants and plant-derived products used as traditional home remedies by Bangladeshi COVID-19 patients to combat SARS-CoV-2. Saudi Journal of Biological Sciences. 2021;28(11):6653–73. https://doi.org/10.1016/j.sjbs.2021.07.036
21. Hontecillas R, O'Shea M, Einerhand A, Diguardo M, Bassaganya-Riera J. Activation of PPAR gamma and alpha by punicic acid ameliorates glucose tolerance and suppresses obesity-related inflammation. Journal of the American College of Nutrition, 2009;28 (2):184–95. https://doi.org/10.1080/07315724.2009.10719770
22. Xu KZ, Zhu C, Kim MS, Yamahara J, Li Y. Pomegranate flower ameliorates fatty liver in an animal model of type 2 diabetes and obesity. Journal of Ethnopharmacology. 2009;123(2):280-87. https://doi.org/10.1016/j.jep.2009.03.035
23. Mayasankaravalli C, Deepika K, Esther Lydia D, Agada R, Thagriki D, Govindasamy C et.al. Profiling the phyto-constituents of *Punica granatum* fruits peel extract and accessing its *in-vitro* antioxidant, anti-diabetic, anti-obesity and angiotensin-converting enzyme inhibitory properties. Saudi Journal of biological sciences. 2020;27 (12):3228–34. https://doi.org/10.1016/j.sjbs.2020.09.046
24. Nair AB, Jacob S. A simple practice guide for dose conversion between animals and human. J Basic Clin Pharm. 2016;7(2):27-31. https://doi.org/10.4103/0976-0105.177703
25. Fatma Z, Luis MJ, Antonio EL, Laura SR, Ferraez HT, et.al. An aqueous pomegranate peel extract (*Punica granatum*) protect against Elastase-induced pulmonary emphysema in Sprague Dawley rats model. Braz J Pharm Sci. 2022:57. https://doi.org/10.1590/s2175-97902020000418972
26. Abdulredha WS, Shuhaib HO. Flaxseeds using effect as weight loose with or without diet and exercise on liver enzymes and lipids profile in moderate obese men**.** Biochemical and Cellular Archives. 2020; (20):3433. https://connectjournals.com/03896.2020.20.3433
27. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clinical Chemistry. 1972;18(6):499–502.
28. Reddy MK, Gupta SK, Jacob MR, Khan SI, Ferreira D. Antioxidant, antimalarial and antimicrobial activities of tannin-rich fractions, ellagitannins and phenolic acids from *Punica granatum* L. Planta Medica. 2007;73(5):461–67. https://doi.org/10.1055/s-2007-967167
29. Hagag OYA, Younis FE, Al-Eisa RA, Fayad E, El-Shenawy NS. Effect of feeding pomegranate (*Punica granatum*) peel and garlic (*Allium sativum*) on antioxidant status and reproductive efficiency of female rabbits. Veterinary Sciences. 2023;10(3):179. https://doi.org/10.3390/vetsci10030179
30. Imbabi TA, Ahmed-Farid O, Selim DA, Sabeq II. Antioxidant and anti-apoptotic potential of whole-pomegranate extract promoted growth performance, physiological homeostasis and meat quality of V-line rabbits under hot summer conditions. Anim Feed Sci Technol. 2021;276:114911. https://doi.org/10.1016/J.ANIFEEDSCI.2021.114911
31. Grabez M, Skrbic R, Stojiljkovic M, Rudic Grujic V, Paunovic M, Arsic A, et al. Beneficial effects of pomegranate peel extract on plasma lipid profile, fatty acids levels and blood pressure in patients with diabetes mellitus type-2: a randomized, double-blind, placebo-controlled study. J Funct Foods. 2019;64:103692. https://doi.org/10.1016/j.tifs.2021.06.014
32. Rahnama Z, Poozesh Jadidi R, Nasir Zadeh MR. Effect of two month aerobic training and pomegranate peel extract (PPE) supplementation on Insulin resistance index levels in obese rats. Journal of Applied Health Studies in Sport Physiology. 2017;4 (1):1-10. https://doi.org/10.22049/jassp.2019.26522.1197
33. Faddladdeen KAJ. Ameliorating effect of pomegranate peel extract supplement against type 1 diabetes-induced hepatic changes in the rat: Biochemical, morphological and ultrastructural microscopicstudies. Foliamorphologica. 2021;80 (1):149–57. https://doi.org/10.5603/FM.a2020.0034
34. Fatimah A, Alqahtani1 F. The role of olive leaves and pomegranate peel extracts on diabetes mellitus induced in male rats. The Egyptian Journal of Hospital Medicine. 2018;71(5):3079-85.
35. Raheema RH. Effect of pomegranate peel extract on some biochemical and histopathological parameters in experimental induced mice with *Staphylococcus aureus*. J Anim Health Prod. 2016;4(2):42-9.
36. Faddladdeen KA, Ojaimi AA. Protective effect of pomegranate (*Punica granatum*) extract against diabetic changes in adult male rat liver: Histological study. Journal of microscopy and ultrastructure. 2019;7(4):165–70. https://doi.org/10.4103/JMAU.JMAU_6_19
37. Arun K, Jayamurthy P, Anusha C, Mahesh S, Nisha P. Studies on activity guided fractionation of pomegranate peel extracts and its effect on anti-diabetic and cardiovascular protection properties. J Food Process Preserv. 2017;41(1):e13108. http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1745-4549
38. Barghchi H, Milkarizi N, Belyani S, Norouzian Ostad A, Askari VR, Rajabzadeh F, et al. Pomegranate (*Punica granatum* L.) peel extract ameliorates metabolic syndrome risk factors in patients with non-alcoholic fatty liver disease: a randomized double-blind clinical trial. Nutrition Journal. 2023;22(1):40. https://doi.org/10.1186/s12937-023-00869-2
39. Al-Shaaibi SN, Waly MI, Al-Subhi L, Tageldin MH, Al-Balushi NM, Rahman MS. Ameliorative effects of pomegranate peel extract against dietary-induced nonalcoholic fatty liver in rats. Preventive Nutrition and Food Science. 2016;21(1):14–23. https://doi.org/10.3746/pnf.2016.21.1.14
40. Al-Sallami AS, Al-bideri AW, Alsaaedi SH. Hepatoprotective effect of pomegranate peel (*Punica granatum* L.) against thioacetamide-induced cirrhosis. The Egyptian Journal of Experimental Biology. 2018;14:41-7.
41. Abd El-Aziz YM, Hendam BM, Al-Salmi FA, Qahl SH, Althubaiti EH, Elsaid FG, et al. Ameliorative effect of Pomegranate Peel Extract (PPE) on hepatotoxicity prompted by Iron oxide nanoparticles (Fe_2O_3-NPs) in mice. Nanomaterials (Basel, Switzerland). 2022;12 (17):3074. https://doi.org/10.3390/nano12173074

42. Kaplan M, Hayek T, Raz A, Coleman R, Dornfeld L, Vaya J, et al. Pomegranate juice supplementation to atherosclerotic mice reduces macrophage lipid peroxidation, cellular cholesterol accumulation and development of atherosclerosis. The Journal of Nutrition. 2001;131(8):2082–89. https://doi.org/10.1093/jn/131.8.2082

43. Al-Muammar MN, Khan F. Obesity: the preventive role of the pomegranate (*Punica granatum*). Nutrition (Burbank, Los Angeles County, Calif.). 2012;28(6):595–604. https://doi.org/10.1016/j.nut.2011.11.013

44. Altunkaya A. Potential antioxidant activity of pomegranate peel and seed extracts and synergism with added phenolic antioxidants in a liposome system: a preliminary study. Ir J Agricultural food Res. 2014:121–31. http://hdl.handle.net/11019/757

45. Lv O, Wang L, Li J, Ma Q, Zhao W. Effects of pomegranate peel polyphenols on lipid accumulation and cholesterol metabolic transformation in L-02 human hepatic cells via the PPARγ-ABCA1/CYP7A1 pathway. Food and function. 2016;7(12):4976–83. https://doi.org/10.1039/c6fo01261b

46. Sadeghipour A, Eidi M, Ilchizadeh Kavgani A, Ghahramani R, Shahabzadeh S, Anissian A. Lipid lowering effect of *Punica granatum* L. peel in high lipid diet fed male rats. Evidence-based complementary and alternative medicine: eCAM. 2014:432650. https://doi.org/10.1155/2014/432650

47. Banihani S, Swedan S, Alguraan Z. Pomegranate and type 2 diabetes. Nutrition research (New York, NY). 2013;33(5):341–48. https://doi.org/10.1016/j.nutres.2013.03.003

48. Stockton A, Al-Dujaili, EAS. Effect of pomegranate extract consumption on satiety parameters in healthy volunteers: A preliminary randomized study. Foods (Basel, Switzerland). 2022;11(17):2639. https://doi.org/10.3390/foods11172639

49. Rafraf M, Haghighian MK, Molani-Gol R, Hemmati S, Asghari Jafarabadi M. Effects of pomegranate (*Punica granatum* L.) peel extract supplementation on markers of inflammation and serum matrix metalloproteinase 1 in women with knee osteoarthritis: A randomized double-blind placebo-controlled study. Nutrition and metabolic insights. 2024;17:11786388241243266. https://doi.org/10.1177/11786388241243266

50. Lamiaa ML, Eman SA. The impact of pomegranate peel-fortified cupcakes on weight loss. Int J Pharm Res Allied Sci. 2019;8(3).

51. Aviram M, Dornfeld L, Rosenblat M, Volkova N, Kaplan M, Coleman R, et al. Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL and platelet aggregation: Studies in humans and in atherosclerotic apolipoprotein E-deficient mice. The American Journal of Clinical Nutrition. 2000;71(5):1062–76. https://doi.org/10.1093/ajcn/71.5.1062

52. Asgary S, Sahebkar A, Afshani MR, Keshvari M, Haghjooyjavanmard S, Rafieian-Kopaei M. Clinical evaluation of blood pressure lowering, endothelial function improving, hypolipidemic and anti-inflammatory effects of pomegranate juice in hypertensive subjects. Phytotherapy research: PTR. 2014;28(2):193–99. https://doi.org/10.1002/ptr.4977

53. Dos Santos RL, Dellacqua LO, Delgado NT, Rouver WN, Podratz PL, Lima C, et al. Pomegranate peel extract attenuates oxidative stress by decreasing coronary angiotensin-converting enzyme (ACE) activity in hypertensive female rats. Journal of Toxicology and Environmental Health. Part A. 2016;79(21):998–1007. https://doi.org/10.1080/15287394.2016.1213690

54. Ali MY, Jannat S, Chang MS. Discovery of potent angiotensin-converting enzyme inhibitors in pomegranate as a treatment for hypertension. Journal of Agricultural and Food Chemistry. 2023;71(30):11476–90. https://doi.org/10.1021/acs.jafc.3c02115