The Potential Hypolipidemic Effect of Pomegranate Peel and Licorice Extracts in Rats

Asmaa H. Arafat[1], Omnia E. Kilany[2], Haidy G. Abdel-Rahman[2]
[1] Free Veterinarian
[2]Department of Clinical Pathology, Faculty of Veterinary Medicine, Suez Canal University
E-mails:
Asmaa H. Arafat[1]: semsemarafat73@gmail.com
Omnia E. Kilany[2]: omniakilany@vet.suez.edu.eg
Haidy G. Abdel-Rahman[2]: hgdody@yahoo.com

Abstract
Hyperlipidemia constitutes a major problem causing serious health problems. The current study was conducted to investigate the effect of Pomegranate peel (PC) and Licorice (LC) extracts as anti-hyperlipidemic agents in rats. Sixty male Wister rats were used in current study. They were divided into 6 groups; Group I: Control (C), Group II: Pomegranate control (PC), Group III: Licorice Control (LC), Group IV: Hyperlipidemia control (H), Group V: Hyperlipidemia pomegranate (HP), Group VI: Hyperlipidemia licorice (HL). Pomegranate was administrated 200 mg/kg body weight, while licorice was administrated 400 mg/kg body weight. All doses were given by oral gavage. The results showed that pomegranate peel and licorice extract significantly reversed the levels of serum lipid profile, glucose and hepatic damage markers, and antioxidant of hyperlipidemic rats. Histopathological examination of liver tissues was in concurrence with the biochemical results. It is logical to consider that the antihyperlipidemic and antioxidative properties of pomegranate and licorice are mechanistically achieved. So, pomegranate and licorice could be used as protective agents against hyperlipidemia and subsequent resulted metabolic disorders.

Key words: Hyperlipidemia, pomegranate, licorice, lipid profile, liver, rats.

Introduction:

Hyperlipidemia is defined as a group of disorders that are characterized by increase in blood lipids which include cholesterol, triglyceride, low density

lipoprotein and decrease in high density lipoprotein in blood stream **(*Shattat, 2014*)**. Hyperlipidemia consider as a serious risk of cardiovascular disease which leads high mortality worldwide **(*Smith et al., 2004*).** There are many types of hyperlipidemias which have different effects on the body **(*Singh and Nain, 2018*).** The elevated levels of cholesterol and triglycerides in the blood has been reported as the main risk factor associated with atherosclerosis by the American Heart Association. So, it is thought that the treatment of hyperlipidemia is one of the fundamental approaches towards decreasing the atherogenic process **(*Moss and Dajani, 1971*).**

Hypolipidemic drugs are present in large scale, however, their side effects and complications have diminished their popularity. Nowadays, natural hypolipidemics have overcame these shortages **(*Lal et al., 2004*).** Pomegranate (*Punica granatum*) is an essential origin of various bioactive compounds with useful properties, such as antioxidant, anti-inflammatory, anti-aging, prebiotic and anticancer effects, as well as its defensive role against metabolic disorders and cardiovascular diseases. (***Lavoro et al., 2021*).** Many articles were recorded on the capability of pomegranate leaves extracts to combat obesity, cancer, and other diseases **(*Lansky and Newman, 2007*)**, and their ability of ameliorating hyperlipidemia and hypertension **(*Sohrab et al., 2019*).** Licorice (*Glycyrrhiza glabra*), herbaceous plant native to Europe and Asia. This plant is used as a native medicine as it owns antibacterial, antiviral, anti-allergic, antidiabetic, hepatoprotective, and anti-carcinogenic activities **(*Kalita and Hazarika, 2021*).** The dried roots of the licorice plant have been used as flavoring and sweating compounds, and as anti-allergic and anti-inflammatory agents in Japan and China **(*Simmler et al., 2014*).** Alcoholic extract of licorice root has reduced low-density lipoprotein (LDL) oxidation in atherosclerotic mice and in hypercholesterolemic, in addition to normal lipidemic humans **(*Fuhrman et al., 2002*).** This investigation was carried out to check the efficacy of pomegranate and licorice extracts as anti-hyperlipidemic agents.

Materials and Methods:

Sixty male Wistar rats weighing between 100-115 g were purchased from Animal Vaccine Institute, Helwan, Egypt and acclimated for 2 weeks prior to experimental use at the laboratory animal house of Vet. Medicine Faculty, Suez Canal University

Tested plant extracts:

A- Pomegranate peel extract: Methanol pomegranate peel extract was purchased from Golden Horizon (Chengdu) Technology Co., Ltd., China. it was used at 200 mg/kg b.wt per day orally. This dose was selected on the basis of previous reports of ***Abdel Moneim et al.* (*2011*)**.

B- Licorice oil extract: Licorice oil extract was purchased from Dongatai Hanfangyuan Biological Technology Co., Ltd, China It used by dose of 400mg/kg b.wt This dose was selected according to ***Shalaby* (*2004*).**

Experimental design

The experimental period was (15 weeks) which consists of two periods, the first for induction of hyperlipidemia (9 weeks) and the second for the treatment with pomegranate and licorice extracts (6 weeks). Rats were divided to six group: **Group I (C):** Rats received balanced control diet fulfill nutritional requirements of rats all over the experimental period and received 0.2 ml of normal saline daily by oral gavage for the last 6 weeks. **Group II (PC):** Rats received balanced control diet fulfill nutritional requirements of rats all over the experimental period and received (200 mg/kg b.wt) pomegranate peel extract daily by oral gavage for the last 6 weeks. **Group III (LC):** Rats received balanced control diet fulfill nutritional requirements of rats all over the experimental period and received (400 mg/kg b.wt) licorice root extract daily by oral gavage for the last 6 weeks. **Group IV (H):** Rats received HFD all over the experimental period. **Group V (HP):** Rats received HFD all over the experimental period and received (200 mg/kg b.wt) pomegranate peel extract daily by oral gavage for the last 6 weeks. **Group VI (HL):** Rats received HFD all over the experimental period and received (400 mg/kg b.wt) licorice root extract daily by oral gavage for the last 6 weeks.

Sampling

A-blood sampling

Blood samples were collected from overnight fasted rats from retro-orbital venous under the effect of light anesthesia. Blood sample was collected in a plain, clean and sterile centrifuge tube without anticoagulant for serum separation for biochemical analysis, antioxidant and cytokines analysis.

B- Tissue sampling

After scarification, liver samples were obtained and fixed in 10% formalin for histopathological examination.

Determination of serum lipid profile:

A-Total cholesterol (TC) Serum TC (mg/dl) was determined according to ***Richmond (1973).***

B-Triglyceride (TG) Serum TG (mg/dl) was determined according to ***Fossati and Prencipe (1982)*.**

C-High density lipoprotein cholesterol (HDL-C) Serum HDL-C (mg/dl) was determined according to ***Burstein et al., (1970)*.**

D-Low-density lipoprotein cholesterol (LDL-C)

Serum LDL-C (mg/dl) was determined according to the formula of ***Friedewald et al. (1972).***

Serum LDL-C (mg/dl) = TC -- HDL-C -- TG/5

E-Very low-density lipoprotein cholesterol (VLDL-C)

Serum VLDL-C (mg/dl) was determined according to the formula of ***Friedewald et al. (1972).*** Serum VLDL-C (mg/dl) = TG/5

Determination Serum biochemicals

A-Determination of serum total protein level was determined calorimetrically according to ***Henry (1974).***

B-Determination of serum albumin and globulin level (gm/dl) was determined calorimetrically according to ***Drupt (1974).***

C-Determination of A/G ratio was calculated by dividing albumin over globulin according to ***Noveraz (1953).***

D-Determination of liver transaminases Serum ALT and AST (IU/l) activities were determined calorimetrically according to ***Reitman and Frankel (1957)*.**

E- Determination of serum fasting blood glucose (mg/dl) was determined according to ***Nagel et al. (2006).***

Oxidant/antioxidants analysis

1. Serum Malondialdehyde (MDA) was determined according to ***Yagi (1998).***

2. Serum Superoxide Dismutase (SOD) (µg/mL) was determined according to ***Koivunen and Krogsrud, (2006)*.**

3. Serum reduced Glutathione (GSH) (µg/mL) was determined according to ***Mytilineou et al., (2002)*.**

Histopathological examination: Tissue specimens from liver of rats were taken after sacrification. The microscopic slides were then stained by Hematoxylin and eosin stain (H&E stain) ***(Bancroft et al., 1996).***

Statistical analysis: Data of the current study were analyzed using One Way Analysis of Variance for all tested groups according to ***Snedecor and Cochran* (*1971*)**. Means separations were done by Duncan′s Multiple Range test according to ***Duncan (1955)***. The current data were analyzed using **(SPSS, 16)** for windows. Results are considered significant at probability level of 0.05 ($P \leq 0.05$).

Results:

The effect of administration of pomegranate and licorice on the body weight and liver relative weight after 3 and 6 weeks from pomegranate and licorice administration

After 3 weeks, a significant increase was recorded in body weight in HC group when compared with C group. While, there was a significant decrease in body weight in both HP and HL treated groups compared with HC group. Liver relative weights showed a significant increase in HC groups compared with C groups. While, liver relative weight exhibited significant decrease in both HP and HL treated groups compared with HC groups.

After 6 weeks, HC group induced significant increase in body weight than C group. HP and HL groups revealed significant decrease in body weight than HC groups. Meanwhile, Liver relative weight exhibited non-significant change in both HP and HL treated groups compared with HC groups as shown in table (1).

Lipid profile at 3 and 6 weeks from pomegranate and licorice administration

After 3 weeks of treatment, in HC group there was a significant increase in the value of cholesterol than C group. Both HP and HL induced a significant decrease compared with HC groups. The values of T.G and VLDL showed significant increase in HC groups than C groups. Besides, HP and HL groups significantly reduced the values of T.G and VLDL. There was significant decrease in HDL value in HC group compared with C group. Meanwhile, there were significant increases in HDL values of both HP and HL groups compared with HC group. In addition, LDL showed highly significant increase in HC group compared with C group. Meanwhile, HP and HL groups induced significant decrease in the value of LDL compared with HC group as shown in table (2).

After 6 weeks post treatment, HC group showed significant increase in the values of cholesterol, T.G, LDL and VLDL compared with C groups. However, the HP and HL groups exhibited significant decline in the values of cholesterol, T.G, LDL and VLDL when compared with HC group. HC group showed significant decrease in HDL compared with C group, but HP and HL groups revealed significant increase in HDL compared with HC groups, as shown in table (3).

Serum biochemical parameters at 3 and 6 weeks from pomegranate and licorice administration

After 3 weeks, HC groups showed significant decrease in T.P,

albumin and globulin without significant changes in A/G ratio compared with C group, but there was significant increase in ALT, AST and glucose. The HP and HL groups revealed significant rise in the concentrations of total protein and albumin, meanwhile, globulin and A/G ratio were non-significantly increased in correspondence with HC rats. The values of ALT, AST, glucose decreased in both HP and HL groups as shown in table (4).

After 6 weeks, the content of total protein and albumin were significantly decreased in HC while there were non-significant changes in globulin and A/G ratio when compared with C groups. Both HP and HL showed non-significant changes in T.P, globulin and A/G ratio compared with HC groups. Meanwhile, they showed significant increase in albumin when compared with HC groups. ALT, AST and glucose were significantly increased in HC group compared with C. Moreover, the values of ALT, AST and glucose were significantly decreased in HP and HL groups compared with HC groups as shown in table (5).

Serum lipid peroxidation and antioxidants at 3 and 6 weeks from pomegranate and licorice administration

After 3 weeks, the level of MDA was significantly increased in HC group, whereas the levels of GSH and SOD were significantly declined in the HC group compared with the C group. Besides, the levels of GSH and SOD were significantly increased, while the level of MDA significantly decreased in both HP and HL groups compared with HC groups as shown in table (6).

After 6 weeks, HC groups showed significant decrease in both GSH and SOD and increase in MDA. Besides, the level of MDA was significantly decreased in both HP and HL groups compared with HC groups. Furthermore, the levels of GSH and SOD were significantly increased in HP groups compared HL group, as shown in table (7)

Histopathological results of liver after 6 weeks:

Liver of control groups I, II and III showed normal histological structures, regarding licorice group mild congestion of central vein were observed (Photos 1, 2 & 3). Group IV (hyperlipidemia) demonstrated different degrees of fat infiltration inside the hepatic cells along with focal necrosis of some hepatic cells and mild proliferation of hepatic areas, in addition to proliferation of Von kupffer cells (Photo 4). The livers of group V (pomegranate treated group), revealed marked improvement of the hepatic tissue alterations. It revealed mild fat vacuoles of various sizes inside

some hepatic cells (Photo 5). Group VI (treated licorice), showed mild to minimal vacuoles along with mild congestion of hepatic blood vessels and sinusoids (Photo 6).

Table (1): *Body weight and Liver relative wright (Mean ±SE) at 3 and 6 weeks from pomegranate and licorice administration in different treated groups*

Parameters / Groups	3 weeks		6 weeks	
	Body weight (g)	**Liver relative weight (%)**	**Body weight (g)**	**Liver relative weight (%)**
C	203.00± 1.73^{d}	2.79± 0.84^{de}	215.67± 2.60^{d}	3.62± 0.61^{ab}
PC	207.67± 1.45^{d}	3.02± 0.12^{c}	252.33± 1.45^{bc}	3.22± 0.95^{c}
LC	221.33± 1.76^{c}	3.37± 0.55^{b}	245.33± 1.45^{c}	3.41± 0.13^{bc}
HC	246.67± 3.53^{a}	3.75± 0.95^{a}	275.00± 3.78^{a}	3.75± 0.04^{a}
HP	234.33± 4.41^{b}	2.96± 0.77^{cd}	255.00± 2.89^{b}	3.62± 0.71^{ab}
HL	223.67± 2.03^{c}	2.70± 0.15^{e}	258.33± 3.48^{b}	3.60± 0.91^{ab}

Within the same column, mean with different superscripts are significantly differ (*P≤0.05*).

Table (2): *Lipid profile parameters changes in the different treated groups after 3 weeks of pomegranate and licorice administration (Mean ±SE)*

Parameters / Groups	**Cholesterol (mg/dl)**	**TG (mg/dl)**	**HDL (mg/dl)**	**LDL (mg/dl)**	**VLDL (mg/dl)**
C	201.53± 0.53^{e}	112.67± 1.45^{f}	56.00± 0.58^{a}	123.00± 0.58^{e}	22.53± 0.30^{f}
PC	189.07± 0.71^{f}	142.00± 1.15^{d}	37.67± 1.45^{c}	123.00± 1.52^{e}	28.40± 0.23^{d}
LC	216.60± 2.66^{d}	133.00± 1.73^{e}	41.33± 0.88^{b}	148.67± 1.45^{d}	26.60± 0.35^{e}
HC	304.67± 2.17^{a}	178.33± 0.88^{a}	23.67± 0.88^{e}	245.33± 1.45^{a}	35.67± 1.77^{a}
HP	240.47± 0.43^{c}	167.33± 1.20^{b}	28.00± 0.58^{d}	179.00± 0.58^{c}	33.46± 0.24^{b}
HL	272.87± 0.87^{b}	159.33± 0.66^{c}	27.67± 0.88^{d}	213.33± 1.20^{b}	31.87± 0.13^{c}

Within the same column, mean with different superscripts are significantly differ (*P≤0.05*).

Table (3): *Lipid profile parameters changes in the different treated groups after 6 weeks of pomegranate and licorice administration (Mean ±SE)*

Parameters / Groups	Cholesterol (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
C	242.80± 0.76^{e}	177.33± 1.45^{d}	42.33± 0.89^{a}	190.00± 0.58^{d}	35.46± 0.29^{d}
PC	240.47± 1.27^{e}	145.67± 0.67^{e}	40.67± 0.67^{a}	188.67± 0.67^{d}	36.00± 0.13^{d}
LC	240.33± 1.33^{e}	131.67± 1.67^{f}	41.67± 0.89^{a}	198.33± 0.88^{d}	34.33± 0.33^{d}
HC	393.27± 0.96^{a}	304.67± 1.20^{a}	25.33± 0.89^{c}	307.00± 1.52^{a}	60.93± 0.24^{a}
HP	310.00± 0.80^{b}	221.67± 0.88^{b}	29.00± 0.58^{b}	236.67± 1.20^{b}	44.33± 0.18^{b}
HL	291.60± 2.078^{c}	203.00± 1.73^{c}	30.00± 1.15^{b}	225.00± 2.87^{c}	40.60± 0.35^{c}

Within the same column, mean with different superscripts are significantly differ (*P≤0.05*)

Table (4): *Serum biochemical parameters changes in the different treated groups after 3 weeks of pomegranate and licorice administration (Mean ±SE)*

Parameters / Groups	**T.P (g/dl)**	**Albumin (g/dl)**	**Globulin (g/dl)**	**A/G**	**ALT (IU/I)**	**AST (IU/I)**	**Glucose (mg/dl)**
C	6.23± 0.15^{a}	3.50± 0.25^{a}	2.73± 0.15^{a}	1.30± 0.16^{ab}	47.67± 1.45^{cd}	51.00± 1.52^{b}	52.00± 1.52^{d}
PC	6.10± 0.10^{a}	3.80± 0.57^{a}	2.30± 0.57^{ab}	1.65± 0.04^{a}	48.67± 1.33cd	51.67± 1.66^{b}	49.00± 0.57^{d}
LC	6.06± 0.16^{a}	3.50± 0.57^{a}	2.57± 0.22^{ab}	1.39± 0.13^{ab}	43.67± 0.88^{d}	50.33± 0.33^{b}	52.00± 1.53^{d}
HC	4.50± 0.58^{c}	2.40± 0.12^{c}	2.10± 0.15^{b}	1.16± 0.14^{b}	71.67± 0.88^{a}	72.67± 0.88^{a}	87.00± 1.15^{a}
HP	5.20± 0.10^{b}	2.83± 0.12^{b}	2.37± 0.89^{ab}	1.20± 0.84^{b}	53.00± 1.00^{b}	54.67± 2.33^{b}	72.00± 1.15^{b}
HL	5.30± 0.58^{b}	2.97± 0.67^{b}	2.33± 0.12^{ab}	1.28± 0.9^{ab}	52.33± 2.33^{b}	54.00± 2.08^{b}	58.33± 0.88^{c}

Within the same column, mean with different superscripts are significantly differ (*P≤0.05*)

Table (5): *Serum biochemical parameters changes in the different treated groups after 6 weeks of pomegranate and licorice administration (Mean ±SE)*

Parameters / Groups	T.P (g/dl)	Albumin (g/dl)	Globulin (g/dl)	A/G	ALT (IU/I)	AST (IU/I)	Glucose (mg/dl)
C	7.23± 0.34^{a}	4.17± 0.15^{a}	3.07± 0.38^{a}	1.39± 0.21^{a}	59.67 ±2.60^{b}	57.66± 1.45^{d}	92.67± 1.45^{d}
PC	6.97± 0.17^{a}	4.06± 0.88^{a}	2.90± 0.17^{a}	1.31± 0.25^{a}	57.33± 0.33^{b}	67.33± 1.66^{b}	87.33± 0.73^{d}
LC	7.03± 0.32^{a}	4.03± 0.88^{a}	3.00± 0.23^{a}	1.34± 0.81^{a}	56.67± 1.67^{b}	61.00± 1.52^{bcd}	89.83± 1.34^{d}
HC	6.17± 0.22^{b}	3.33± 0.18^{b}	2.83± 0.17^{a}	1.43± 0.34^{a}	73.00± 1.53^{a}	76.00± 0.58^{a}	125.00± 2.89^{a}
HP	6.87± 0.33^{ab}	3.96± 0.33^{a}	2.90± 0.57^{a}	1.31± 0.17^{a}	60.33± 1.20^{b}	65.33± 1.86^{bc}	115.00± 2.89^{b}
HL	6.63± 0.33^{ab}	3.39± 0.58^{a}	2.73± 0.33^{a}	1.33± 0.23^{a}	57.67± 0.88^{b}	60.33± 1.53^{cd}	102.00± 1.73^{c}

Within the same column, mean with different superscripts are significantly differ ($P \leq 0.05$)

Table (6): *Serum lipid peroxidation and antioxdants at 3 weeks from pomegranate and licorice administration in different treated groups (Means ± SE)*

Groups / Parameters	GSH (µg/ml)	SOD (µg/mL)	MDA (µm/ml)
C	17.24±0.06^{a}	6.41±0.02^{b}	0.57±0.01^{d}
PC	17.46±0.08^{a}	6.56±0.05^{a}	0.56±0.01^{d}
LC	17.39±0.02^{a}	6.49±0.04 ^{ab}	0.56±0.001^{d}
HC	13.00±0.08^{d}	4.16±0.02^{e}	0.94±0.01^{a}
HP	15.12±0.14^{b}	5.35±0.04^{c}	0.76±0.01^{c}
HL	14.00±0.08^{c}	4.90±0.02^{d}	0.85±0.01^{b}

Within the same row, means with different superscripts are significantly differ ($P \leq 0.05$)

Table (7): *Serum lipid peroxidation and antioxidants at 6 weeks from pomegranate and licorice administration in different treated groups (Means ± SE)*

Groups / Parameters	GSH (µg/ml)	SOD (µg/mL)	MDA (µm/ml)
C	17.34±0.03^{b}	6.38±0.02^{b}	0.58±0.01^{d}
PC	17.65±0.05^{a}	6.59±0.01^{a}	0.55±0.0035^{e}
LC	17.51±0.05^{ab}	6.50±0.02^{a}	0.56±0.0038^{de}
HC	14.00±0.07^{e}	4.94±0.06^{e}	0.85±0.01^{a}
HP	16.97±0.09^{c}	5.98±0.04^{c}	0.61±0.01^{c}
HL	16.00±0.06^{d}	5.59±0.01^{d}	0.73±0.01^{b}

Within the same row, means with different superscripts are significantly differ ($P \leq 0.05$)

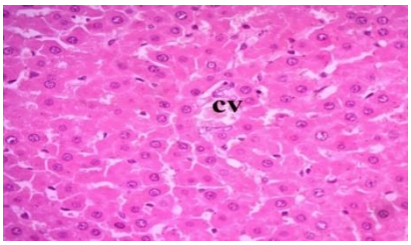

Photo (1): Liver, control group I, after 6 weeks, showing normal hepatic cells with normal cytoplasm and centrally located nuclei. H&E. X 400

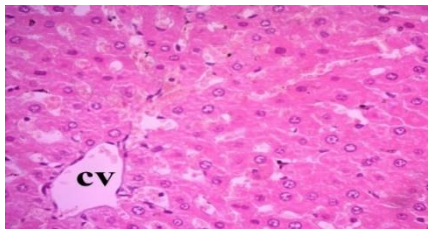

Photo (2): Liver, control group II, after 6 weeks, showing normal hepatic cells with normal cytoplasm and centrally located nuclei. H&E. X 400.

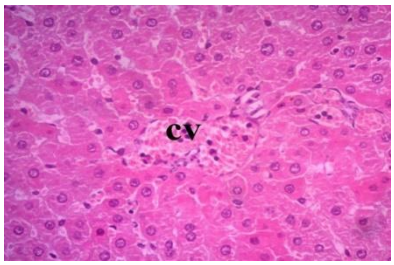

Photo (3): Liver, control group III, after 6 weeks, showing normal hepatic cells with normal cytoplasm and centrally located nuclei with mild congestion of central veins. H&E. X 400.

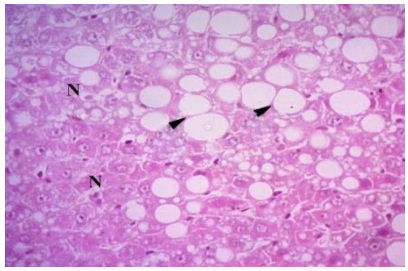

Photo (4): Liver, group IV, after 6 weeks, showing marked fat globules inside hepatocytes represented by vacuoles of various sizes and shapes inside the hepatocytes. Hyperplasia of Von Kopfer's cells and focal necrosis (N) H&E. X 400.

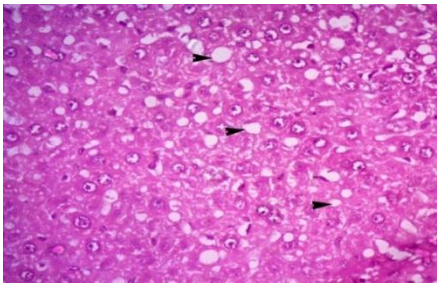

Photo (5): Liver, treated group IV, after 6 weeks, showing focal mild fat globules inside hepatic cells (arrow heads). H&E. X 400

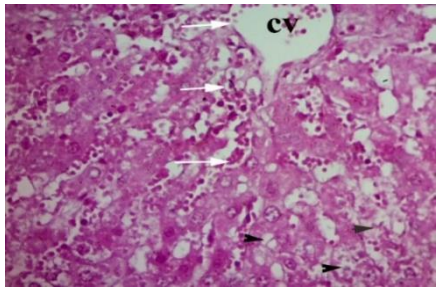

Photo (6): Liver, treated group VI, after 6 weeks, showing moderate vacuoles of fat infiltration inside the hepatocytes (arrow heads) and congestion of sinusoids (white arrows). H&E. X 400.

Discussion

In the present investigation, hyperlipidemia was induced in rats through a HFD for justifying the metabolic effect of pomegranate and licorice on the different clinicopathological parameters. Our study showed that feeding rats on high-fat diet significantly increased the body weight in the hyperlipidemic group compared with control group. These results are and this is in harmony with ***Onyeike et al. (2012)*** who reported that more weight acquired by the hyperlipidemic group because the high fat diet (cholesterol) utilised to induce hyperlipidemia in the rats enhanced energy intake and storage. ***Chao et al., (2009)*** cleared that enhancement of body weight may be due to the biological function of pomegranate polyphenols including ellagic and tannic acids which increases total serum protein and protein synthesis in the body. While, ***Gabr (2017)*** reported that in terms of body weight, there were no notable differences. between pomegranate treated groups when compared to control group. Moreover, our result showed that pomegranate decrease liver relative weight compared with control. The same findings were sound by **Ramzy (2019)** who stated that the supplemented diabetic groups had a significant decrease in the liver feeding rats on pomegranate peel.

The concentrations of TC, TG, LDL and VDL were significantly increased in hyperlipidemic group compared with control. These results seem similar to ***Miao et al. (2015)*** who showed that serum TC, TG and LDL-C were significantly increased, whereas HDL-C level was significantly decreased in diet-induced hyperlipidemic rats compared to the control group. Similarly, it was concluded that treatment with pomegranate for hyperlipidemic groups showed significant decrease in the TC, TG, LDL and VDL compared with hyperlipidemic group. ***Al-Muslehi (2013)*** concluded that pomegranate peel powder can improve lipid profile and reduce the risk of atherosclerosis in hypercholesterolemic rats. He also suggested that pomegranate peel powder consumption may modify the risk of hypercholesterolemia and that it has more potential as a health supplement rich in natural antioxidants. It was found that treatment with licorice for hyperlipidemic groups displayed significant decrease in the TC, TG, LDL and VDL compared with hyperlipidemic group. These results are in the line with ***Akinseye, (2016)*** who stated that treatment with different doses of licorice tea significantly decreased the levels of TC and LDL-C with respect to the normal control without tea extract. Similarly,

Awad, (2017) resulted that water extract of licorice significantly lowered TC and plasma triacylglycerols, which may be back to the good number of bioactive compounds in the water extract.

Our results showed that a high fat diet results in significant decrease in total protein, albumin, globulin, in the hyperlipidemic group compared with control group. This is due to fatty liver, where liver is responsible for production of protein so fatty liver impaired albumin synthesis. ***Ramadan et al. (2011)*** reported that rats fed on high fat diet led to a significant reduction of albumin when compared with control group. The content of albumin was improved a result of treatment with pomegranate and licorice for hyperlipidemic groups.

Our results demonstrated that the content of ALT and AST were significantly decreased in hyperlipidemic pomegranate and licorice groups compared with hyperlipidemic group after 3 and 6 weeks. In agreement with ***Sadeghipour et al. (2014)*** found that pomegranate extract reduced blood ALT and AST in high-fat diet-fed rats as compared to saline-treated rats, and that the various portions of the pomegranate have been known to be a reservoir of bioactive chemicals with potential biological activity.

Our results were confirmed by histopathological examination of liver where liver tissue showed that hyperlipidemic rats produced some pathological changes in liver tissues especially during the last 6 weeks of experiment. Our results are corresponding with ***Mahmoud (2019)*** who stated that these changes are such as the unique signet ring look is caused by significant fat deposition inside the hepatocytes. Treatment of hyperlipidemic rats with pomegranate and licorice improved the microscopic picture of liver. These results were coincided with, ***Aboonabi et al., (2014)*** noticed some positive attributes of pomegranate may be the ability to lower the oxidative stress.

Our results showed that a high fat diet results in significant rise in serum glucose level, these are compatible with ***Amin and Nagy, (2009)*** who concluded that a high fat diet results significant increase in serum glucose level and insulin resistance. Also, **Eu *et al.* (2010)** reported that blood glucose concentration was elevated in high-fat diet-induced hyperlipidemic rats for 28 days compared to the controls. The content of glucose was significantly decreased in hyperlipidemic groups treated with pomegranate and licorice compared with hyperlipidemic

group. The previously mentioned data are in harmony with those reported by **Salwe et al. (2015)** found that pomegranate leaves and peels protect the pancreas from damage, increase beta cells, lead to an excess of insulin, increase beta cell and insulin receptor regeneration, and lower blood sugar levels.

Our results showed that the level of MDA was significantly increased in hyperlipidemic group, whereas the concentrations of GSH and SOD were decreased in the hyperlipidemic group compared with the control group. These findings are in harmony with that reached by ***Humaish et al. (2017)*** who find significant increase in the serum concentration of MDA and decline in the concentration of serum reduced GSH in rats treated with high cholesterol diet, these results may be due to stimulation of enzyme fatty acyle CoA oxidase and increase oxidation of fatty acids lead to increase ROS production involving H2O2 which in turn lead to increase lipid peroxidation that caused disturbance of cell membrane homeostasis and damage of cell, so MDA will be increased. Similarly, ***Reed and Farries, (1984)*** concluded that dyslipidemia led to disturbance of antioxidant status causing oxidative stress, thus decrease of serum GSH may be due to participation of GSH in preventing of oxidation in oxidative stress status either by direct scavenger of free radicals or due to formation glutathione peroxidase. Equally, a study was carried out by ***Murry et al., (2003)*** who showed that lipid peroxidation happened due to increase production of free radicals, which lead to destruction of poly unsaturated fatty acids of cell membrane, thus increase concentration of MDA. Furthermore, we have found that treatment of hyperlipidemic rats with pomegranate and licorice extracts were significantly promoted the concentrations of GSH and SOD, While, significantly lead to decrease the level of MDA than hyperlipidemic rats. ***Mahmud et al., (2011)*** concluded that the anti-hyperlipidemic effect of pomegranate is related to the presence of phenolic and flavonoid compounds that remove free radicals through their ability to hydrogenate phenolic groups, which serve to neutralize free radicals and protect the body from oxidative stress.

Conclusion

From the result of the present work, we can conclude that pomegranate and licorice plants have hypolipidemic and antioxidant activities.

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التأثير الخافض للدهون المحتمل لمستخلصي قشر الرمان و العرقسوس في الفئران

أسماء حسيني عرفات[1]، أمنية السيد كيلاني[2]،هايدي جلال عبد الرحمن[2]

[1]طبيب بيطري حر

[2] قسم الباثولوجيا الإكلينيكية, كلية الطب البيطري, جامعة قناة السويس

الملخص العربي

تشكل زيادة الدهون في الدم مشكلة كبيرة تسبب مشاكل صحية خطيرة. أجريت الدراسة الحالية لمعرفة تأثير مستخلصات قشر الرمان والعرقسوس كعوامل مضادة لزيادة الدهون في الدم. تم استخدام 60 فأر في التجربة وتم تقسيمهم إلى 6 مجموعات، المجموعة الأولى:هي المجموعة الضابطة, المجموعة الثانية: تم تجريعها بمستخلص قشر الرمان، المجموعة الثالثة: تم تجريعها بمستخلص العرقسوس الزيتي ، المجموعة الرابعة: وقد تّلقت عليقة عالية في الكولوستيرول لرفع الدهون في الدم طوال فترة التجربة، المجموعة الخامسة: وقد تّلقت عليقه عالية في الكولوستيرول طوال فترة التجربة وقد تم تجريعها بمستخلص قشر الرمان، المجموعة السادسة: وقد تلقت عليقة عالية في الكولوستيرول طول فترة التجربة وقد تم تجريعها بمستخلص العرقسوس الزيتي. تم إعطاء الرمان بجرعة 200 مجم / كجم من وزن الجسم من مستخلص قشر الرمان ، بينما تم إعطاء عرقسوس بجرعة 400 مجم / كجم من وزن الجسم. أعطيت جميع الجرعات عن طريق الفم. أظهرت النتائج أن مستخلص قشر الرمان ومستخلص العرقسوس قد خفضوا بشكل كبير مستويات الدهون في الدم والجلوكوز ومؤشرات التلف الكبدي ومضادات الأكسدة في الفئران التي تعاني من ارتفاع نسبة الدهون في الدم. وكان الفحص المرضي لأنسجة الكبد متوافقا مع النتائج البيوكيميائية. ويمكن استخدام مستخلصات قشر الرمان والعرقسوس كعوامل وقائية ضد ارتفاع نسبة الدهون في الدم والاضطرابات الأيضية الناتجة عنها.