دراسة تأثير الدوم والشمر كعوامل مضادة لارتفاع دهون الدم في فئران التجارب

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الملخص العربي

أقرت العديد من الدراسات الوبائية والسريرية أن ارتفاع دهون الدم هو مساهم رئيسي في مرض تصلب الشرايين القلبي الوعائي . لذلك ؛ أجريت الدراسة الحالية لمعرفة تأثير الدوم والشمر كعوامل مضادة لارتفاع دهون الدم في فئران التجارب.

تم استخدام ستة وثلاثين من ذكور الجرذان البيضاء وزنها 130 ± 20 جرامًا وتم تقسيمهم إلى مجموعتين رئيسيتين . كل مجموعة تحتوي علي (6 فئران لكل منها) ، المجموعة الرئيسيةالأولى تم تغذيتها على الغذاء الأساسي طوال فترة التجربة (سبع أسابيع) واستخدمت كمجموعة ضابطة سالبة (٧ –) ، بينما المجموعة الرئيسية الثانية (30 فأر) تم تغذيتها على الغذاء المرتفع الدهن لمدة ثلاث اسابيع لاحداث ارتفاع دهون الدم . بعد تلك الفترة تم سحب عينات دم للتأكد من حدوث الاصابة وبعد ذلك تم تقسيم المجموعة الرئيسية الثانية الى خمس مجموعات فرعية . االمجموعة الأولي هي المجموعة الضابطة الموجبة المجموعة الثانية والثالثة تغذت على الغذاء الأساسي مدعما بالدوم بنسبة (5٪) و (10٪) على التوالي ، بينما المجموعة الرابعة والخامسة تغذت على الشمر بنسبة (5٪) و (10٪) على التوالي لمدة أربعة أسابيع.

تم إجراء التحليل الكيميائي لكلا من النباتين. أظهرت النتائج أن كمية الفينولات الكلية في نخيل الدوم والشمر كانت (0.270 و 0.357٪ على التوالي). بينما كانت كمية الفلافونويد الكلية (23.015 و 34.227 ملجم / 100 جم على التوالي).

وفي نهاية التجربة تم حساب البيانات البيولوجية وأخذ عينات الدم للتحليل البيوكيميائي. بالإضافة إلى ذلك ، تم إجراء فحص الأنسجة للكبد. وأظهرت النتائج

أن النظام الغذائي المرتفع الدهن في المجموعة المصابة الموجبة أدي إلى زيادة نسبة كلا من وزن الجسم ، ووزن الأعضاء النسبي ، ونسبة الدهون في الدم ، و انزيم المالون داى الدهيد (مؤشر حدوث الكسدة) ، وإنزيمات الكبد وجلوكوز الدم بينما انخفض البروتين الدهني عالي الكثافة في الدم ((HDL)، و سوبر أكسيد ديسميوتاز وانزيم الجلوتاثيون بيروكسيديز. وقد أظهرت جميع المجموعات المعاملة في كلا من النباتين تحسنًا في المؤشرات السابقة مقارنة بالمجموعة المصابة الموجبة .في الختام ، يمكن استخدام الدوم والشمر (5 ، 10 %) لتحسين مستوى الدهون ووظائف الكبد والحماية من عوامل الخطورة الناتجة من ارتفاع دهون الدم في فئران التجارب.

الكلمات المفتاحية : دهون الدم – النباتات – الانزيمات المضادة للأكسدة – وظائف الكبد

Study the Effect of DOUM-PALM and FENNEL as ANTI-HYPERLIPIDEMIC AGENTS in Experimental RATS

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ABSTRACT

Several epidemiological and trial clinical studies have reported that
dyslipidemia is a major contributor to atherosclerotic cardiovascular disease (ASCVD), So that; the present study was carried out to investigate the effect of Doum-palm and Fennel as anti-hyperlipidemic agents in experimental rats. Thirty-six male albino rats weighing 130 ± 20 g were used in this study and divided into two main groups, the first main group (6 rats) kept as a negative control group (v -) received a basal diet throughout the experiment period (seven weeks), while the second main group (30 rats) fed on a high-fat diet for three weeks to induce hyperlipidemia . After that the rats in the second main group (30) were divided into five subgroups, the first was the (v +) control group, the second and third given a basal diet supplemented with doum-palm (5%) and (10 %) , respectively . the four and five given a basal diet supplemented with fennel (5%) and (10%) , respectively for four weeks. The chemical composition for both plants was done. The results showed that the amount of total phenolics in doum palm and fennel were (0.270 and 0.357 % respectively). While , the amount of total flavonoids were (23.015 and 34.227 mg/100g respectively). At the end of the experiment, biological data were calculated; blood samples were taken to biochemical analysis. In addition, a histopathological examination for the liver was done. The results revealed that high fat diet in the (v +) control group increased body weight gain %, relative organ

weight, serum lipid profile, Malondialdehyde (MDA), liver enzymes and serum glucose, decreased in serum HDL-C, serum Superoxide Dismutase (SOD), and Glutathione Peroxidase (GPx). All treated groups with two plants showed improvement previously parameters compared with the positive control group. In conclusion, the consumption of doum-palm and fennel (5 and 10%) could be used for improving lipid profile, liver function and protect from the risk factor of hyperlipidemia in experimental rats.

Key words: lipid profile - plants – antioxidant enzymes- liver function

INTRODUCTION

Hyperlipidemia is a group of conditions which leads to elevate the levels of lipids in the bloodstream such as triglycerides (TG), cholesterol and low density lipoprotein (LDL) increase, or the level of high density lipoprotein (HDL) decrease in the blood. Hyperlipidemia is becoming a major health problem in the world recently even in humans **(Karam *et al.*, 2019).** Most people don't usually knowledge any symptoms but having hyperlipidemia which increases the risk of atherogenic dyslipidemia, a pro-inflammatory and pro-thrombotic state, high blood pressure, central obesity and cardiovascular disease (CVD) **(Lasker *et al.*, 2019).**

Medicinal plants are a principal source in health care in the form of plant extracts or their active components as a result of their properties **(Shorinwa and Monsi, 2020)**. Phenols in fruits and vegetables are bioavailable and protect against oxidative stress and free radicals **(Luna-Vázquez, *et al.*, 2013).** Nowadays, most hypolipidemic drugs have relatively side effects during the treatment of CVD. Thus, a certain component from food with slight side-effect or free of side effects has been paid more and more attention to the treatment of hyperlipidemia **(Yue *et al.*, 2018).**

Doum palm (*Hyphaene thebaica*) is a type of palm tree with edible oval fruit. It is native to the Nile valley in Egypt. It

was considered sacred by the Ancient Egyptians and the seed was found in many pharaohs' tombs. The fruits are oval, shiny, and red to orange in color, with an average length and diameter of 6 and 5 cm. The benefits of doum are including lowering blood pressure in hypertensive patients and changing blood lipids and lipoproteins in a manner that decreases the risk to the cardiovascular system **(AL-amer and Rashwan, 2012).**

Fennel (*Foeniculum vulgare*) is an aromatic herb belonging to the Parsley family. It is used as a spice and possesses a sweet taste that is similar to anise. Fennel seed shape is oval and has a strong scent, while the fruit has slightly sweet and slightly spicy. The seeds contain fiber and complex carbohydrates **(Elghazaly *et al.*, 2019).** Fennel seeds were found to have a hypotensive effect, hepatoprotective, anti-inflammatory, antidementia, protective effect against ethanol induced gastric mucosal lesions, anticancer **(Rezq, 2012).** Several studies reported the pharmacological properties for doum- palm and fennel so this study was carried out to investigate the effect of Doum-palm and Fennel as anti-hyperlipidemic agents in experimental rats.

MATERIALS AND METHODS

Plant materials: Doum-palm and fennel were purchased from The private Company for Herbs and Medicinal Plants, Cairo Governorate, Egypt.

Preparation of plant: doum-palm and fennel were homogenized into a fine powder, and then stored in dark glass containers in room temperature until use. Chemical composition (protein, fat, moisture, ash and carbohydrates calculated by difference) determined according to **(A.O.A.C, 2010).** Total phenolic was determined according to the method described by **Ranganna (2001)**. Total flavonoids were determined according to the procedure of **Marckam(1989).**

Animals: Thirty six adult male albino rats Sprague Dawley strain weighing (130 ± 20 g) were housed in well- aerated cages under hygienic conditions and were fed on a basal diet for one week to adapt.

Experimental design: Animals were divided into two main groups, the first (6 rats) kept as a negative control group (v -) received basal diet according to **Jerome *et al.*,(2002)**throughout the experiment period (seven weeks), while the second (30 rats) fed on a high-fat diet for three weeks to induce hyperlipidemia according to **Rashwan (1994**) , After this period blood samples were obtained to ensure the occurrence of hyperlipidemia and to estimate lipid profile. After that the rats in the second main group (30) were divided into five subgroups ,the first was the (v +) control group, the second and third given basal diet supplemented with doum-palm (5%)and(10 %) , respectively . the four and five given basal diet supplemented with fennel (5 %)and(10%) , respectively for four weeks. At the end, animals were weighed, fasted overnight, and then sacrificed under very light ether anaesthesia. Blood samples were collected from the hepatic portal vein of each rat into dry clean centrifuge tubes. Serum was carefully separated by centrifugation of blood samples at 3500 rpm (round per minute) for 15 minutes at room temperature, transferred into dry clean ebendorf tubes, and then kept frozen at -20˚C for latter determinations. Livers, hearts and spleen will be removed from rats by careful dissection, washed in saline solution (0.9%), dried using filter paper and independently weighed.

Biological evaluation

During the experiment (7weeks), feed intake was recorded every day and body weight was recorded every week. Biological evaluation of the different diets was carried out by calculating body weight gain % (BWG %) and feed efficiency ratio (FER) according to **Chapman *et al.*, (1959).**

Biochemical analysis of serum

Serum was analyzed for various biochemical parameters like lipid profile , total cholesterol, triglycerides and HDL-C were evaluated on the authority of **Allain *et al.*, (1974); Trinder and Ann., (1969)** and **Lopes -Virella *et al.*, (1977)** but LDL-C and VLDL-C calculated according to **Friedwald *et al.*, (1972).** The atherogenic indices were calculated according to **Tilvis and Miettinen (1986).** Antioxidant enzymes superoxide dismutase (SOD), glutathione peroxidase (GPx) and Malondialdehyde (MDA) level as a parameter for the lipid peroxidation were determined according to **Kakkar *et al.*,(1984), Ellman (1959) and Draper *et al* ., (1993).** Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP) were measured according to **Bergmeyer *et al.*, (1986)** and **Roy, (1970).** Glucose was determined in the serum according to the method described by **Trinder (1959)**.

Histopathology investigation

The liver was fixed in 10% buffered neutral formalin immediately following excision from animals. Fixed tissues were subsequently processed for histopathology examinations as previously described by **Carleton (1979).**

Statistical analysis

Results are expressed as mean ± standard deviation (SD). Differences between means indifferent groups were tested for significance using a one-way analysis of variance (ANOVA) followed by Duncan's test and a probability value of 0.05 or less was considered significant. Comparative means were performed according to the least

significant differences test (LSD) according to **Snedecor, (1969)** using SPSS (version 20).

RESULTS

Table (1) showed the total phenolic and total flavonoid contents in doum palm and fennel, The amount of total phenolics in doum palm and fennel were (0.270 and 0.357 % respectively) . While, the amount of total flavonoids in doum palm and fennel were (23.015 and 34.227 mg/100g respectively).

Table (2): showed the averages (g) of moisture, protein, fat, carbohydrate and ash per 100g Doum Palm and Fennel powder. The results of chemical compositions for Doum palm powder revealed that carbohydrate recorded the highest average (81.42) followed by moisture (9.2), ash (5.99), protein (2.94) and fat(0.45) respectively. While The results of chemical compositions for Fennel powder revealed that carbohydrate recorded the highest average(60.73) followed by protein(15.24) , moisture(9.1) , ash(8.33) and fat(6.60) respectively.

Table (3): showed the effect of Doum Palm, (5%and 10%), and Fennel (5% and 10 %) on feed intake (FI), body weight gain (BWG %) and feed efficiency ratio (FER) in hyperlipidemic rats. The results showed that previous mentioned parameters recorded increase in a positive control group as compared to negative control group. All the treated groups with Doum Palm and Fennel (5 %, 10 %) showed a significant decrease ($P<0.05$) as compared to the positive control group.

Table (4) showed the effect of doum palm (5% and 10%) and fennel (5% and 10%) on relative organs weight in hyperlipidemic rats. Relative liver weight value showed a significant increase in the positive control group as compared to the negative control group . All treated groups indicated significant decrease as compared to positive control group. The

best result was found in the treated group with (doum Palm10%) and closed to the normal group .Also, The relative heart weight value showed a significant increase in the positive control group as compared to the negative control group . Rats treated with (doum Palm10% and fennel 5%) indicated a significant decrease ($P<0.05$) in relative heart weight and recorded the best results as compared to the positive control group and closed to the normal group . However, the relative spleen weight value showed non-significant differences between negative and positive control group, as shown in table (4).

Table (5) showed the effect of Doum Palm (5% and10%) and Fennel (5% and 10%) on serum glucose in hyperlipidemic rats. Serum glucose showed a significant increase in the positive control group as compared to the negative control group (139.67±6.06 and 70±9.25 mg/dl respectively). All treated groups indicated a significant decrease as compared to the positive control group. The best result was found in the treated group with (Fennel 10%) and closed to the normal group as shown in table (5).

Table (6) Showed the effect of Doum Palm, (5% and 10%), and Fennel (5% and 10%) on Total cholesterol (T.C) and Triglycerides (T.G) in hyperlipidemic rats. The result revealed that, a significant increase in total cholesterol and triglyceride in the positive control group as compared to the negative control group. While, these parameters decreased in all treated groups especially treated group with (fennel 10%) which showed non-significant differences in serum cholesterol, as compared to the negative control group as shown in table (6).

Table (7) Showed the effect of Doum Palm, (5% and 10%), and Fennel (5% and 10%) on lipid profile (HDL, LDL, VLDL) and atherogenic index (AI) in hyperlipidemic rats . The result

revealed that, a significant decrease in (HDL) in the positive control group as compared to the negative control group. While, this parameter (HDL) recorded a significant increase in the treated groups with Doum Palm (10%),and Fennel (5% and 10%) as compared to the positive control group . On the other hand, (LDL, VLDL and AI) parameters recorded a significant increase in the positive control group as compared to the negative control group While, these parameters decreased in all treated groups especially treated group with (fennel 10%) which recorded the best result and closed to the normal group as shown in table (7) .

Table (8) Showed the effect of Doum Palm (5% and 10%), and Fennel (5 % and 10 %) on liver enzymes in hyperlipidemic rats. Serum AST value showed a significant increase in the positive control group as compared to the negative control group. All treated groups indicated a significant decrease as compared to the positive control group. The best result was found in the treated group with (Fennel 10 %) and closed to the normal group. Also, the mean value of serum ALT and ALP showed significant increase in positive control group as compared to negative control group. All treated groups recorded significant decrease as compared to positive control group. The best result found in treated groups with Doum palm (10%) and Fennel (10%) as shown in table (8) .

Table (9) Showed the effect of Doum Palm (5% and 10%), and Fennel (5 % and 10 %) on Serum antioxidant enzymes in hyperlipidemic rats. The mean value of SOD and GPx value showed a significant decrease in the positive control group as compared to the negative control group. All treated groups indicated a significant increase as compared to the positive control group. The best result was found in the treated groups with doum palm (10%), and fennel (10%). Finally, value of MDA showed a significant increase in the positive control group as compared to

the negative control group. All the treated groups indicated a significant decrease (P<0.05) as compared to the positive control group. The best result was found in the treated groups with doum palm (10%) and fennel (10%) as shown in table (9).

Table (1): Total phenolic and total flavonoid contents in Doum Palm and fennel .

Herbs	Total phenols %	Total Flavonoids mg/100 g.
Doum Palm	0.270±0.01	23.015±2.00
Fennel	0.357±0.01	34.227±4.00

Table (2) : The averages of moisture , protein , fat , carbohydrate and ash (g/100g) in Doum Palm and Fennel powder .

Proximate composition (g / 100g)	Doum	Fennel
Moisture	9.2±2.05	9.1±0.08
Crude Protein	2.94±1.05	15.24±0.04
Crude Fat	0.45±0.05	6.60±0.02
Ash	5.95±1.94	8.33±0.05
Carbohydrate	81.42±0.99	60.73±0.03

Table (3): Effect of diets supplemented with Doum palm and Fennel on Total feed intake , feed efficiency ratio and BWG% in hyperlipidemic rats

Parameters / Groups	Total feed intake (g)	Feed efficiency ratio	BWG %
Control – ve	612 ± 9.21^{c}	0.128 ± 0.009^{bc}	62.22 ± 5.74^{c}
Control + ve	873.55 ± 11.40^{a}	0.134 ± 0.002^{ab}	89.85 ± 20.47^{a}
Doum palm 5%	842.10 ± 10.88^{b}	0.127 ± 0.006^{c}	86.87 ± 8.42^{a}
Doum palm 10%	826.93 ± 25.45^{b}	0.122 ± 0.004^{c}	81.47 ± 6.43^{ab}
Fennel 5%	836 ± 20.44^{b}	0.136 ± 0.004^{a}	90.25 ± 4.60^{a}
Fennel 10%	825.47 ± 13.88^{b}	0.109 ± 0.004^{d}	72 ± 3.81^{bc}
LSD	19.20	0.01	11.79

Means in the same column with different superscript letters are significantly different at $p \leq 0.05$.

Table (4): Effect of diets supplemented with Doum palm and Fennel on Relative organs weight in hyperlipidemic rats

Parameters / Groups	Liver	Heart	Spleen
Control – ve	3.67 ± 0.73^{b}	0.24 ± 0.04^{b}	0.30 ± 0.06^{abc}
Control + ve	4.71 ±0.50^{a}	0.31 ± 0.05^{ab}	0.28 ± 0.05^{bc}
Doum palm 5%	4.27 ± 0.46^{ab}	0.33 ± 0.09^{a}	0.39 ± 0.16^{a}
Doum palm 10%	3.77 ± 0.46^{b}	0.25 ± 0.07^{b}	0.27 ± 0.03^{bc}
Fennel 5%	4.09 ± 0.41^{ab}	0.26 ± 0.02^{b}	0.36 ± 0.06^{ab}
Fennel 10%	4.22 ± 0.33^{ab}	0.30 ± 0.03^{ab}	0.25 ± 0.02^{c}
LSD	0.59	0.07	0.09

Means in the same column with different superscript letters are significantly different at $p \leq 0.05$.

Table (5): Effect of diets supplemented with Doum palm and Fennel on serum glucose in hyperlipidemic rats

parameters / Groups	Serum Glucose (mg/dl)
Control – ve	70 ± 9.25^{d}
Control + ve	139.67 ± 6.06^{a}
Doum palm 5%	111.50 ± 17.38^{b}
Doum palm 10%	95.17 ± 11.23^{c}
Fennel 5%	105.33 ± 14.11^{bc}
Fennel 10%	73.83 ± 12.21^{d}
LSD	14.43

Means in the same column with different superscript letters are significantly different at $p \leq 0.05$.

Table (6): Effect of diets supplemented with Doum palm and Fennel on Total cholesterol (T.C) and Triglycerides (T.G) in hyperlipidemic rats

parameters / Groups	Total cholesterol (mg/dl)	Triglycerides (mg/dl)
Control – ve	58.17 ± 10.87^{d}	85.50 ± 13.43^{c}
Control + ve	107.83 ± 9.72^{a}	171.17 ± 22.59^{a}
Doum palm 5%	80.67 ± 16.97^{bc}	131.33 ± 19.34^{b}
Doum palm 10%	77.33 ± 11.11^{bc}	109.67 ± 17.95^{b}
Fennel 5%	84.83 ± 10.61^{b}	124.67 ± 19.28^{b}
Fennel 10%	69.33 ± 8.12^{cd}	109.50 ± 16.86^{b}
LSD	13.64	21.76

Means in the same column with different superscript letters are significantly different at $p \leq 0.05$.

Table (7): Effect of diets supplemented with Doum palm and Fennel on lipoprotein fractions (HDL-C, LDL-C, VLDL-C) and atherogenic index (AI) in hyperlipidemic rats

Parameters / Groups	HDL-C mg/ dl	LDL-C mg/ dl	VLDL-C mg/ dl	AI
Control – ve	41.67 ± 0.55^{a}	0.81 ± 0.31^{e}	17.10 ± 2.69^{c}	0.39 ± 0.19^{e}
Control + ve	28.50 ± 4.59^{b}	44.10 ± 3.04^{a}	34.23 ± 4.52^{a}	2.61 ± 0.04^{a}
Doum palm 5%	29.33 ± 5.24^{b}	27.73 ± 5.45^{b}	26.27 ± 3.87^{b}	1.28 ± 0.33^{b}
Doum palm 10%	39.33 ± 6.44^{a}	16.90 ± 1.79^{d}	21.93 ± 3.59^{b}	0.98 ± 0.19^{c}
Fennel 5%	36.67 ± 6.95^{a}	23.23 ± 3.06^{c}	24.93 ± 3.86^{b}	1.34 ± 0.22^{b}
Fennel 10%	41.67 ± 7.03^{a}	4.30 ± 10.10^{e}	21.90 ± 3.37^{b}	0.68 ± 0.15^{d}
LSD	7.11	3.52	4.35	0.24

Means in the same column with different superscript letters are significantly different at $p \leq 0.05$.

Table (8): Effect of diets supplemented with Doum palm and Fennel on serum liver function enzymes in hyperlipidemic rats

Parameters / Groups	AST U/L	ALT U/L	ALP U/L
Control – ve	53.17 ± 12.66^{e}	18 ± 2.19^{d}	136.33 ± 17.76^{c}
Control + ve	276 ± 40.70^{a}	69 ± 12.62^{a}	247 ± 22.57^{a}
Doum palm 5%	154 ± 25.47^{bc}	56.67 ± 9.48^{b}	209.33 ± 17.76^{b}
Doum palm 10%	132 ± 21.71^{cd}	43 ± 9.42^{c}	157.33 ± 23.26^{c}
Fennel 5%	164.67 ± 27.34^{b}	54 ± 5.37^{b}	187.33 ± 21.62^{b}
Fennel 10%	102.67 ± 18.27^{d}	37.67 ± 8.12^{c}	145 ± 20.22^{c}
LSD	30.51	10.07	24.08

Means in the same column with different superscript letters are significantly different at $p \leq 0.05$.

Table (9): Effect of diets supplemented with Doum palm and Fennel on SOD , GPX and MDA in hyperlipidemic rats

Parameters / Groups	SOD U/L	GP_X ng/ml	MDA m mol/gm
Control – ve	59.57 ± 5.87^{a}	131 ± 8.73^{a}	6.07 ± 0.95^{e}
Control + ve	25.27 ± 4.92^{d}	59.97 ± 8.93^{e}	18.87 ± 2.33^{a}
Doum palm 5%	37.50 ± 4.23^{c}	84.60 ± 9.31^{d}	13.87 ± 1.17^{b}
Doum palm 10%	48.37 ± 4.85^{b}	116.23 ± 7.92^{b}	9.60 ± 0.93^{c}
Fennel 5%	40 ± 4.97^{c}	94.80 ± 5.61^{c}	13 ± 1.35^{b}
Fennel 10%	51.73 ± 4.83^{b}	119.47 ± 9.33^{b}	7.83 ± 1.25^{d}
LSD	5.82	9.91	1.66

Means in the same column with different superscript letters are significantly different at $p \leq 0.05$.

Histopathological results:

Liver

Microscopic pictures of H&E stained hepatic sections from control group showing normal arrangement of hepatic cords around the central vein (CV) with normal portal areas (PA) and sinusoids (s) high magnification X: 400 bar 50 **(photo 1 – 2)** . Meanwhile, liver of hyperlipidemic rat without treatment (control +ve group) showed disrupted hepatic architecture due to congestion (red arrows), swelling of hepatocytes (black arrows) around central vein (CV), hydropic degeneration (black arrows) with multiple large cytoplasmic vacuoles in hepatocytes (black arrowheads) around portal areas (PA) with occluded sinusoids. **(photo 3 - 4)** Some Microscopic pictures of hepatic sections from treated group with fennel 5% showed partial disruption of hepatic architecture characterized by congestion (red arrows), few large cytoplasmic vacuoles in hepatocytes (black arrowheads) around portal areas (PA) with normal sinusoids (s) **(photo 5)** . Hepatic sections from treated group with fennel 10% showing retained normal hepatic architecture characterized by normal arrangement of hepatic cords around central vein (CV) with normal portal areas (PA) and sinusoids (s) **(photo 6 - 7)** . Whereas , other Hepatic sections from treated group with Doum palm5% showing partial disruption of hepatic architecture characterized by hydropic degeneration (black arrows) in few hepatocytes (black arrows) around central vein (CV), with few small and large cytoplasmic vacuoles in hepatocytes (black arrowheads) around portal areas (PA) with normal sinusoids (s) **(photo 8 - 9)** . How ever Hepatic

sections from treated group with Doum palm 10% showing great improvement of hepatic architecture normal hepatocytes around central vein (CV), with few minute cytoplasmic vacuoles in hepatocytes (black arrowheads) around portal areas (PA) with normal sinusoids (s) **(photo 10 - 11) .**

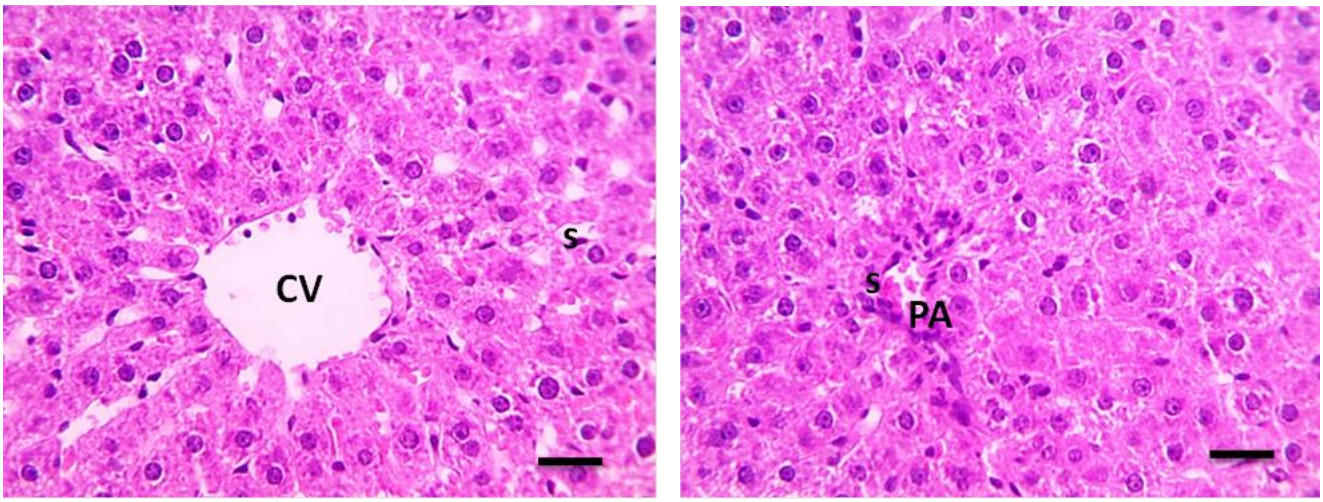


photo (1 – 2) : Microscopic pictures of H&E stained hepatic sections from control group showing normal arrangement of hepatic cords around the central vein (CV) with normal portal areas (PA) and sinusoids (s) high magnification X: 400 bar 50 .

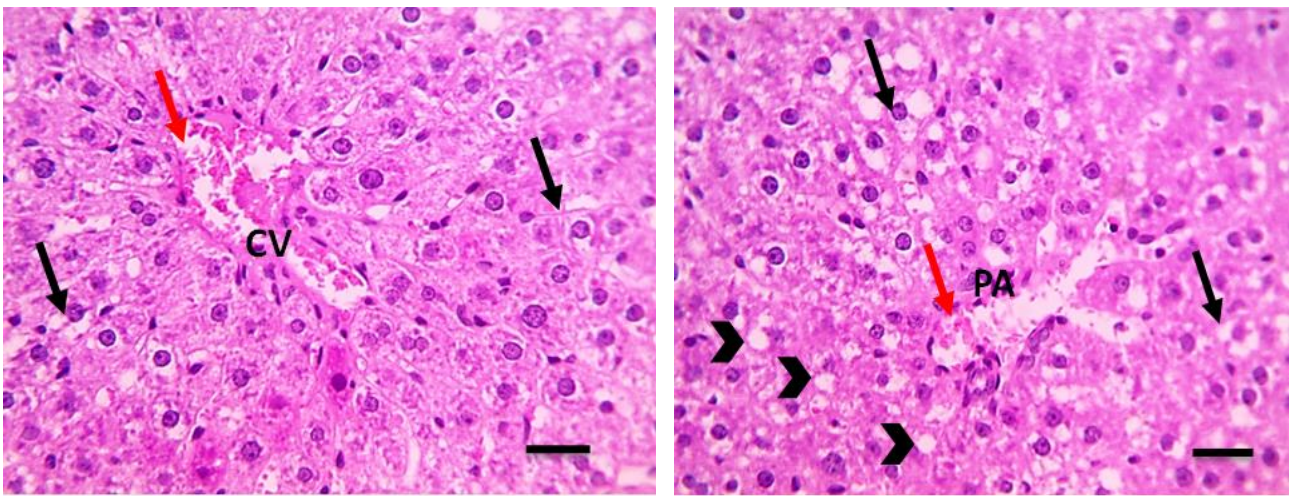


Photo (3 - 4) : liver of hyperlipidemic rat without treatment (control +ve group) showed disrupted hepatic architecture due to congestion (red arrows), swelling of hepatocytes (black arrows) around the central vein (CV)), hydropic degeneration (black arrows) with multiple large cytoplasmic vacuoles in hepatocytes (black arrowheads) around portal areas (PA) with occluded sinusoids**.**

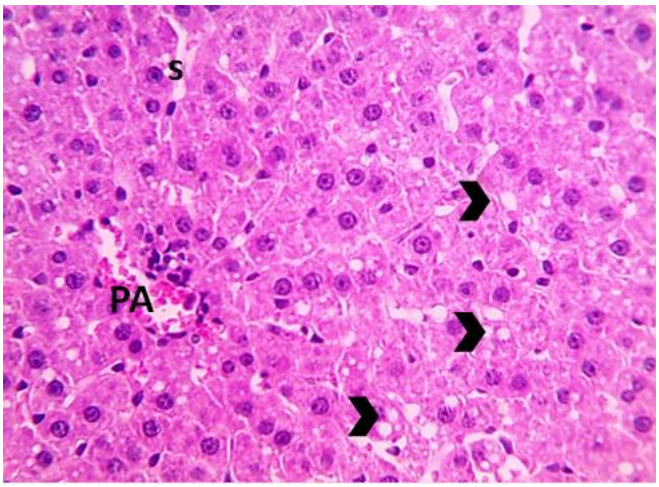
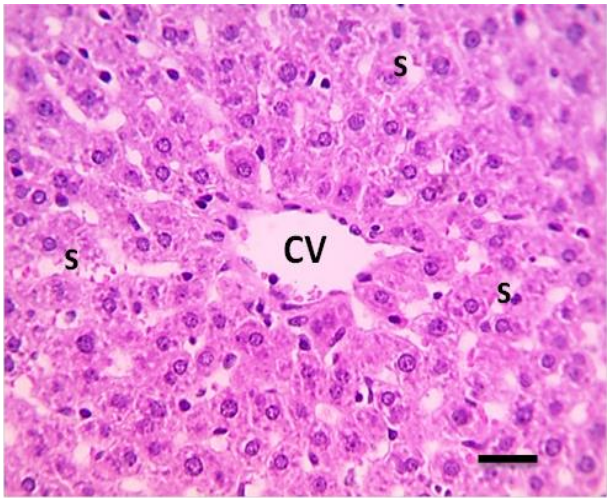
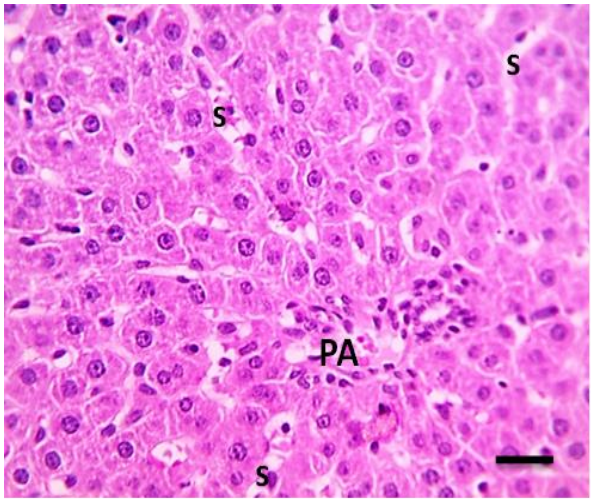
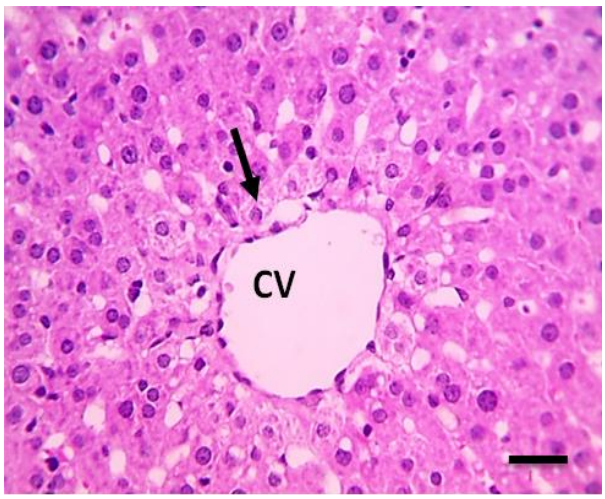


Photo (5) : Microscopic picture of hepatic sections from the treated group with fennel 5% showed partial disruption of hepatic architecture characterized by congestion (red arrows), few large cytoplasmic vacuoles in hepatocytes (black arrowheads) around portal areas (PA) with normal sinusoids (s) .





P hoto(6 - 7) : Hepatic sections from the treated group with fennel 10% showing retained the normal hepatic architecture characterized by normal arrangement of hepatic cords around the central vein (CV) with normal portal areas (PA) and sinusoids (s) .



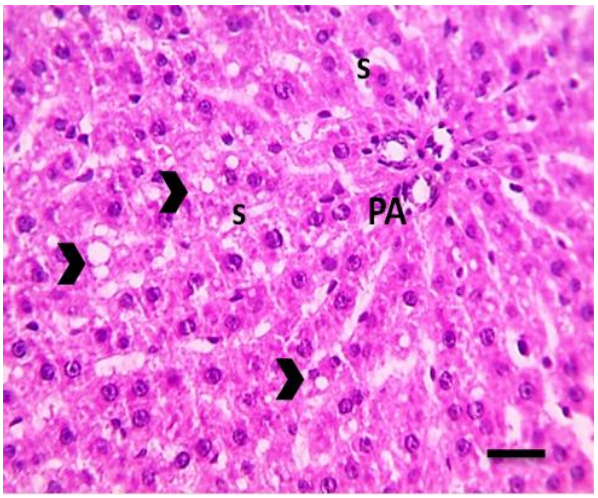


Photo (8 - 9) : Hepatic section from the treated group with Doum palm5% showing partial disruption of hepatic architecture characterized by hydropic degeneration (black arrows) in few hepatocytes (black arrows) around the central vein (CV), with few small and large cytoplasmic vacuoles in hepatocytes (black arrowheads) around portal areas (PA) with normal sinusoids (s) .

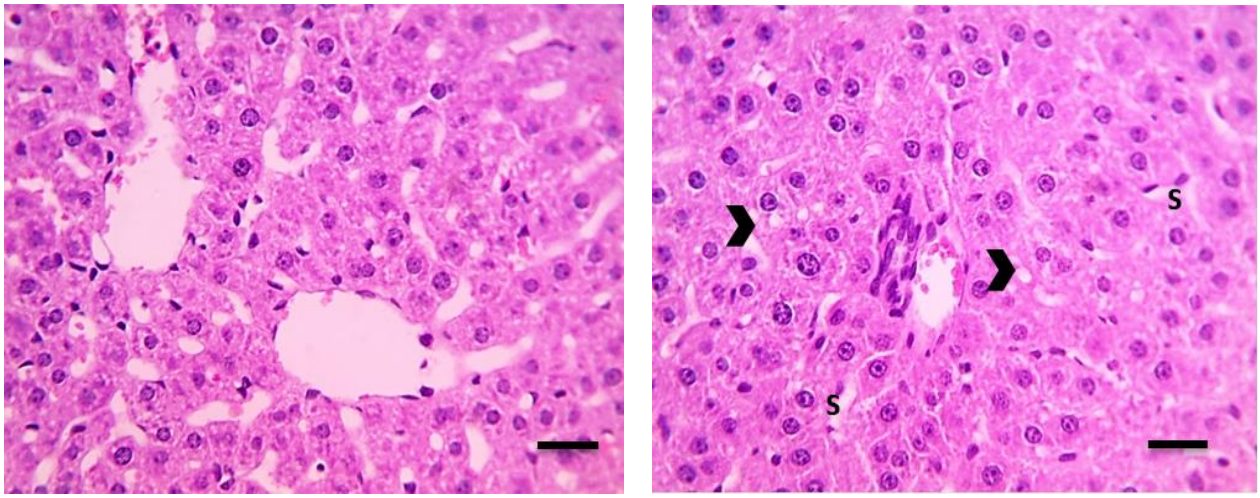


Photo (10 - 11) : Hepatic section from the treated group with Doum palm 10% showing great improvement of hepatic architecture normal hepatocytes around the central vein (CV), with few minute cytoplasmic vacuoles in hepatocytes (black arrowheads) around portal areas (PA) with normal sinusoids (s) .

Discussion

Hyperlipidemia is known as a risk factor for cardiovascular disease, especially atherosclerosis, which is one of the major causes of premature death globally and is expected to be the most important cause of mortality. It has been well established that nutrition plays an important role in the etiology of hyperlipidemia and atherosclerosis. The current study was aimed to investigate the effect of doum palm and fennel as anti- hyperlipidemic agents in experimental rats.

Hyperlipidemia is a metabolic disorder characterized by elevated levels of total cholesterol in the blood. Hypercholesterolemia may develop as a consequence of an unbalanced diet, obesity , inherited (genetic) diseases (familial hypercholesterolemia),or other diseases .

Polyphenols have antioxidant actions that increased interested with them in treatment of several diseases **(Reis *et al.*, 2016).** Phenols in fruits and vegetables are bioavailable and protect against oxidative stress and free radicals **(Luna-Vázquez, *et al.*, 2013).** Our result agrees with **Hossam *et al* ., (2018)** who suggested that the fruit of ***((Hyphaene thebaice))*** is a source of potent antioxidants and contains important substances including saponins , tannins , Flavonoids , terpenes and terpinoids . According to ***(Bayad, 2016)*** the fruits of *H. thebaica* have aphonolic , Flavonoids compounds, antimicrobial, antioxidant, antidiabetic, antihypertensive and hypolipidemic effects. **Abbas *et al* ., (2019)** reported that ***(Foeniculm vulgar)*** is a rich source of natural antioxidants , phonolic compounds and flavonoids . It also known to promote menstruation , being useful in child birth , anti-bacterial , hepato protective and anti - in flammatory activities in many in vitro and invivo settings . Also, **Rather *et al* ., (2016)**

confirmed that ***(Foeniculum vulgar)*** is abiennial aromatic and medicinal member of Apiacecae Family. It contains several types of phenolic and flavonoids that is known as antioxidants and had strong free radical scavenging and it is of the most effective antioxidants in the food industry. Also **Jamwal *et al* ., (2013)** who reported that medicinal plants are a principal source in health care about 80 % word's population in the form of plant extracts or their active components as a result of their properties **.** *Foeniculum vulgar* belong to the group of medicinal herbs which are used for the treating various ailments because of their antioxidant action and phenolic compounds .

Our result agree with **Nwosu *et al* ., (2018)** who reported that the Doum palm fruits contains 8.10 % ash, 0.95 %ether extract, 0.01 %protein, 89.25 %carbohydrate, 3655.9 Kcal/kg Metabolizable energy . Also ***Aboshora et al., (2014)*** who reported that doum palm contained high amount of amino acids valine, leucine, and some nonessential amino acids such as (alanine, aspartic acid, glutamic acid, glycine, serine and proline). Also it was very rich in minerals such as potassium (K) and phosphorous . Also, **Elghazaly *et al.*, (2019)** who reported that The seeds of fennel contain fiber and complex carbohydrates**.** Additionally, fennel volatile oil is amixture of different chemicals and the main ingredients are: trans- anethole ، fenchone and estragole .

The obtained findings, showed significant increase of BWG% in positive control group as compared to negative control group .All treated groups with doum-palm and fennel recorded significant decrease in BWG% as compared to control positive group . It may be due to polyphenols in fennel and doum that decrease oxidative stress . Our results in line with **Lozano *et al.*, (2016)** who confirmed that high fat diet increase body weight and demonstrated the role of oxidative stress in pathogenesis as well as in complications (hepatic and vascular). Also, **Zeng-Jie Xu *et***

***al,* (2009)** noticed that the high fat diet (HFD) fed rats were observed as significantly increased in point of body weight, epididymal fat weight and liver index comparing to the control group rats.

Our results agree with **A-Lamer , (2012)** who shows that BWG% was significantly increased in the rats group that treat with doum additionally, FI and FER as compared to negative control group but reduce the BWG comparing with positive control group , The increase in body weight could be explained due to the high level of nutrients (carbohydrates, sugar, amino acids, and fatty acids) in doum fruits which has effect on body weight gain in mice **(Aboshora *et al.*, (2017); Mohammed and Zidan, (2018) and El-Ghany *et al.*,(2014)**. Also **El-Masry, Soheir (2012)** reported that consumption of doum has a best significant treatment effect against increasing of weight gain, food efficiency ratio of hepatic rats.

Also, **Parsaeyan, (2016)** reported that the effect of diet supplemented with fennel on hyperlipidemic rats was a great significant treatment against increasing of weight gain which reduce body weight gain and food intake as compared to positive control group.

Results obtained in present study showed that there was a significant decrease in the relative liver weight on hyperlipidemia male rats that used different doses from doum fruit and fennel powder when compared to the control positive group. These results were confirmed by histopathological examination of liver which showed the presence of fatty changes of hepatocytes. Our finding are agreement with those results obtained by **(Matos et al., 2005)** who reported that increasing relative liver weight of hyperlipidemia male rats could be a consequence of the higher fat content on liver.

Our result agree with **Nanees, (2010)**who reported that feeding hyperlipidemic rats doum palm with diet significantly reduced liver , Heart and Spleen weight compared to control positive group. This result could be explained as follows, the possible mechanism underlying the hepatoprotective properties of the doum fruit is having five flavone glycosides were isolated and identified namely, luteolin 7-Oßglucuronoide, apigenin 7-O-ß-glucuronoide, luteolin O-ß-glycoside, luteolin 7-O-rutinoside and chrysoeriol 7-O-rutinoside. Antioxidant property is claimed to be one of the mechanisms of hepatoprotective . Also **Zafar *et al.*, (2009)** who reported that Feeding hyperlipidemic rats fennel with diet significantly reduced liver amd Spleen weight compared to control positive group. This action may be due to the presence of hepatoprotective activity of fennel.

In the present study, Serum glucose showed significant increase in positive control group of hyperlipidemic rats as compared to negative control group. This study agree with **Anon , (2015)** who reported that treated groups with doum palm recorded significant decrease in Serum glucose as compared to positive control group. Also, **Salah *et al* ., (2011)** reported that *H. thebaica* reduced the serum glucose levels significantly when compared with the positive control group. It may be due to presence of saponins in the constituents of doum palm which have hypoglycemic activity. Also, these results are in agreement with those found by **Bayad, (2016)** who reported that using doum with diets led to significant decrease in blood glucose. The doum has an effective ability in reducing blood glucose because it plays the role of insulin when glucose enters to the cells and achieving optimal use of glucose. Also, **Srinivasan *et al* ., (2012)**who reported that Doum is from medicinal plants that contain flavonoids. It was found that the administration of flavonoids extracts to diabetic rats significantly increased adiponectin levels that stimulate the hypoglycemic

action of insulin without altering the concentration of insulin in blood. Also, this study agreed with **parsaeyan,(2016)** who reported that hyperlipidemic rats treated with fennel had significant decrease in Serum glucose and increase the serum insulin levels and suggested that this hypolipedemic activity of fennel could be attributed to the presence of the valuable polyphenolic compounds and flavonoids. Also, **Anitha *et al* .,(2014)** reported that the hypoglycemic effect of fennel herb may be due to the increased level of serum insulin by increasing the pancreatic secretion of insulin from cells of islets of Langerhans or its release from bound insulin, and also may be due to the enhancement of peripheral metabolism of glucose .

In the present study, HFD in (positive control group) significantly ($p<0.05$) increased TC, TG, LDL-c and a significantly ($p< 0.05$) decreased HDL-c level compare with control negative group. These results in line with **Adekiya *et al.*, (2018)** who reported that keeping the animal on high fat-diet resulted in dyslipidemic changes as illustrated by the significant increase in serum TG, TC, LDL-C and VLDL-C, as well as a significant reduce in serum HDL-C level . These results were consistent with the studies of **Mariee *et al.*, (2012), and Harb *et al.*, (2018).** The results showed significant ($p< 0.05$) decrease in TC, TG, LDL-C levels accompanied with significant ($p< 0.05$) increased in HDL-c level in all treated groups with doum palm compared with control positive group. These results were consisting with **ElGendy et al., (2008) and Bayad, (2016)** studies which report that the administration of doum palm was significantly ($p<0.05$) reduced total cholesterol،triglycerides and LDL-C levels while significantly increasing the concentrations of HDL . Also **(Al-Amer and Huda; Rashwan, 2012)** who reported that using seeds of doum palm in experimental diet showed decreasing of serum atherogenic index (Al) of hyperlipidemic rats .

Also **Anitha *et al*., (2014)** confirmed that when high fat-diet was supplemented with the different levels of fennel seeds (5 and 10%), the elevated levels of TL, TG, TC, LDL-C and VLDL-C condition has shown considerable decline which were significantly. This decline as effect by feeding fennel seeds was more detectable with increasing the level of it. Moreover, serum level of HDL-C was significant increase, compared to feeding rats with high fat-diet only. Elevated level of HDL-C is considered as cardio protective effect. **Parsaeyan, (2016)** who reported that hyperlipidemic rats treated with fennel extract had significant decrease in plasma levels of TL, TG, TC, LDL-C and VLDL, and significant increase in HDL-C level. This result suggests that cholesterol-lowering activity of the fennel can result from a rapid catabolism of LDL-C through its hepatic receptors for final elimination in the form of bile acids as demonstrated by **Anitha *et al* .,(2014)**who suggested that the hypolipedemic activity of fennel could be attributed to the presence of the valuable polyphenolic compounds especially tannins, and flavonoids. Also **parsaeyan,(2016)** reported that hypolipedemic effect of fennel may be due to the high content of polyunsaturated fatty acids from omega-6 and omega3 families that found in this plant and these compounds have strong biological properties in low concentrations.

Liver function tests, which include liver enzymes, are groups of clinical biochemistry laboratory blood assays designed to give information about the state of liver functions. The used serum liver chemistry test in the present study includes serum AST, ALT and ALP. The activities of AST and ALT are cytosolic marker enzymes reflecting hepatocellular necrosis as they are released into the blood after cell membrane damage. Therefore, we used the activities of AST, ALT and ALP in the circulation as indicators of hepatic functions **(McGill, 2016)**.

In the current study data revealed that significant increase in the activities of liver enzymes (AST, ALT and ALP) in feeding rats with high fat-diet. These elevations in liver enzymes may be attributed to their release from the cytoplasm into the blood circulation after rupture of the plasma membrane, cellular damage. This result confirmed by histological changes of liver sections of positive control rats .

This observed in the elevations were agreed with **McGill, (2016)** who reported that elevated activity of serum AST are a common sign of liver and cardiovascular diseases. The observed increases in serum AST and ALT levels may be attributed to excessive release of such enzymes from the damaged liver cells as a result of hyperlipidemia into the blood circulation. Where, there is an inverse relationship between the liver activity and the level of enzymes in serum. Since AST and ALT were significantly higher in fatty liver and the severity of fatty liver was positively related to increases in hyperlipidemia, so AST and ALT were significantly higher in hyperlipidemic cases. **El-Masri (2012) and AL-amer *et al.*, (2012** reported that treatment of the hyperlipidemic rats with Hyphaene thebaica showed reduction in ALT, ALP, AST as compared with untreated group which revealed that administration of doum can improve liver functions .

Also, **Zafar *et al.*, (2009)** who revealed that feeding rats with high fat-diet supplemented with different levels of fennel seeds produce significant decrease in serum AST, ALT and ALP levels and improved liver functions compared to the feeding rats with high fat diet only. This effect may be related to antioxidant properties of fennel. Also **Ozbek *et al* ., (2006)** reported that essential oil of fennel had hepatoprotective activity against carbon tetrachloride (CCl_4) which induces liver injury in rat's model as it decreases levels of serum AST, ALT, ALP and bilirubin. Fennel contains several types of phenolic and flavonoids that is known as

antioxidants and had strong free radical scavenging. It is of the most effective antioxidants in the food industry. Also **Jamwal *et al* ., (2013)** reported that fennel have D-limonene and ß-myrcene compounds found in fennel (Foeniculum vulgare) have a potent hepatoprotective action.

Our study showed that lipid–peroxidation was increased significantly in hyperlipidemic control rats as indicated by the increased in serum MDA level compared with the normal control rats. The activities of SOD and GP_X enzymes were significantly decreased in hyperlipidemic control rats when compared with normal control rats. This study agreed with **Prasad *et al*., (2006)** showed significant increase in serum MDA levels, a decrease in SOD and GP_X activity in hypercholesterolemic. These results suggest that hypercholesterolemia produces oxidative stress in the myocardium which may be due to a decrease in the antioxidant reserve. This results agreement with **El-Masri, (2012)** who reported that doum powder supplements showed a significant increase in the values of liver SOD and GP_X and significant decrease in MDA when compared with control positive group . Our finding agreed also with **Abd el Halim, (2020)** who showed that doum fruit can increase the level of GPX and SOD in hyperlipidemic rats but decrease the level of MDA . Also **(Huyut et al., 2017)** who suggested that Doum contains high levels of flavonoids and phenols that have antioxidant properties also, it is known that phenolic compounds act as antioxidants because of their ability to give the hydrogen molecule and in addition to molecule inhibiting lipid oxidation . Our result in line with **(Yogendrasinh and Rajendra.,2010)** who reported that Feeding rats with high fat-diet supplemented with (5%and 10%) fennel seeds produced significant reduce in serum MDA and significant increase the activities of GP_X and SOD enzymes compared to the feeding rats with high fat-diet only. Therefore, fennel seeds

reduced oxidative stress and improve antioxidant defense. This action of fennel may be related to its antioxidant activity. This result agreed with **Eman *et al*.,(2011).** who showed that fennel has antioxidant effects, reducing MDA level and increasing plasma SOD as well as GP_X activities. Aqueous extracts of fennel provide to have antioxidant activity higher than some well-known antioxidant such as ascorbic acid.

Finally Histopathological analysis of liver section of rats that treated with doum and fennel powder showed Amelioration improvement of histological changes caused by high level of hyperlipidemia when compared with control positive group.

Conclusion

In conclusion, this study evaluated the effect of Doum-palm and Fennel as anti-hyperlipidemic agents in experimental rats. Which in Doum-palm and Fennel have contained amount of phenolic compounds and flavonoids, which may play important role as natural antioxidants. The consumption of doum-palm and fennel (5 and 10%) could be used for improving lipid profile, liver function and protect from the risk factor of hyperlipidemia in experimental rats.

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