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TIKRIT JOURNAL OF PURE SCIENCE

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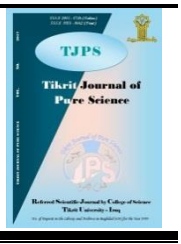

Comparison of the effect of the alcoholic extract of leaves and fruits of hawthorn plant *Crataegus azarolus* with the drug simvastatin in its effect in reducing cardiovascular disease in male rabbits with experimental fat disorder

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ARTICLE INFO.

Article history:

-Received: 13 / 11 / 2017

-Accepted: 20 / 2 / 2018

-Available online: / / 2018

Keywords: *Crataegus azarolus*, Cholesterol, High Density Lipoprotein, Low Density Lipoprotein, Triglycerides, HMG-CoA Reductase.

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Abstract

This study designed to investigate the role of both Ethanolic extracts of hawthorn leaves and fruits in reducing cardiovascular risk factors in male with experimental lipid disorders. 50 male rabbits of New Zealand, 1250-1500g and 8-10 months old used in this study. Rabbits divided into 10 groups (each group 5 male rabbits). The (I) group as a control group, which given the free standard diet and water. The (II) group given high cholesterol (260 mg/Kg) of the weight as a standard diet, the (III) group, which given high cholesterol diet with extracts of *C.azarolus* (200 mg/kg) of body weight, the (IV) group which given high cholesterol diet with hawthorn fruit extract (20 mg/kg) Of the body weight, the the (V) group, which was given high cholesterol diet of body weight, the (VI) group, which given high cholesterol diet with vitamin C (100 mg / kg) of body weight, group (VII), which is the drug of simvastatin, group (VIII), which given vitamin C, the(IX) group given Hawthorn leaf extract, the (X) group, which given extracts fruit of hawthorn plant. The experiment conducted for six weeks. Statistical analysis showed a significant increase ($P<0.05$) in the lipid profile variables (total cholesterol, triglyceride, LDL, VLDL and HDL) in the serum and liver extract in the high cholesterol group compared with the control group. Fruits play a more effective role in the prevention of hyperlipidemia compared with vitamin C and the drug of simvastatin and leaf extract. The study also showed a significant decrease ($P< 0.05$) in the effectiveness of HMG-CoA reductase (HMGR) in the group treated with the drug Simvastatin compared with the control group, while there were no significant differences in the group which given high cholesterol , vitamin C group , extracts of leaves and fruits of the plant group. The conclusion, have found that ethanolic extracts of *C. azarolus* Low levels of lipids (cholesterol and triglycerides) in the serum of animals experiment with the use of the drug Simvastatin and the fruits of hawthorn plant the largest role compared with vitamin C and extract leaf hawthorn. On the other hand, the non-change in the concentration of the enzyme HMG-CoA reductase in the serum and liver extract indicates that the role of the extract in the normalization of lipid variables is centered on other mechanisms related to the digestive system, such as absorption.

Introduction

Atherosclerosis is a chronic inflammatory disease that occurs in the large and medium arteries and is usually associated with hyperlipidemia at baseline or with other risk factors [1,2]. These factors can be divided into two categories of undetermined risk factors including age, gender, heredity and adjustable risk factors, including hypertension, dyslipidemia, diabetes, autoimmune disease [3]. The disease affects the coronary arteries and the cerebral arteries in particular, where the deposition of fatty substances

and cholesterol and the remnants of cellular products and platelets on the inner wall of the vessel consists of the so-called clot or plug (Plaque), which may close the blood vessel and prevent feeding the heart or the organ that supplies the artery causing the blood clot when detonated and damage to tissues of those organs [4]. The liver is the main organ in the process of controlling and regulating the levels of cholesterol in the body. In mammalian cells, the concentration of cholesterol within cells is regulated by internal construction and extrusion (by the diet). The internal structure is mediated by feedback by hepatic HMG-CoA reductase, while the external source is controlled by LDL receptors. The HMG-CoA reductase enzyme reduces the HMG-CoA to mevalonate, which is the specific step for the cholesterol biosynthesis [5]. For the purpose of atherosclerosis treatment, the current studies have been directed to plant extracts because of its antioxidant, anti-inflammatory and lipid properties. Among these plants are *Crataegus azarolus*, which is present in many countries including Europe, Asia and North Africa [6,7]. Alcoholic and aquatic extracts of leaves, flowers and wild hawthorn fruits have high therapeutic and pharmacological properties, as they contain very important chemicals such as flavonoids, triterpenic acids, phenol carboxylic acids and oligomericprocyanidins (OPC). These substances have antioxidant properties. which is the cause of atherosclerosis and many diseases related to fat imbalance [8,9,10]. Chronic inflammation is non-inflammatory T controlled increase the risk of atherosclerosis and that the use of fruits and leaves extracts blocks hawthorn acts as an anti-inflammatory to reduce the ferocity of atherosclerosis [11,12].

The present study aims to investigate the role of both alcoholic extracts of wild hawthorn leaves and fruits in reducing and improving the cardiovascular risk factors in male New Zealand rabbits infected with experimental lipid disorder.

Materials and Methods

Collection and preparation of plant extracts

Leaves and fruits of the wild hawthorn plant *Crataegus azarolus* were used. The samples collected in October 2016 from the Kordi-Merkban districts of Sulaymaniyah Governorate. Clean the leaves and fruits and then dried and crushed using an electric grinder. Leaf and fruit powder extracted based on the method used by [13]. The leaves and fruits extracted by 1 g of leaf powder per 10 ml of ethyl alcohol at a concentration of 90%.

Experiment animals

In this study, 50 male Albino Rabbit, aged 6-8 months, and weight (1000-1250 g) obtained from the local market. It ascertained that there were no skin lesions and diseases by detecting them before Veterinarians from the Faculty of Veterinary Medicine \ University of Tikrit. Rabbits were randomly divided into 10 groups (5 rabbits per group) as follows:

1. The I group (control group): This group treated by giving them a standard cholesterol-free diet with distilled water daily throughout the experiment.
2. The II group (cholesterol group): This group treated by giving a standard diet plus hyperlipidemic diet (HLD) with a concentration of 260 mg/kg [14] of the weight of the diet on a daily basis for the duration of the experiment.
3. The III group (cholesterol group and hawthorn extract): This group treated with a standard meal (HLD) and was extracted with the extract of hawthorn leaves at a concentration of 200 mg / kg body weight [15].
4. The IV group (cholesterol group and hawthorn extract): This group treated with a standard meal (HLD) and was extracted with hawthorn fruit extract at a concentration of (20 mg / kg) of body weight [16] daily throughout the experiment.
5. The V group (the cholesterol group and Simvastatin): This group treated with a standard meal (HLD) and Simvastatin was injected with a concentration of 0.3 mg / kg [14] of body weight on a daily basis throughout the trial period.
6. Group VI (cholesterol and vitamin C group): This group treated with a standard meal (HLD) and was treated with vitamin C at a concentration of 100 mg / kg [15] of body weight on a daily basis throughout the trial period.
7. The group VII (Simvastatin group only): This group treated with Simvastatin only at a concentration of 0.3 mg/kg body weight on a daily basis throughout the trial period.
8. Group VIII (vitamin C group only): This group treated with vitamin C only at a concentration of 100 mg / kg body weight daily throughout the trial period.
9. The IX group (Hawthorn extract group only): This group treated with hawthorn leaf extract only at a concentration of 200mg/kg body weight daily throughout the experiment.
10. The group X (Hawthorn fruit extract group only): This group treated with the extract of hawthorn fruits at a concentration of (20 mg / kg) of body weight on a daily basis throughout the experiment.

Determination of Total Cholesterol, Triglycerid, High density Lipoprotein Concentration

The concentration of total cholesterol, triglycerides and high density lipoproteins (HDL-C) in serum and liver extract estimated using the Kit manufactured by the French company BIOLABO SA, based on Tietz et.al. [17] and Allan and Dawson[18]. Low-density lipoproteins (LDL-C) only concentrated by [17], whereas the concentration of very low-density proteins (VLDL-C) according to [19], according to [20].

Determination of HMG - CoA Reductase Concentration: The concentration of the HMG-CoA Reductase enzyme estimated using MyBiosource analysis kit. using Elisa technology.

Analysis Statistical

The values were statistically analyzed using the Minitab statistical analysis program and the results presented in the mean arithmetic mean ± standard error. The results of the present study were statistically analyzed by the ANOVA test for the purpose of detecting significant differences by comparing the arithmetic averages of the different experimental groups and using the Duncun Multiple Rang test.

Results

The results of the present study showed significant differences (P <0.05) in all lipid parameters at treated group compared with control group. Table 1 shows that there are significant differences (P <0.05) in the concentrations of total cholesterol, triglycerides, low density lipoproteins, very low density lipoproteins and the indication of harvest in serum fed on a high fat diet (213.5 ± 6.4, 240.5 ± 9.2, 136.9 ± 8.5, 48.1 ±1.4, 7.49 ± 0.032mg/100 ml serum) respectively compared with control group. It was also observed that the total cholesterol concentrations in the group fed on a high-fat diet and treated with leaf extract (141±5.7) was significantly reduced. In the group fed on a high-fat diet and treated with vitamin C (156 ± 4.2) With the control group (119.5±17.7). The total cholesterol levels in the group fed on a high-fat diet and treated with simvastatin (125.5 ± 19.1), and in the group fed on a high-fat diet and treated with fruit extract (129±14.1) showed no significant differences (P<0.05) compared with control group as shown in Table (1). The results showed a significant increase (P<0.05) in serum triglycerides (240.5± 9.2) in the group of animals fed on a high-fat diet compared with the control group (138.5±6.4). It is also noted that the groups of animals fed on a high-fat diet and its dosage by the alcoholic extract of leaves and fruits of wild hawthorn plant and the drug Simvastatin and vitamin C showed a significant decrease (P<0.05) in the concentration of triglycerides (182.5± 6.4, 171± 19.8,160.5± 6.4, 192 ±11.3) respectively compared to the HLD control group. While the extracts of the leaves of the hawthorn plant and of the simvastatin and vitamin C alone showed a significant decrease in the concentrations of triglycerides (113.5±13.4, 102±11.3, 101±15.6, 110±9.9), respectively, compared to the control group. The results showed a significant decrease (P<0.05) in HDL-c (28.5±2.3) group of animals fed on a high-fat diet compared to the control group (41±5.7). It is also noted that the groups of animals fed on a high-fat diet and its dosage by the alcoholic extract of leaves and fruits of wild hawthorn plant and the drug Simvastatin and vitamin C showed a significant increase (P <0.05) in the concentrations of HDL-c (39 ± 1.4, 46 ± 4.8, 43.5 ± 3.4 , 38.5 ± 2.1) respectively compared to the HLD infected control group. The groups of animals with the extract of the leaves and fruits of hawthorn plant and the drug of the simvastatin and vitamin C alone did not show significant differences in the concentrations of HDL-c (41 ± 3.8, 50 ± 1.7, 42 ± 4.2, 40± 7.1), respectively, compared to the control group sound. On the other hand, the results of the current study also showed a significant increase (P<0.05) in the concentrations of LDL-c (136.9±8.5) in the serum group of animals fed on a high-fat diet compared to the control group sound (50.8 ± 15.7). It is also noted that the groups of animals fed on a high-fat diet and its dosage by the alcoholic extract of leaves and fruits of wild hawthorn plant and the drug Simvastatin and vitamin C showed a significant decrease (P <0.05) in the concentration of LDL-c (65.5±1.4,48.8 ± 12.6, 49.9 ± 2.1, 79.1 ± 13.2) respectively compared with the HLD infected control group. While the serum extracts of the leaves of the hawthorn plant and of the simvastatin and vitamin C alone showed a significant decrease in LDL-c (22.7 ± 2.8, 20.4 ± 2.1, 20.2 ± 2.8, 28 ± 28), respectively, compared to the control group.

The results showed a significant decrease (P <0.05) in VLDL-c (48.1±1.4) serum group of animals fed on a high-fat diet compared with the control group (27.7 ±1.4). It is also noted that the groups of animals fed on a high-fat diet and its dosage by the alcoholic extract of leaves and fruits of wild hawthorn plant and the drug Simvastatin and vitamin C showed a significant decrease (P <0.05) at the concentrations of VLDL-c (36.5 ± 0.7, 34.2 ± 3.5, 32.1 ± 1.5 , 38.4 ± 2.1) respectively compared to the HLD infected control group. The groups of animals with the extract of the leaves and fruits of Hawthorn plant and the drug Simvastatin and vitamin C alone did not show significant differences in the concentrations of VLDL-c (21.3 ± 2.7, 11.6 ± 3.9, 16.3 ± 12, 22 ±1.3), respectively, compared to the control group. The results of the assessment of the serum Atherogenic index of the group animals fed on a high fat diet (7.49±0.032) showed a high morale (P<0.05) compared to the control group (2.91±0.031). In addition, the results indicated that the dosage of animal groups fed with high-fat diets with leaf extract and fruits of hawthorn, simvastatin and vitamin C resulted in a significant decrease (P<0.05) in the Atherogenic index (3.61 ± 0.233, 2.8 ± 0.026, 2.88 ± 0.03, 4.05±0.042) respectively compared to the group of animals fed on a high-fat HLD diet. The total number of animals fed with hawthorn leaves and fruits extract and vitamin C alone showed a significant decrease in the Atherogenic index (2.07±0.031,1.64±0.023,1.86±0.029,2.25±0.019), respectively, compared with the control group. As for the concentration of the enzyme, the results showed no significant differences in the effectiveness of the enzyme HMG-CoA reductase (1.355±0.078) in rabbit serum, which was fed on a diet high in fat compared with the group of rabbits in the control of sound (1.41±0.057). In addition, the efficacy of the enzyme in the rabbits fed on a high-fat diet with the leaf and fruit extract of hawthorn and vitamin C showed no significant differences (1.352±0.035,1.33± 0.028,1.36 ± 0.051), respectively, compared to the HLD control

group . On the other hand, the group of animals fed high-fat diets and simvastatin showed a significant increase (P<0.05) in enzyme concentration (1.145± 0.049) compared to the HLD control group. The results indicated that there was no significant difference in the efficacy of the enzyme in the rabbits with the extract of leaves and fruits of hawthorn plant and vitamin C only (1.355 ± 0.05, 1.3 ± 0.041, 1.35 ± 0.077), respectively, compared to the control group. While the experimental animals showed only a significant reduction in the concentration of enzyme HMG-CoA reductase of simvastatin alone (p<0.05) (1.05 ± 0.057) compared to the control group as shown in Table (1).

Table (1): The effect of the treatment of cholesterol and the alcoholic extract of leaves and fruits of wild hawthorn plant and the drug of the simvastatin and vitamin C in the lipid profile and the concentration of the enzyme HMGR and the Atherogenic index in the blood serum of male rabbits.

Parameters / Groups	Total Cholesterol mg/dl	Triglyceride mg/dl	HDL mg/dl	LDL mg/dl	VLDL mg/dl	HMGR ng/ml	Atherogenic index
Control	119.5±17.7 c	138.5±6.4 c	41±5.7 ab	50.8±15.7 c	27.7±1.4 c	1.41±0.057 a	2.91±0.031 c
hyperlipidemic diet	213.5±6.4 a	240.5±9.2 a	28.5±2.b	136.9±8.5 a	48.1±1.4 a	1.355±0.078 a	7.49±0.032 a
leaf extract +HLD	141±5.7 b	182.5±6.4 b	39±1.4 ab	65.5±1.4 bc	36.5±0.7 b	1.352±0.035 a	3.61±0.233 b
fruit extract +HLD	129±14.1 c	171±19.8 bc	46±4.8 ab	48.8±12.6 c	34.2±3.5 bc	1.33±0.028 a	2.8±0.026 c
simvastatin + HLD	125.5±19.1 c	160.5±6.4 bc	43.5±3.4 ab	49.9±2.1 c	32.1±1.5 bc	1.145±0.049 b	2.88±0.03 c
vit.C + HLD	156±4.2 b	192±11.3 b	38.5±2.1 ab	79.1±13.2 b	38.4±2.1 b	1.36±0.051 a	4.05±0.042 b
simvastatin only	78.5±7.8 d	101±15.6 d	42±4.2 ab	20.2±2.8 d	16.3±12 d	1.05±0.057 b	1.86±0.029 e
vit.C only	90±4.2 d	110±9.9 d	40±7.1 ab	28±28 d	22±1.3 d	1.35±0.077 a	2.25±0.019 d
leaf extract only	85±5.7 d	113.5±13.4 d	41±3.8 ab	22.7±2.8 d	21.3±2.7 d	1.355±0.05 a	2.07±0.031 de
fruit extract only	82±8.5 d	102±11.3 d	50±1.7 a	20.4±2.1 d	11.6±3.9 d	1.3±0.041 a	1,64±0.023 e

As for liver tissue extract, the results in Table (2) showed a significant increase (P<0.05) in the total cholesterol concentrations (123±7.1) in the liver tissue of the group of animals fed on a high fat diet compared with the control group (87.5±3.5). It is also noted that the groups of animals fed on a high-fat diet and its dosage by the alcoholic extract of leaves and fruits of wild hawthorn plant and the drug Simvastatin and vitamin C showed a significant decrease (P<0.05) in total cholesterol concentrations (97.5±5,93.5±7.8, 90.5±3.5,104.5±5) respectively compared to the HLD infected control group. The total number of animals in the alcoholic extract of leaves and fruits of Hawthorn and Simvastatin alone showed a significant decrease (P<0.05) in the total cholesterol concentrations (76±6.4, 72±4.9,70±7.1), respectively, compared with the control group. While the vitamin C group (80±4.2) did not show a significant difference compared with the control group. The results of the current study, as shown in Table 2, showed a significant increase (P<0.05) in the concentrations of triglycerides (172.5±7.8) in the liver tissue of the group of animals fed on a high fat diet compared to the control group (98.5±12.1). It is also noted that the groups of animals fed on a high-fat diet and its dosage by the alcoholic extract of leaves and fruits of wild hawthorn plant and the drug Simvastatin and vitamin C showed a significant decrease (P<0.05) in the concentration of triglycerides (126.5±7.7,106 ±7.8,102±2.8,120.5±3.5) respectively compared to the HLD infected control group. While the serum groups of the hawthorn leaf, the simvastatin and the vitamin C alone did not show a significant difference in the concentrations of triglycerides (84.5±3.6,85±2.8,98.5±13.4), respectively, compared to the control group. (80±4.2) showed a significant decrease compared with the control group. On the other hand, the results showed a significant decrease (P<0.05) in HDL-c (25.4±3.3) in the liver tissue of the group of animals fed on a high-fat diet compared with the control group (31.5 ± 0.7). It is also noted that the groups of animals fed on a high-fat diet and its dosage by the alcoholic extract of wild hawthorn leaves and fruits and the drug Simvastatin and vitamin C showed a significant increase (P<0.05) in HDL-c(30±1.4,31±1.4,32±1.3,29±2.1) respectively compared to the HLD infected control group. The animal extracts of the hawthorn leaves and the fruits of the hawthorn plant and the simvastatin and vitamin C alone did not show a significant difference in HDL-C(32.5±3.7.34.5±3.1,34.3±1.4,30.5±7.1), respectively , compared to the control group.

The results of the present study showed a significant increase (P<0.05) in the concentrations of LDL-c (63.1±4.3) in the liver tissue of the group of animals fed on a high-fat diet compared with the control group (36.3±2.9). It is also noted that the groups of animals fed on a high-fat diet and its dosage by the alcoholic extract of leaves and fruits of wild hawthorn plant and the drug Simvastatin and vitamin C showed a significant decrease (P<0.05) in the concentration of LDL-c (42.2 ± 3.5,41.3 ± 6.4, 38.1 ± 5.4,51.4±3.6) respectively compared to the HLD infected control group. While the serum extracts of hawthorn leaves and fruits of the hawthorn plant and of the simvastatin and vitamin C alone showed a significant

decrease in LDL-c (26.6±5.1,21.5±2.4,18.7±5.7, 29.8±4.1) respectively compared to the control group. The results showed a significant decrease (P<0.05) in VLDL-c (34.5± 2.2) in the liver tissue of the group of animals fed on a high-fat diet compared with the control group (19.7±2.1). It is also noted that the groups of animals fed on a high-fat diet and its dosage by the alcoholic extract of leaves and fruits of wild hawthorn plant and the drug simvastatin and vitamin C showed a significant decrease (P<0.05) at the concentrations of VLDL-c (25.3±1.4, 21.2±1.4, 20.4±0.7,24.1±0.7) respectively compared to the HLD infected control group. The groups of animals with the extract of the leaves and fruits of Hawthorn plant and the drug simvastatin and vitamin C alone did not show significant differences in the concentrations of VLDL-c (16.9±0.7,16±0.8,17±0.8, 19.7±6.4), respectively, compared to the control group. Also, the results of the assessment of the evidence in the liver tissue of the group animals fed on a high fat diet (4.84 ± 0.065) (Table 2) showed a high morale (P <0.05) compared with the control group (2.77 ± 0.014). In addition, the results indicated that the dosage of animal groups fed with high-fat diets with leaf and fruit extracts of hawthorn, simvastatin and vitamin C resulted in a significant decrease (P <0.05) in the Atherogenic index (3.25 ± 0.017,3.01±0.045,2.82±0.039,3.6±0.028) respectively compared to the group of animals fed on a high-fat HLD diet. The groups of animals fed by the fruit extract of Hawthorn and simvastatin alone showed a significant decrease in the Atherogenic index (2.08±0.011,2.04±0.047), respectively, compared with the control group. The animal groups of the leaf extract for hawthorn and vitamin C (2.33±0.038, 2.62±0.013) did not show a significant difference compared to the control group. As for the effectiveness of the enzyme, the results of the present study showed no significant differences in the effectiveness of the enzyme HMG-CoA reductase (1.73 ± 0.021) in rabbit liver tissue, which was fed on a diet high in fat compared with the group of rabbits in the control of sound (1.78± 0.065) . In addition, the efficacy of the enzyme in the rabbits fed on a high-fat diet with the leaf and fruit extract of hawthorn and vitamin C showed no significant differences (1.71± 0.045,1.69±0.205,1.77±0.056) respectively compared to the HLD control group . On the other hand, the group of animals fed high-fat diets and simvastatin showed a significant increase (P<0.05) in enzyme efficacy (1.59 ± 0.036) compared to the HLD control group. The results indicated that there was no significant difference in the efficacy of the enzyme in the rabbits with the extract of leaves and fruits of hawthorn plant and vitamin C only (1.71±0.049, 1.75±0.318,1.76±0.035), respectively, compared to the control group. (P<0.05) (1.38 ± 0.057) compared with the control group as shown in Table (2).

Table (2): The effect of the treatment of cholesterol and the alcoholic extract of leaves and fruits of wild hawthorn plant and the drug of the simvastatin and vitamin C in the lipid profile and the concentration of the enzyme HMGR and the Atherogenic index in the liver extract of male rabbits.

Parameters / Groups	Total Cholesterol mg/dl	Triglyceride mg/dl	HDL mg/dl	LDL mg/dl	VLDL mg/dl	HMGR ng/ml	Atherogenic index
Control	87.5±3.5 b	98.5±12.1 b	31.5±0.7 b	36.3±2.9 b	19.7±2.1 c	1.78±0.065 a	2.77±0.014 c
hyperlipidemic diet	123±7.1 a	172.5±7.8 a	25.4±3.3 c	63.1±4.3 a	34.5±2.2 a	1.73±0.021 a	4.84±0.065 a
leaf extract +HLD	97.5±5 ab	126.5±7.7 ab	30±1.4 b	42.2±3.5 b	25.3±1.4 b	1.71±0.045 a	3.25±0.017 b
fruit extract +HLD	93.5±7.8 b	106±7.8 bc	31±1.4 b	41.3±6.1 b	21.2±1.4 c	1.69±0.205 a	3.01±0.045 b
simvastatin + HLD	90.5±3.5 b	102±2.8 b	32±1.3 b	38.1±5.4 b	20.4±0.7 c	1.59±0.036 b	2. 82±0.039 c
vit.C + HLD	104.5±5 ab	120.5±3.5 ab	29±1.5 bc	51.4±3.6 ab	24.1±0.7 b	1.77±0.056 a	3.6±0.028 b
simvastatin only	70±7.1 c	85±2.8 bc	34.3±1.4 a	18.7±5.7 c	17±0.8 d	1.38±0.057 b	2.04±0.047 d
vit.C only	80±4.2 bc	98.5±13.4 b	30.5±4.1 bc	29.8±4.1 c	19.7±6.4 c	1.76±0.035 a	2.62±0.013 c
leaf extract only	76±6.4 c	84.5±3.6 bc	32.5±3.7 bc	26.6±5.1 c	16.9±0.7 d	1.71±0.049 a	2.33±0.038 cd
fruit extract only	72±4.9 c	80±4.2 c	34.5±3.1 a	21.5±2.4 c	16±0.8 d	1.75±0.318 a	2.08±0.011 d

Discussion

As mentioned above, hyperlipidemia events in rabbits have led to a rise in total cholesterol, triglyceride, low density lipoprotein, very low density lipoprotein, low concentrations of high density lipoprotein Both serum and liver extracts. Where the results of the current study agreed with the results of Al-Ashlash [21] in the study and attributed the researcher caused the high concentration of cholesterol in the group treated with cholesterol to a defect in the process of fat metabolism, or a defect in the process of absorption and subtraction of steroids or perhaps because of low concentration of bile salte. Simvastatin and its role in lowering body fat levels have been agreed with

Trapani et.al.[22], who noted that the low concentration of cholesterol in Simvastatin is due to the inhibition of the HMG-CoA reductase enzyme responsible for the formation of cholesterol in liver cells, Inside the cells. In addition, the drug plays an important role in increasing the effectiveness of the lipoprotein lipase enzyme and thus lowering the levels of triglycerides [23]. Simvastatin's ability to raise the concentration of HDL-C is unknown, but Barter et.al.[24] Simvastatin can increase the composition of ApoA, a protein that enters the structure of HDL-C, which increases its concentration and concentration in the serum.

The role of vitamin C against high levels of fat and arteriosclerosis was important in terms of lowering total cholesterol, triglyceride, LDL and VLDL levels and raising HDL levels in both serum and liver extracts. This indicates the role of vitamin C in the fight against body fat. Al-Guary [25] noted the role of vitamin C in lowering levels of cholesterol, low-density lipoproteins and low-density lipoproteins. The researcher explained the reason is to prevent the process of oxidation of low-density lipoprotein and cholesterol-breaking or by converting cholesterol to bile acid and thus lead to lowering the concentrations of cholesterol. The reason for vitamin C's ability to reduce the concentration of cholesterol, LDL-c and triglycerides, and raise the concentration of HDL-C to its vital antioxidant role is to reduce free radicals by analyzing and minimizing damage by preventing membranes cellular and inhibition of lipid peroxidation and its derivatives and LDL-c oxidation [26].

The results of the present study showed the effective role of hawthorn extracts in the fight against and reduction of body fat concentrations. The extract of hawthorn extract on both vitamin C and simvastatin has been shown to reduce cholesterol and triglyceride concentrations. The researcher Wang et.al.[27] extract of Hawthorn fruit works to lower concentrations of cholesterol, triglyceride, LDL and VLDL. In a study carried out by Xu et.al.[28] for the purpose of detecting the role of wild hawthorn fruit extract, mice were fed a high-fat diet. After extracting the fruit extract and the simvastatin drug, there was a decrease in the concentrations of triglyceride and total cholesterol as well as low fat and low-density lipoproteins. What explains the role of extracts of hawthorn, especially fruits and their role in fat reduction is due to its ability to inhibit the effectiveness of acyl CoA, called cholester Acyltransferase (ACAT). Triterpenic acids, which are mainly fruits, have a direct effect on lowering cholesterol concentrations and tissues [29]. The extract of both fruits and leaves has the inhibitory effect of the acyl-CoA enzyme called cholester acyltransferase. At the same time, the effect of the extracts on 3-hydroxy-3-methyl glutaryl coenzyme A reductase (HMG-CoA-R) and cholesterol 7α-hydroxylase. Mnafgui et.al.[30] pointed out that hawthorn extract has the ability to inhibit the effectiveness of pancreatic triacylglycerol lipase, which in turn causes lower concentrations of body fat. And the role of the extract is due to the presence of flavons, which in turn inhibit this enzyme. This explains the role of extracts, especially fruits in reducing fat concentrations. On the other hand, the reason for the ability of the extract in reducing cholesterol to increase the flow of plasma cholesterol to the liver by increasing the activity of LDL-c receptors and increase regulation and also increase the destruction of cholesterol to bile acids and remove these acids, which is one of the mechanisms important to remove cholesterol from the body [31].

In terms of the enzyme HMG-CoA reductase, the results showed that the concentrations of the enzyme in the group given high cholesterol diet decreased but no significant differences found with the control group. The slight decrease in enzyme concentrations that were not significant with the group could be explained by the fact that the concentration of cholesterol inside the cells is regulated by Internal construction and taking from outside (via diet). Internal construction is done by hepatic HMG-CoA reductase feedback, while the external source is controlled by LDL receptors [5]. Therefore, the high concentrations of cholesterol as a result of nutrition reduced the need for the manufacture of hepatic cells and thus reduce the activity of HMG-CoA reductase. The results of the present study found that the drug simvastatin has an effective ability to inhibit the work of the enzyme HMG-CoA reductase and thus prevent and reduce the production of cholesterol by liver cells and this is consistent with Investigator Istvan [33] suggests that the drug Simvastatin has a disincentive effect on the action of the enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) thus preventing and reducing the production of cholesterol and triglyceride in the body. The researchers noted that statins in general and simvastatin in particular are linked to the active site on the enzyme and thus discourage its work. In vitamin C and its ability to reduce fat concentrations and its role in the effect of the enzyme HMG-CoA reductase and thus reduce the manufacture of cholesterol in hepatocytes, Wong et.al. [34] of the ability of vitamin to inhibit the work of the enzyme HMG-CoA reductase and depends on the amount of inhibition at the dose. The study indicated that the plant extracts were not effective in inhibiting the work of the enzyme HMG-CoA reductase and this is consistent with the findings of the researchers Abu-Gharbieh and Gamil [35]. When using *C.azarolus* extract as an anti-hyperlipidemia found in rats, the ability of the extract was found to reduce total cholesterol, triglyceride, LDL and VLDL concentrations with increased HDL concentrations. However, when measuring the concentrations of HMG-CoA, there were no significant changes in enzyme concentrations. Therefore, the researcher suggested other mechanisms to work on the gene

expression of PPAR-α genes, which are involved in lipid metabolism, in addition to the ability of the extract to reduce cholesterol and triglyceride concentrations in liver cells. During oxidation Fatty acids and inhibition of additional synthesized.

Conclusion: we have found that ethanolic extracts of *C. azarolus* Low levels of lipids (cholesterol and triglycerides) in the serum of animals experiment with the use of the drug Simvastatin and the fruits of hawthorn plant the largest role compared with vitamin C and extract leaf hawthorn. On the other hand, the non-change in the concentration of the enzyme HMG-CoA reductase in the serum and liver extract indicates that the role of the extract in the normalization of lipid variables is centered on other mechanisms related to the digestive system, such as absorption.

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مقارنة تأثير المستخلص الكحولي لأوراق وثمار نبات الزعرور البري *Crataegus azarolus* مع عقار السمفاستاتين في تأثيرها في الحد من الامراض القلبية الوعائية عند ذكور الارانب المصابة باضطراب الدهون التجريبي

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الملخص

صممت هذه الدراسة للبحث عن دور كل من المستخلصات الكحولية لأوراق و ثمار نبات الزعرور البري في خفض وتحسين عوامل الخطورة على الجهاز القلبي الوعائي في ذكور الارانب النيوزلندية المصابة باضطراب الدهون التجريبي. استخدام 50 ذكر ارنب نيوزلندي بالغ بوزن 1000−1250 غم وبعمر 6−8 شهر وقسمت الارانب الى 10 مجاميع (كل مجموعة 5 ذكور ارانب) وكما يلي: المجموعة الاولى وهي مجموعة السيطرة واعطيت عليقة قياسية, المجموعة الثانية واعطيت عليقة عالية الكوليسترول (260ملغم\ كغم) من وزن العليقة القياسية, المجموعة الثالثة واعطيت عليقة عالية الكوليسترول مع المستخلص الكحولي لاوراق نبات الزعرور *C.azarolus*(200ملغم\كغم) من وزن الجسم, المجموعة الرابعة واعطيت عليقة عالية الكوليسترول مع مستخلص ثمار نبات الزعرور (20ملغم\كغم) من وزن الجسم, المجموعة الخامسة واعطيت عليقة عالية الكوليسترول مع عقار السمفاستاتين (0.3ملغم\كغم) من وزن الجسم, المجموعة السادسة واعطيت عليقة عالية الكوليسترول مع فيتامينC (100ملغم\كغم) من وزن الجسم, المجموعة السابعة واعطيت عقار السمفاستاتين فقط, المجموعة الثامنة وجرعت فيتامينC فقط, المجموعة التاسعة وجرعت مستخلص اوراق نبات الزعرور فقط والمجموعة العاشرة وجرعت مستخلص ثمار نبات الزعرور فقط. أجريت التجربة لمدة ستة أسابيع. أظهرت التحليل الاحصائي ارتفاع معنوي ($P<0.05$) في متغيرات الدهون (الكوليسترول الكلي, الشحوم الثلاثية, LDL, VLDL وانخفاض HDL) في المصل ومستخلص الكبد في المجموعة المعطاة عليقة عالية الكوليسترول مقارنة مع مجموعة السيطرة السليمة, اما المعاملة بمستخلصات النبات فقد اظهر مستخلص الثمار دور فعال جدا في الوقاية من فرط الدهون مقارنة مع مستخلص الاوراق وفيتامين C وعقار السمفاستاتين. كما أظهرت الدراسة ايضاً انخفاض معنوي ($P<0.05$) في تركيز الانزيم HMG-CoA reductase (HMGR) في المجموعة المعاملة بعقار السمفاستاتين مقارنة مع مجموعة السيطرة، في حين لم يكن هناك فروقات معنوية في كل من المجموعة المعطاة عليقة عالية الكوليسترول ومجموعة فيتامين C ومجاميع مستخلصات أوراق وثمار النبات. يستنتج من نتائج الدراسة الحالية بأن للمستخلص الكحولي لثمار نبات الزعرور اهمية كبيرة في خفض الامراض القلبية الوعائية. وقد استنتج من خلال هذا البحث انخفاض مستويات الدهون (الكوليسترول والشحوم الثلاثية) في أمصال حيوانات التجربة عند استعمال عقار السمفاستاتين وكان لثمار نبات الزعرور الدور الأكبر مقارنة مع فيتامين C ومستخلص أوراق نبات الزعرور. ومن جهة أخرى فإنَّ عدم تغير تركيز أنزيم HMG-CoA reductase في مصل الدم ومستخلص الكبد يؤشر بأنّ دور المستخلص في تطبيع متغيرات مرتسم الدهون يتمحور نحو آليات أخرى ذات علاقة بالجهاز الهضمي كالامتصاص مثلاً.