



Influence of pumpkin peels and olive leaves extract on liver enzymes and lipid profile in serum of male mice

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Abstract

Pumpkin fruit is a highly popularly produced vegetable that is extremely rich in essential vitamins and antioxidants. It is a member of the Cucurbits family, one of the most significant plant groups that produces delicious products as well as valuable fibers with many different hypoglycemic polysaccharides present in fruit pulps. A total of 30 albino mice were used for two months. The animals were divided into three different groups: the control group (G1), the second group (G2), treated with pumpkin oral administration, and the G3 group, which included the animals that were orally administered olive leaf extract. The present study was used to find the biological effects of pumpkin and olive leaf on liver enzyme activity levels and lipid profiles. Results showed a statistically considerable difference in the concentration of liver enzymes and lipid profiles in the serum of animals; this indicates that pumpkin and olive leaf extracts help to lower atherosclerosis risk, and there was a reduction in serum cholesterol level, a marker of inflammation, due to the presence of anthocyanin. It has been suggested that pumpkin and olive leaves extractions may be used as a nutritional supplement or as a prophylactic measure against chemotherapy due to its diverse spectrum of biochemical and pharmacological properties.

Keywords Pumpkin · Olive leaves · Cholesterol · Liver enzyme · Cucurbita

Introduction

Cucurbits (*C. pepo*) are a significant plant family that provides a wide variety of hypoglycemic polysaccharides found in fruit pulps, as well as food items and valuable fibers. Biologically active components of pumpkin (genus Cucurbita; family Cucurbitaceae) are squash-like fruits like polysaccharides, proteins, para-aminobenzoic acid, carotenoids, peptides, fixed oils, sterols, proteins, vitamins, and gamma-aminobutyric acid (Applequist et al. 2006; Caili et al. 2006). Therefore, it has been considered beneficial for health. The fruit pulps of pumpkin are used as an insulin secretor and sensitizer because they contain D-chiro-inositol. There are other applications that are identified in pumpkin, such as

blood-coagulatory effects, anti-inflammatory effects, inhibition of kidney stone formation, and hypotensive effects. Pumpkins are an excellent source of several nutrients, such as protein, healthy fats, and minerals (Provesi et al. 2011). Significant amounts of dietary zinc, iron, copper, and magnesium are supplied by pumpkins. Based on ethnopharmacological investigations, several countries use *C. pepo* to cure a wide range of illnesses, including urinary problems, ulcers, diabetes, and antivirals (Choi et al. 2001). Additionally, it has been demonstrated that several plant parts, such as pumpkin fruit and seeds, have important physiological advantages, such as the capacity to heal wounds, inhibit tumor growth, have hypoglycemic effects, and control the immune system (Marianna et al. 2009; Glew et al. 2006). The seeds can be used to treat a number of conditions, such as high blood pressure, elevated erysipelas skin enzyme, urinary tract problems, kidney stone prevention, prostate illness, and vermifuge. *C. pepo* contains significant levels of vitamin A, C, niacin, folic acid, iron, and vitamin E, especially gamma-tocopherol. They have been demonstrated to increase vitality in general and energy in particular, in addition to omega-6 and omega-3 fatty acids (Fissore

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et al. 2009). Pumpkin seed has strong inhibitory activity against gram-positive bacteria and significant nutritional content, including proteins, minerals, and unsaturated fatty acids, primarily linoleic and oleic acids. High protection against oxidative stress was linked to substances found in *Curcubita maxima* seed oil (Leichtweis et al. 2022). Pumpkin seeds have long been used to cure bladder infections, worms, and parasites. Pumpkin seeds are a good source of zinc, which increases serotonin production and encourages a good night's sleep (Stevenson et al. 2007; Yadav et al. 2010). Pumpkin peels include high levels of protein, fiber, and minerals, including calcium and magnesium, as well as bioactive elements. However, it has a lower nutritional content than pumpkin pulp in terms of carbohydrates, fats, and potassium. In addition to carotenoids that can improve health, and they are abundant in pumpkin skin (Gavril et al. 2024).

Many studies on herbal medicines and their various constituents, which are used to treat a wide range of diseases, have been reported. Herbal medicines have progressively fewer toxic side effects than manufactured medications (Huang and Sumpio 2008).

Improved lipid profiles, blood glucose, insulin resistance, lower blood pressure, inflammatory biomarkers, and overall mortality are just a few of the numerous positive benefits of the Mediterranean diet that have been linked to its effectiveness in the treatment and prevention of cardiovascular disorders (Martinez-Gonzalez et al. 2009). Variable levels of triacylglycerols are present in olive oil, along with trace amounts of phenols, free fatty acids, aroma compounds, sterols, pigments, tocopherols, glycerol, and additional components that are not yet identified. Olive leaves, which contain large amounts of polyphenols with relatively little oleic acid, provide a unique opportunity to examine the impact of polyphenols discovered in olive oil on metabolic profile, cardiovascular, and hepatic structure and function. Oleic acid, the main fatty acid in olive oil, together with the oleuropein and polyphenols hydroxytyrosol, have been linked to the cardioprotective properties of this oil, which is one of the keystones of the Mediterranean diet (Gorzynik-Debicka et al. 2018).

The olive tree (*Olea europaea*) belongs to the family Oleaceae. Olive leaf extract contains some chemical compounds, such as polyphenols with their antioxidant activity and oleuropein with its hydrolysis product, hydroxytyrosol. The primary ingredient in olive leaves is oleuropein, a monoterpene from the iridoide family that is assumed to provide medicinal benefits. Additionally, olivin, luteolin, apigenine, rutin, and other flavonoids, as well as triterpenes such as oleanolic and maslinic acid, are present in olive leaves (Meirinhos et al. 2005; Pereira et al. 2007).

Olive leaf extract has been used in treated of wounds, fever, diabetes, gout, atherosclerosis, and hypertension (Hamad 2015). Furthermore, olive leaf used as anti-atherosclerotic, cholesterol-lowering, antimicrobial, anti-tumor,

and anti-viral activities. Olive leaf extract has the ability to lessen the effects of a high-carbohydrate, high-fat diet on rats' livers, hearts, and metabolism. Due to their high phenolic content, olive oil, olive fruit, and olive leaves have been acknowledged for their pharmacological qualities as vital parts of both medicine and a balanced diet (Abdel-Hamid et al. 2011; Waterman and Lockwood 2007).

The current study aimed to determine how the extraction of pumpkin and olive leaves affected the activity of liver enzymes, including alanine aminotransferase (GPT), alkaline phosphatase (ALP), aspartate aminotransferase (GOT), and gamma-glutamyltransferase (gGT), in addition to the experimental animals' blood lipid profile values.

Materials and methods

Preparation of pumpkin and olive leaves

Pumpkin peels have been collected from pumpkins fruit in Baghdad, washed, dried by air for 2 days, then crushed into powder and weighed 250 gm of crushed powder with 250 gm of dried crushed olive leaves. The extraction procedure for the pumpkin and olive leaves was the same, 500 mL of 70% ethanol was added to each of them in a soxhlet extraction apparatus, which was then placed at 50 °C for 60 min. The mixture was then allowed to cool while being continuously stirred slowly, and a thick solution was prepared by filtering the mixture in a rotary evaporator set at 60 °C. The obtained solution was removed and kept in a refrigerator at 4 °C after being dried in an incubator for two days at 37 °C until it became pulverized. The resultant deposit was dissolved in distilled water to generate the 20 mg/mL doses.

Blood Sample Collection and Laboratory Animals

Male albino mice have been obtained from the University of Technology's Animal Production Laboratory Unit at the Biotechnology branch. A 12 h light/dark cycle was maintained for all mice, along with stable temperature ranges of 24 to 26 °C and 55 to 60% humidity. In addition to having unlimited access to food and tap water, they were kept in wood-dust-filled polypropylene cages. The guide for the Care and usage of Laboratory Animals in the Biotechnology Division' was followed in the acquisition, upkeep, and usage of the animals, and the University of Technology's Animal Ethical Committee gave its approval in accordance with the guidelines of Animal Research: Reporting of In Vivo Experiments (ARRIVE) in 2020.

A total of 30 healthy albino mice weighing between 35 and 50 g were acquired from the University of Technology, Baghdad's Animal House of the Biotechnology Division. The animals were divided into three groups of 10 each for



the experimental groups. The control groups, or group G1, did not receive the extracts. The rats in groups G2 and G3 received oral doses of pumpkin and olive leaf extract (20 mg/mL/day), respectively. Following two months of extract administration, all the animals were killed at the end of the trial using the intravenous anesthesia method, and blood samples were obtained via puncture for hepatic enzyme activity and serum lipid profile biochemical analysis.

Blood samples collection

After receiving the extracts for two months, blood samples were collected. The serum was subsequently separated by centrifuge at 3500 rpm for fifteen minutes and kept in a plain tube before being used to test biological variables.

Biochemical assay

Serum cholesterol (Cat. No.: E-BC-K205-S, Elabscience Bionovation Inc., USA), Very Low-Density Lipoprotein (VLDL) (Cat. No.: KA1671, Novus Biologicals Inc., USA), High-Density Lipoprotein (HDL) (Cat. No.: E-BC-K221, Elabscience Bionovation Inc., USA), Low-Density Lipoprotein (LDL) (Cat. No.: E-BC-K205-S, Elabscience Bionovation Inc., USA), triglyceride (TC) (Cat. No.: E-BC-K109-S, Elabscience Bionovation Inc., USA), GOT (Cat. No.: E-BC-K236-S, Elabscience Bionovation Inc., USA), GGT (Cat. No.: E-BC-K126-M, Elabscience Bionovation Inc., USA), GPT (Cat. No.: E-BC-K235-S, Elabscience Bionovation Inc., USA) and ALP (Cat. No.: E-BC-K009-M, Elabscience Bionovation Inc., USA), levels were measured using colorimetric method.

Statistical analysis

The data has been demonstrated as mean $\pm$ SD. In order to obtain the desired data, each individual value was tabulated in a Graph Pad Prism version 5.01 (Graph Pad Software, Inc., La Jolla, CA, USA) statistical program sheet.

Results

Pumpkin is a commonly grown vegetable that is very rich in vitamins and important antioxidants. Herbs have reportedly been used as food and medicine for hyperlipidemia, which may help lower the risk of cardiovascular disease and alterations in metabolism in the liver (Marianna et al. 2009; Glew et al. 2006). The present investigation was done to study some biochemical effects of olive oil and pumpkin extracts in the serum of albino mice. Results are demonstrated in Tables 1, 2, 3 and 4.

Table 1 illustrates the effect of olive leaf extract (20 mg/mL/day) on serum liver enzyme activities in white albino male mice. The group that received olive leaf treatment showed improvements in the activity of the liver enzymes GGT, ALP, GOT, and GPT. The results show a significant decrease in the serum enzyme activities of GGT, ALP, GOT, and GPT ($p \leq 0.05$, $p \leq 0.001$, $p \leq 0.001$, $p \leq 0.05$), respectively.

The results in Table 2 represent the effect of olive leaves at 20 mg/mL/day on the concentration of serum lipid profiles in white albino mice. It shows a statistically significant decrease in cholesterol, triglycerides, VLDL-cholesterol, and LDL-cholesterol ($p \leq 0.001$). However, a significant rise in HDL-cholesterol levels ($p < 0.001$) was seen in treated animals when compared to untreated ones.

Table 3 illustrates the effect of pumpkin peel extract (20 mg/mL/day) on serum values of liver enzyme activities GGT, ALP, GOT, and GPT in animal mice. The results show that serum enzyme activities (GGT, ALP, and GOT) were significantly lower in pumpkin extract-treated compared to untreated mice ($p < 0.001$), and the difference in GPT activity was $p \leq 0.02$.

Table 4 results show how pumpkin peel extract affects the concentration of the lipid profile. LDL-cholesterol, VLDL-cholesterol, cholesterol, and triglycerides all showed statistically significant decreases ($p < 0.001$), whereas HDL-cholesterol levels significantly increased ($p \leq 0.001$) in the treated animals compared to the untreated group.

Table 5 results show how olive leaves and pumpkin peels extract affects the LDL/HDL ratio which its show a statistically significant decrease ($p \leq 0.001$) in the treated animals compared to the control group.

Discussion

The results showed that there is a mild decrease in the level of liver enzymes after treatment of animals with pumpkin peel extract, this is attributed to the hepatoprotective effect of the extract; due to the presence of different

Table 1 Effect of olive leaves extract (20 mg/mL/day) on serum liver enzyme activities in white albino male mice

Case	Mean $\pm$ SD			
	GGT U/L	GPT U/L	GOT U/L	ALP U/L
Control Group n = 10	71 $\pm$ 2.3 CV = 3.2%	56.8 $\pm$ 2.29 CV = 4%	48.2 $\pm$ 1.75 CV = 3.6%	66.3 $\pm$ 2.62 CV = 3.95%
Treated Group n = 10	33.6 $\pm$ 2.79 CV = 8.3%	12.2 $\pm$ 1.1 CV = 9%	20.5 $\pm$ 2.01 CV = 9.8%	39.1 $\pm$ 2.68 CV = 6.8%
p value	($p \leq 0.05$)	($p \leq 0.05$)	($p \leq 0.001$)	($p \leq 0.001$)

Table 2 Effect of olive leaves (20 mg/mL/day) on serum lipid profile in white albino male mice

Case	Mean $\pm$ SD				
	Cholesterol mg/dL	VLDL mg/dL	LDL mg/dL	HDL mg/dL	Triglyceride mg/dL
Control group n = 10	197.6 $\pm$ 13.2 CV = 6.6%	98.30 $\pm$ 2.1 CV = 6.7%	122.2 $\pm$ 11.9 CV = 9.7%	41.5 $\pm$ 2.41 CV = 5.8%	154.9 $\pm$ 13.6 CV = 8.7%
Treated group n = 10	146.5 $\pm$ 3.5 CV = 2.3%	92.17 $\pm$ 3.2 CV = 16.0%	27 $\pm$ 2.4 CV = 8.8%	63.4 $\pm$ 4.7 CV = 7.4%	99.6 $\pm$ 5.6 CV = 5.6%
p value	(p $\leq$ 0.001)	(p $\leq$ 0.001)	(p $\leq$ 0.001)	(p $\leq$ 0.001)	(p $\leq$ 0.001)

Table 3 Effect of pumpkin peel extract (20 mg/mL/day) on serum liver enzyme activities in white albino male mice

Case	Mean $\pm$ SD			
	GGT U/L	GPT U/L	GOT U/L	ALP U/L
Control Group n = 10	42.7 $\pm$ 8.4 CV = 19.6%	24.9 $\pm$ 24 CV = 9.6%	29.2 $\pm$ 2/5 CV = 8.5%	50.7 $\pm$ 7.24 CV = 14.2%
Treated Group n = 10	33.6 $\pm$ 2.79 CV = 8.30%	12.2 $\pm$ 1.4 CV = 11.4%	20.5 $\pm$ 2.01 CV = 9.80%	39.1 $\pm$ 2.68 CV = 6.85%
p value	(p $\leq$ 0.01)	(p $\leq$ 0.02)	(p $\leq$ 0.001)	(p $\leq$ 0.001)

Table 4 Effect of pumpkin peel extract (20 mg/mL/day) on serum lipid profile

Parameter	Control group n = 10	Treated animal n = 10	Significant
Total cholesterol mg/dL	230.9 $\pm$ 4.31 CV = 1.8%	142.2 $\pm$ 12.47 CV = 8.7%	(p $\leq$ 0.001)
VLDL mg/dL	34.4 $\pm$ 2.3 CV = 6.6%	28.76 $\pm$ 3.18 CV = 11%	(p $\leq$ 0.001)
LDL mg/dL	147.5 $\pm$ 3.5 CV = 2.3%	30.84 $\pm$ 3.0 CV = 9.7%	(p $\leq$ 0.001)
HDL mg/dL	49 $\pm$ 6.6 CV = 13.46%	82.6 $\pm$ 5.41 CV = 6.5%	(p $\leq$ 0.001)
Triglycerides mg/dL	172 $\pm$ 3.4 CV = 1.9%	143.8 $\pm$ 16.2 CV = 11.2%	(p $\leq$ 0.001)

Table 5 Effect of olive leaves and pumpkin peels extract on the LDL/HDL ratio

Case	LDL/HDL ratio with olive leaves	LDL/HDL ratio with pumpkin peels
Control group n = 10	2.94	3.01
Treated group n = 10	0.43	0.37
p value	(p $\leq$ 0.01)	(p $\leq$ 0.01)

phytochemicals like tocopherol, carotenoid, and triterpenes. Secondary metabolites like sitosterol, dehydrodi coniferyl alcohol, and tetrasaccharide glycerol glycolipid were also present (Isin et al. 2007). Abou Seif HS et al. (Abou Seif 2014) showed that giving pumpkin extract to animals had a protective effect against hepatotoxicity, which is in agreement with our results. In addition, there is evidence that pumpkin seed oil has a high concentration of tannins, flavonoids, and polyphenols, which have antioxidant activity as well as hepatoprotective abilities that reduce hepatic damage leading to decreased liver enzyme activity (Rouag et al. 2020).

The lipid-reducing effects of pumpkin are probably due to the presence of fibers, which act to decrease plasma LDL-C levels by interrupting or inhibiting cholesterol and bile acid absorption and increasing LDL receptor activity. The present result is in agreement with (Makni et al. 2008), which shows that intestinal acyl coenzyme A cholesterol acyltransferase (ACAT) is inhibited by unsaturated fatty acids. Since reverse cholesterol transport and pre- β HDL-C are stimulated, the effect of pumpkin seeds on the serum concentrations of TC in atherogenic rats could be explained by their rich source of polyunsaturated fatty acids and the rate-limiting step in cholesterol absorption (Lcumberri et al. 2007). Elevated levels of HDL-C may be responsible for some of its anti-atherogenic qualities, such as its ability to prevent LDL oxidation and shield endothelial cells from the damaging effects of oxidized LDL. Moreover, a diet high in fiber lowers triglycerides by inhibiting the liver's lipogenesis. Rats' cholesterol levels are lowered when unsaturated fatty acids like oleic and linoleic acids found in pumpkin seeds are present. This plant's ability to reduce lipids is partially attributed to the pectin that it contains (Isin et al. 2007; Al-Attar and Shawush 2015).

The effect of olive leaf extract (20 mg/mL/day) on serum liver enzyme activities in albino male mice is due to the presence of a large amount of the phenol group and large phytochemical compounds. This, in agreement with the obtained result of Hamad I. (Hamad 2015), demonstrated the significant impact of olive leaf extract on liver damage, as well as its high phenol content and robust antioxidant activity. This improved serum GOT and GPT and increased



serum antioxidant capacity when compared to the treated group receiving CCl_4 treatment, indicating that olive leaves have a positive effect on antioxidant levels (Al-Attar and Shawush 2015; Afify et al. 2018). On the other hand, the protective action of olive leaf extract can be attributed to various phytoconstituents like flavonoids and fatty acids (especially oleuropein and hydroxytyrosol), which show hepatoprotective abilities and have a role in preserving the structural integrity of the hepatocellular membrane that may be responsible for the membrane stabilizing- activity (Taha et al. 2020). It was demonstrated that the combination of flavonoids, oleuropeosides, and substituted phenols produced an antioxidant activity in whole olive leaf extract that was greater than that of vitamins C and E (Khalil 2004). The aqueous extract of olive leaves contains antioxidant properties that, due to the hepatoprotective impact of the polyphenol chemicals present, might prevent liver damage. Olive leaves are essential for the stability of the plasma membrane, liver damage healing, and the prevention of intracellular enzyme leakage (Fki et al. 2020).

Pectin-rich diets have been shown to be helpful in increasing bile acid excretion, which increases the liver's synthesis of these acids from cholesterol. Pectin increases the activity of lipoprotein lipase in the heart and adipose tissue, which raises the absorption of VLDL, chylomicron, and triglyceride-rich lipoproteins in tissues other than the liver and promotes their breakdown, lowering triglyceride levels (Isin et al. 2007; Lcumberri et al. 2007). Since LDLs have the greatest concentration of cholesterol and cholesterol is essential for lipoprotein production, LDLs are expected to decrease if cholesterol levels are lowered. Conversely, a rise in LDL catabolism might be the cause of the LDL decrease. By regulating the LDL receptors, flavonoids can increase the quantity of LDL receptors on the liver's surface. However, it is removed from the circulation in mice after being carried into the hepatocyte (Makni et al. 2008; Lcumberri et al. 2007).

There is evidence of risk factors for cardiovascular disease (CVD), particularly with elevated levels of total and LDL cholesterol and lower levels of HDL cholesterol (Herrington et al. 2016). In this case, the results show a significant decrease in the treated animals compared to the control group with both olive leaves and pumpkin peels, that indicates the possibility of these extractions to be a savior in CVD (Hussain et al. 2022; Stevens et al. 2021).

Conclusions

Results demonstrated the therapeutic effects of pumpkin peel extracts, which included a substantial decrease in blood enzyme activity and concentrations of LDL, VLDL, total cholesterol, and triglycerides while also raising HDL levels.

It will need further research to determine the exact mechanism behind the pumpkin's hypocholesterolemic impact; however, it may be related to the plant's fiber contents. The obtained results of olive leaves showed that olive leaf ethanol extract has strong antioxidant activity due to its high polyphenol content and has a significant effect on liver cells, resulting in decreased serum GGT, GOT, ALP, and GPT.

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Data availability The data supporting the findings are available when requested.

Declarations

Conflict of interest The authors declare that they have no competing interests.

Ethical approval The research was approved by the University of Technology (UOT) Animal Ethical Committee in accordance with the guidelines of Animal Research: Reporting of In Vivo Experiments (ARRIVE) 2020.

Consent for publication Not applicable.

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