

RESEARCH ARTICLE

The Effects of L-Carnitine and Garlic Oil on Hypercholesterolemia in Albino Rats Fed a High-Cholesterol Diet

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Abstract

This study was performed to examine the progress of hypercholesterolemia as a result of an elevated cholesterol diet and to estimate the impact of L-carnitine and garlic oil on serum lipid profiles, serum free fatty acids (FFAs), glucose, serum insulin, serum insulin resistance, serum malondialdehyde (MDA), and liver homogenates for glutathione and liver lipid percentages. Two hundred eighty-eight adult male albino rats were divided into four groups as follows: control group, high cholesterol diet (HCD) group received 1 g, 2 g, and 3 g cholesterol /Kg of paddy feed for 8 weeks, protective group (fed HCD either with L-carnitine at a dose of 200 mg/kg. BW per diem or garlic oil at a dose of 28 mg/kg. BW. per diem for 8 weeks), and treated group was fed on HCD for 4 weeks, then after that treated by L-carnitine or garlic oil for another 4 weeks. In protective groups (L-carnitine and garlic oil supplementations with HCD) the obtained results revealed a significant decrease in serum total cholesterol (TC), triacylglycerols (TG), low-density lipoprotein-cholesterol (LDL-C), very low-density lipoprotein-cholesterol (VLDL-C), FFAs, MDA, glucose, insulin and insulin resistance. Also, revealed a significant decrease in liver lipid percent and oxidized glutathione and significantly increase in serum high-density lipoprotein-cholesterol (HDL-C), liver total glutathione and reduced glutathione. In treated groups, our results affirmed a significant decrease in serum total cholesterol, triacylglycerols, HDL-C, FFAs, MDA, liver lipid percent and oxidized glutathione and significantly increase in liver reduced glutathione (GSH). In addition, our results showed a significant increase of serum LDL-C, VLDL-C, glucose, insulin, and insulin resistance. Based on the results of experiments, it is cleared that garlic oil is more effective than L-carnitine..

Keywords: L-carnitine, Garlic oil, High cholesterol diet, Glutathione, Malondialdehyde.

Introduction

Hypercholesterolemia is a metabolic abnormality identified by increased levels of serum total cholesterol and low-density lipoprotein-cholesterol (LDL-C) [1]. Hypercholesterolemia causes a major problem to many societies because of the close correlation between cardiovascular diseases and lipid abnormalities [2]. Nutritional diet with high carbohydrate and lipid can increase triglyceride level, total

cholesterol and LDL-C with decreased High-density lipoprotein-cholesterol (HDL-C) level; all of these changes increase risk of cardiovascular disease [3].

Hypercholesterolemia causes production of excessive reactive oxygen species (ROS), which promotes oxidative stress that leads to cell death [4]. The excess ROS and/or a decline in the antioxidant defense technique cause an increase in oxidative stress [5]. Also, ROS cause damage of different biomolecules e.g. deoxyribonucleic acid

(DNA), ribonucleic acid (RNA), proteins, lipids, cofactors in enzymes) and distressing ordinary cellular metabolism. Consequently, this may lead to cell death [6].

More aggregations of fat in the liver and muscle cells produce insulin resistances that conclude to beta cell reduction in type 2 diabetes [7]. Glutathione (GSH) has marked antioxidant activities and therefore may prevent cardiovascular disease. The decrease in plasma GSH level in hypercholesterolemia is the main factor for the development of cardiovascular and cerebrovascular diseases [8]. The high cholesterol diet also causes a marked elevation in the levels of plasma malondialdehyde (MDA). MDA is one of the final products of lipid peroxidation [9]. Plasma MDA levels elevated in animals with obesity and diabetes mellitus that indicate marked increases of lipid oxidation in tissues [10].

Carnitine and its acetylated derivatives make the β -oxidation easy and enhance the metabolism of energy reducing the noxious impact of free profiles of long-chain fatty acids in and around mitochondrial membranes and they block permeability transitions and this abolish the discharge of free electrons which consequently develop free radicals [11]. L-carnitine prevents both the mitochondrial destruction produced by oxidative stress and mitochondria reliant apoptosis in different types of cells [12]. Other researches proposed that L-carnitine has a significant function in the balance of oxidative/antioxidative and has an antiperoxidative impact on many tissues [13]. The antioxidant actions of L-carnitine may be direct against oxygen radicals or indirectly via increasing biosynthesis of enzymatic antioxidants, such as GSH and catalase [14].

Numerous attempts are now focused on multiple herbal plant extracts because of their capacity to produce antioxidant impact [15]. The garlic preparations such as garlic powder, aged garlic extract, garlic oil, and fresh garlic lowered significantly the total

cholesterol and LDL-C in comparison with placebo. High-density lipoprotein-cholesterol (HDL-C) concentrations were slightly elevated and triglyceride concentrations were not affected by garlic supplementation [16].

Part of the constituents of garlic may act as inhibitors for some enzymes such as hydroxy methyl glutaryl-CoA reductase that collaborates in cholesterol biosynthesis. Depending on this suggestion, it has been shown that *in vivo* treatment of garlic extract declines the lipid peroxidation outcomes [17].

This study was designed to examine the progress of hypercholesterolemia as a result of an elevated cholesterol diet and to estimate the impact of L-carnitine and garlic oil on serum lipid profiles, serum free fatty acids (FFAs), glucose, serum insulin, serum insulin resistance, serum MDA, liver glutathione, and lipid percentage.

Materials and Methods

The standard and high cholesterol diets

The composition of the experimental diet (g/kg diet) was according to the formula of Kim *et al.* [18]. It included the standard diet (Paddy feed) for control rats (fat 5%, carbohydrates 65%, proteins, 20.3% fiber 5%, salt mixture and 3.7% vitamin mixture 1%). The high cholesterol diet (HCD) formed of standard diet and cholesterol at different concentrations (1 gm, 2 gm, and 3 gm/ Kg of Paddy feed). The standard and high cholesterol diet constituents were purchased from El-Gomhoria Company, Cairo, Egypt. HCD was preserved at 4°C until used.

The drug and its dose

L-carnitine (dietary supplement):

1 mL containing 250 mg carnitine was purchased from the Arab Company for Pharmaceuticals Medicinal Plants (MEPACO, Sharkia Governorate, Egypt). Rats received 200 mg/kg. BW per diem as previously reported [19].

Garlic oil:

Garlic oil has been bought from local markets, Egypt. It was given at a dose of 28 mg / Kg. BW per diem [20].

Animals and experimental design

Two hundred eighty-eight adult male albino rats Spurge-Dawley strain weighting 200-250 gm were used in this study. These animals were obtained from the Central Animals House of Faculty of Veterinary Medicine, Zagazig University. The animals were maintained in stainless steel cage in Biochemistry Department with free access to basal diets and water. All procedures were carried out in accordance with the principles of laboratory Animal Care (**World Health Organization, 1985**) [21]. All animals were acclimatized for minimum period of two weeks prior to the beginning of the study. Rats were divided into four main groups as follows:

Control group (n = 24) rats received normal diet only (paddy feed).

High cholesterol diet group in which rats (n = 72) fed on HCD (1 g cholesterol, 2 g cholesterol, and 3 g cholesterol/Kg of paddy feed).

Protective group:

One hundred and forty-four rats were divided into two subgroups (72 rats for each) and fed on HCD (1g cholesterol, 2 g cholesterol, 3 g cholesterol/ Kg of paddy feed) with either L-carnitine or garlic oil from the beginning of experiment till 8 weeks. The first subgroup was fed on HCD with L-carnitine 250 mg/ Kg. BW The second subgroup was fed on HCD with garlic oil 28 mg/ Kg. B. wt. Eight rats from each subgroup were sacrificed at 2 weeks, 4 weeks and 8 weeks of the experiment and blood and tissues samples were obtained.

Treated group:

Forty-eight rats were divided into three subgroups (16 rats for each). The first subgroup was fed on HCD (1 g cholesterol /Kg of paddy feed) for 4 weeks, then

divided after this duration into two equal parts (first fed on same feed with L-carnitine 250 mg/ Kg. BW and the second on the same feed with garlic oil 28 mg/ Kg for another 4 weeks). Second and third are similar to the first but fed on HCD (2 g cholesterol, 3 g cholesterol/Kg of paddy feed) respectively. Eight rats from each subgroup were sacrificed at the end of experiments and blood and tissues samples were obtained.

Biochemical analysis**Serum analysis**

Blood samples were immediately collected from aorta and placed in a dried clean plain centrifuge tubes and then centrifuged for 15 min at 3000 rpm to separate serum. The separated serum was used to determine the sera total cholesterol (TC), triglyceride (TAG), HDL-C, LDL-C, VLDL-C, FFAs, MDA, glucose, insulin, and insulin resistance concentration. Kits for TC (BioMed Cholesterol-LS- CHO 104060) and TG (BioMed Triglycerides-LS- TG 119060) were obtained from BioMed Company, Egypt. Moreover, HDL-C LDL-C and VLDL-C (Cholesterol Assay Kit-HDL and LDL/VLDL-ab65390-abcaam-untited Kingdom) were measured [22-26]. FFA were determined by using NEFA-Kit-S (Nippon Shoji Kaisha Ltd., 2-30, Koku-machi, Higashi-ku, Osaka, Japan) [27]. MDA was measured by using MDA assay kits (Competitive Elisa-ab238537-abcaam-untited Kingdom) [28]. Glucose (Glucosa-TR-1001191) obtained from Spinreact company, Barcelona, insulin, and insulin resistance (Elisa Kit Cat. #0030) obtained from Alpha Diagnostic International-USA [29-31].

Determination of glutathione system

Liver tissues of the experimental animals were removed by careful dissection. The abdomen was opened and rinsed with physiological saline. Liver tissues were quickly collected, washed by physiological saline to remove any clotted blood. Livers were blotted in filter papers finally kept

frozen at -70°C for biochemical analysis. The homogenate was prepared by homogenized 1.0 gm of each liver sample in 9 ml of distilled water using electrical homogenizer at 3000 rpm for 15 min, the resulting supernatant were collected and used for estimation of glutathione system [32].

Determination of liver lipid percent

Approximately 15 g of wet liver tissue is chemically dried with Hydromatixâ. Samples were extracted with 100% dichloromethane (Shandong S-Sailing Chemical CO., LTD. Shandong, China) by using Dionex ASE200 accelerated solvent extractor (International Equipment Trading Ltd, Mundelein, Illinois, USA) operated at 100°C and 2,000 psi. Extracts are concentrated to 3 mL by evaporative solvent reduction in a water bath at $55 - 60^{\circ}\text{C}$. An aliquot of 100 mL is removed and weighed to the nearest 0.001 mg on a dried, tared glass fiber filter. Percent lipid was calculated based on the extract volume and sample weight [33].

Statistical analysis of the data

Results were evaluated using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). The Kolmogorov-Smirnov test was used to check the normality of distribution. Quantitative data was described using mean \pm standard deviation (SD). Significance of the achieved outcomes was considered at $P \leq 0.05$ [34]. F-test (ANOVA) was employed to compare between more than two groups and Post Hoc test least significant difference (LSD) for pairwise comparisons.

Results

The effects of HCD on serum lipid profile, FFA, MDA, glucose, insulin and insulin resistance were listed in Tables 1 and 2. The statistical analysis of present data revealed a significant elevation in the levels of serum TC, TAG, LDL-C, VLDL-C, FFA, MDA, glucose, insulin and insulin resistance in the experimental groups with different HCD (1g to 3g cholesterol /Kg of

Paddy feed). Also, there was a significant decrease in the amounts of HDL-C.

The Table 3 presented the impact of HCD on the hepatic glutathione state. The total and reduced glutathione concentrations decreased significantly in rats administered high cholesterol diet in a dose of 3g/kg for 4 and 8 weeks as compared with other groups. In contrast the levels of oxidized glutathione increased in rats administered high cholesterol at a dose of 2 and 3 g/kg for 2, 4, and 8 weeks as compared with other groups.

Our findings revealed that TC, TG, LDL-C, VLDL-C, FFAs, MDA, glucose, insulin, and insulin resistance decreased significantly and HDL-C levels increase significantly in rats administered high cholesterol (1, 2 and 3 g cholesterol /kg of Paddy feed) and treated with L-carnitine or garlic oil as compared with corresponding rats administered HCD only. Garlic oil is more effective on some parameters than L-carnitine (Tables 4 and 5).

The total glutathione and reduced glutathione levels increased significantly and the oxidized glutathione levels decreased significantly in rats administered HCD and treated with either L-carnitine or garlic oil as compared with corresponding rats administered high cholesterol diet only (Tables 6 and 7).

The hepatic fat % decreased significantly in rats administered 1g/kg cholesterol and treated either with L-carnitine or garlic oil for 2, 4, and 8 weeks and that received cholesterol in 2 g/kg for 8 weeks as compared with corresponding rats received HCD only. Also, rats administered cholesterol in 1g/kg for 4 weeks then treated with either L-carnitine or garlic oil for other 4 week had a lower hepatic fat % as compared with other treated rats (Table 8).

In the treated groups, cholesterol, triglyceride, free fatty acids and MDA decreased significantly in rats administered HCD (2 and 3 g/kg) for 4 weeks and then treated with L-carnitine or garlic oil for

another 4 weeks. Also, our results show that the serum concentrations of LDL-C, VLDL-C, glucose, insulin, and insulin resistance increased significantly in rats administrated HCD for 4 weeks alone or followed by either L-carnitine or garlic oil treatment for another 4 weeks. In contrast the serum concentrations HDL-C decreased significantly in rats administrated high cholesterol diet for 4 weeks alone or followed by either L-

carnitine or garlic oil treatment for another 4week (Tables 9 and10).Also, our results revealed that, the reduced glutathione increased significantly in rats administrated 3g/kg HCD for 4 weeks then treated with either L-carnitine or garlic oil. In contrast oxidized glutathione levels decreased significantly in rats administrated HCD for 4 weeks and then treated either with L carnitine or garlic oil for other 4 weeks (Table 11).

Table (1): The effect of high cholesterol diet on blood serum cholesterol, triglyceride, high-density lipoproteins, low density lipoprotein and very low density lipoprotein (mg/dL)

		Cholesterol (mg/dL)	Triglyceride (mg/dL)	[†] HDL- cholesterol (mg/dL)	LDL-- cholesterol (mg/dL)	VLDL- cholesterol (mg/dL)	
Control	After 2weeks	107.0 ^h ± 4.34	73.63 ^h ± 2.26	49.38 ^a ± 0.92	46.88 ⁱ ± 3.44	14.73 ^h ± 0.45	
	After 4weeks	108.5 ^h ± 4.50	73.0 ^h ± 3.59	49.88 ^a ± 1.13	50.25 ^{ij} ± 4.74	14.60 ^h ± 0.72	
	After 8weeks	109.6 ^h ± 4.17	74.38 ^h ± 2.92	49.88 ^a ± 1.13	50.38 ⁱ ± 0.92	14.78 ^h ± 0.66	
High cholesterol diet	1gm/Kg	After 2 weeks	119.8 ^g ± 1.98	84.13 ^g ± 1.13	44.0 ^b ± 1.31	55.0 ^h ± 1.77	16.83 ^g ± 0.23
		After 4 weeks	145.1 ^e ± 4.02	94.75 ^{ef} ± 1.83	39.50 ^c ± 1.20	65.25 ^f ± 1.39	18.95 ^{ef} ± 0.37
		After 8 weeks	156.3 ^d ± 9.04	101.9 ^d ± 3.98	37.0 ^{de} ± 1.31	72.0 ^e ± 2.73	20.38 ^d ± 0.80
	2gm/Kg	After 2 weeks	135.4 ^f ± 2.88	89.88 ^{fg} ± 1.13	38.13 ^d ± 1.13	61.75 ^g ± 1.39	17.98 ^{fg} ± 0.23
		After 4 weeks	169.4 ^c ± 4.93	101.9 ^d ± 1.55	36.0 ^{ef} ± 1.31	82.25 ^d ± 4.83	20.38 ^d ± 0.31
		After 8 weeks	194.4 ^b ± 9.10	137.9 ^b ± 9.46	34.0 ^{gh} ± 1.31	101.4 ^b ± 3.25	27.48 ^b ± 1.80
	3gm/Kg	After 2 weeks	147.5 ^e ± 5.90	97.63 ^{de} ± 2.62	35.0 ^{fg} ± 0.93	68.25 ^f ± 1.67	19.53 ^{de} ± 0.52
		After 4 weeks	189.6 ^b ± 9.18	122.6 ^c ± 10.28	33.0 ^h ± 1.31	95.13 ^c ± 3.44	24.53 ^c ± 2.06
		After 8 weeks	255.3 ^a ± 11.97	146.8 ^a ± 12.48	29.38 ⁱ ± 1.77	108.5 ^a ± 6.80	29.35 ^a ± 2.50
[§] F		346.30*	141.20*	257.061*	293.462*	143.044*	
[†] P		<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	
LSD 5%		6.646	5.801	1.239	3.450	1.152	

No. of rats = 8. [†]HDL: high-density lipoproteins, LDL: low density lipoprotein and VLDL: very low density lipoprotein. Data was expressed by using mean ± SD. Means in the same column with common small letters are not significant. [§]F for ANOVA test, pairwise comparison between each 2 groups was done using Post Hoc Test (LSD). [†]P value for comparing between the different studied groups. *Statistically significant at $P \leq 0.05$.

Table (2): The effect of high cholesterol diet on blood serum free fatty acid, malondialdehyde, glucose, insulin, and insulin resistance

		Free fatty acid (mg/dL)	Malondialdehyde (μ mol/L)	Glucose (mg/dL)	Insulin (μ IU/ml)	Insulin Resistance (HOMA-IR)	
High cholesterol diet	Control	After 2weeks	11.81 ^g \pm 0.57	1.76 ^f \pm 0.49	72.0 ^h \pm 2.98	0.77 ⁱ \pm 0.11	0.14 ^g \pm 0.03
		After 4weeks	12.20 ^g \pm 0.40	1.64 ^f \pm 0.63	76.38 ^{gh} \pm 3.70	0.81 ⁱ \pm 0.15	0.15 ^g \pm 0.04
		After 8weeks	12.14 ^g \pm 0.77	1.78 ^f \pm 0.55	78.88 ^g \pm 4.26	0.83 ^{hi} \pm 0.13	0.16 ^g \pm 0.04
	1g/K	After 2 weeks	14.26 ^f \pm 0.18	2.11 ^f \pm 0.64	84.25 ^f \pm 1.98	1.09 ^h \pm 0.14	0.23 ^g \pm 0.04
		After 4 weeks	16.83 ^d \pm 0.27	2.16 ^f \pm 0.57	94.38 ^e \pm 1.77	2.23 ^f \pm 0.14	0.52 ^f \pm 0.04
		After 8 weeks	17.98 ^c \pm 0.51	3.03 ^e \pm 0.63	102.9 ^{cd} \pm 5.19	3.15 ^d \pm 0.37	0.80 ^d \pm 0.14
	2g/K	After 2 weeks	15.48 ^e \pm 0.37	3.06 ^e \pm 0.32	93.25 ^e \pm 3.85	1.94 ^g \pm 0.18	0.45 ^f \pm 0.06
		After 4 weeks	17.70 ^c \pm 0.45	3.30 ^e \pm 0.49	101.9 ^d \pm 1.55	3.16 ^d \pm 0.34	0.80 ^d \pm 0.09
		After 8 weeks	21.64 ^b \pm 0.67	4.25 ^d \pm 0.38	112.0 ^b \pm 4.34	4.76 ^b \pm 0.37	1.32 ^b \pm 0.15
	3g/K	After 2 weeks	17.43 ^c \pm 0.42	4.88 ^c \pm 0.57	102.6 ^d \pm 2.88	2.61 ^e \pm 0.22	0.66 ^e \pm 0.08
		After 4 weeks	21.99 ^b \pm 0.79	5.78 ^b \pm 0.47	107.6 ^{bc} \pm 4.72	4.14 ^c \pm 0.21	1.10 ^c \pm 0.11
		After 8 weeks	21.99 ^b \pm 0.79	6.46 ^a \pm 0.49	133.4 ^a \pm 11.61	5.88 ^a \pm 0.56	1.96 ^a \pm 0.34
	[§] F	426.709*	77.119*	104.663*	295.054*	153.064*	
	[†] P	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	
	LSD 5%	0.586	0.527	4.770	0.275	0.126	

No. of rats = 8. Data was expressed by using mean \pm SD. Means in the same column with common small letters are not significant. [§]F for ANOVA test, pairwise comparison between each 2 groups was done using Post Hoc Test (LSD). [†]P value for comparing between the different studied groups.

*: Statistically significant at $P \leq 0.05$.

Table (3): The effects of high cholesterol diet on hepatic glutathione state (μ mol/g protein)

	Control			High cholesterol diet								
	2 weeks	4 weeks	8	1 g cholesterol /Kg diet			2 g cholesterol /Kg diet			3 g cholesterol /Kg diet		
				2 weeks	4 weeks	8 weeks	2 weeks	4 weeks	8 weeks	2 weeks	4 weeks	8 weeks
	Weeks											
Total glutathione	64.06 \pm 4.1 2 ^b	64.17 \pm 4.0 9 ^b	64.21 \pm 4.21 ^b	63.95 \pm 3.9 9 ^b	64.12 \pm 4.06 ^b	64.19 \pm 4.12 ^b	64.08 \pm 3.96 ^b	64.13 \pm 3.9 8 ^b	64.17 \pm 4.01 ^b	64.22 \pm 4.03 ^b	64.29 \pm 4.11 ^b	64.32 \pm 4.23 ^b
Reduced glutathione	48.59 \pm 3.1 5 ^a	48.06 \pm 3.0 8 ^a	48.11 \pm 2.94 ^a	48.06 \pm 3.06 ^a	48.41 \pm 3.12 ^a	48.05 \pm 3.21 ^a	48.22 \pm 3.18 ^a	48.09 \pm 3.1 9 ^a	48.03 \pm 3.0 8 ^a	48.07 \pm 3.13 ^a	47.39 \pm 3.06 ^b	47.21 \pm 3.13 ^b
Oxidized glutathione	16.47 \pm 1.1 6 ^c	16.11 \pm 1.0 8 ^c	16.1 \pm 1.21 ^c	15.89 \pm 1.15 ^d	15.71 \pm 0.98 ^d	16.14 \pm 1.06 ^c	18.86 \pm 1.19 ^a	16.04 \pm 1.2 1 ^c	16.16 \pm 1.0 7 ^b	16.21 \pm 0.9 6 ^b	16.9 \pm 0.92 ^b	17.11 \pm 1.03 ^b
Glutathione Quotient (GSH/GS.SG)	2.95	2.98	2.99	3.02	3.08	2.98	3.04	2.98	2.97	2.96	2.80	2.76

L.S.D for total glutathione =1.92, L.S.D for reduced glutathione =0.95, L.S.D for oxidized glutathione =0.62.

Table (4): The protective effects of L-carnitine and garlic oil against high cholesterol diet on blood serum cholesterol, triglyceride, high-density lipoproteins, low density lipoprotein and very low density lipoprotein (mg/dL).

		Cholesterol (mg/dL)			Triglyceride (mg/dL)			HDL-cholesterol (mg/dL)			LDL-cholesterol (mg/dL)			VLDLcholesterol (mg/dL)		
		2 weeks	4 weeks	8 weeks	2 weeks	4 weeks	8 weeks	2 weeks	4 Weeks	8 weeks	2 weeks	4 weeks	8 weeks	2 weeks	4 weeks	8 weeks
Control		107.0 ^a ±4.34	108.5 ^a ±4.50	109.6 ^a ±4.17	73.63 ^p ±2.26	73.0 ^p ±3.59	74.38 ^{op} ±2.92	49.38 ^a ±0.92	49.88 ^a ±1.13	49.88 ^a ±1.13	46.88 ^c ±3.44	50.25 ^a ±4.74	50.38 ^a ±0.92	14.73 [±] 0.45	14.60 [±] 0.72	14.78 [±] 0.66
	1g/Kg	119.8 ^{op} ±1.98	145.1 ^{ef} ±4.02	156.3 ^d ±9.04	84.13 ^{kl} ±1.13	94.75 ^{fg} ±1.83	101.9 ^e ±3.98	44.0 ^{cde} ±1.31	39.50 ^{jk} ±1.20	37.0 ^{lm} ±1.31	55.0 ^{op} ±1.77	65.25 ^{ij} ±1.39	72.0 ^b ±2.73	16.83 ^{kl} ±0.23	18.95 ^{fg} ±0.37	20.38 ^e ±0.80
	2g/Kg	135.4 ^{ghi} ±2.88	169.4 ^c ±4.93	194.4 ^b ±9.10	89.88 ^{hij} ±1.13	101.9 ^e ±1.55	137.9 ^b ±9.46	38.13 ^l ±1.13	36.0 ^{mn} ±1.31	34.0 ^{op} ±1.31	61.75 ^k ±1.39	82.25 ^{fg} ±4.83	101.4 ^b ±3.25	17.98 ^{hij} ±0.23	20.38 ^e ±0.31	27.48 ^b ±1.80
High cholesterol diet	3g/Kg	147.5 ^e ±5.90	189.6 ^b ±9.18	255.3 ^a ±11.97	97.63 ^{ef} ±2.62	122.6 ^c ±10.28	146.8 ^a ±12.48	35.0 ^{no} ±0.93	33.0 ^p ±1.31	29.38 ^q ±1.77	68.25 ⁱ ±1.67	95.13 ^c ±3.44	108.5 ^a ±6.80	19.53 ^{ef} ±0.52	24.53 ^c ±2.06	29.35 ^a ±2.50
	1g/Kg	116.1 ^p ±1.55	128.4 ^{klm} ±2.26	132.3 ^{ijk} ±5.26	82.38 ^{klmn} ±1.77	83.0 ^{klmn} ±1.31	87.0 ^{ijk} ±2.98	45.88 ^b ±1.13	42.0 ^{gh} ±0.93	41.88 ^{gh} ±1.55	53.63 ^{op} ±1.77	58.38 ^{lm} ±1.77	61.88 ^k ±3.64	16.48 ^{klm} ±0.35	16.60 ^{klm} ±0.26	17.40 ^{ijk} ±0.60
	2g/Kg	126.8 ^{klmn} ±2.87	133.4 ^{hij} ±4.03	141.0 ^{fg} ±6.65	83.0 ^{klmn} ±1.31	83.0 ^{klmn} ±1.77	115.0 ^d ±8.98	41.0 ^{hi} ±0.93	43.0 ^{defg} ±1.31	41.0 ^{hi} ±1.31	54.88 ^{nop} ±1.55	58.25 ^{lm} ±1.83	93.75 ^c ±3.28	16.60 ^{klm} ±0.26	16.60 ^{klm} ±0.35	23.0 ^d ±2.0
L-carnitine	3g/Kg	128.5 ^{klm} ±4.87	139.3 ^s ±8.08	147.5 ^e ±7.80	86.13 ^{jk} ±4.12	101.4 ^e ±4.66	94.75 ^{fg} ±4.30	38.25 ^{kl} ±1.16	38.25 ^{kl} ±2.25	35.88 ^{mn} ±1.46	62.75 ^{jk} ±2.55	84.0 ^{ef} ±5.50	88.0 ^d ±4.21	17.23 ^{jk} ±0.82	20.30 ^e ±0.97	18.95 ^{fg} ±0.86
	1g/Kg	110.1 ^q ±3.36	124.8 ^{lmno} ±2.87	129.9 ^{ijkl} ±5.79	79.0 ^{no} ±1.77	80.75 ^{lmn} ±1.16	84.50 ^{kl} ±3.12	46.88 ^b ±1.13	44.0 ^{cde} ±1.31	42.63 ^{fg} ±1.77	52.25 ^{pq} ±2.43	57.25 ^{lmn} ±2.25	59.88 ^{kl} ±3.64	15.80 ^m ±0.35	16.15 ^{lm} ±0.23	16.85 ^{kl} ±0.58
	2g/Kg	122.0 ^{no} ±1.77	128.3 ^{ijklm} ±5.60	132.4 ^{ijk} ±7.09	79.13 ^{mno} ±2.42	80.88 ^{lmn} ±1.46	101.9 ^e ±9.85	44.25 ^{cd} ±0.71	44.50 ^c ±1.60	42.75 ^{efg} ±1.98	53.75 ^{op} ±1.39	56.38 ^{mno} ±2.13	86.25 ^{de} ±3.58	15.90 ^{lm} ±0.40	16.18 ^{lm} ±0.29	20.43 ^e ±1.97
Garlic oil	3g/Kg	123.6 ^{mno} ±3.70	127.6 ^{klmn} ±4.10	138.5 ^{gh} ±7.29	83.88 ^{klm} ±3.44	92.63 ^{gh} ±2.07	91.25 ^{ghi} ±4.59	40.75 ^{hij} ±1.39	43.88 ^{cdef} ±1.13	40.13 ^{ij} ±1.55	60.25 ^{kl} ±2.66	79.88 ^s ±2.10	86.25 ^{de} ±3.01	16.75 ^{klm} ±0.62	18.53 ^{gh} ±0.41	18.25 ^{ghi} ±0.92
	§F		218.122 [*]			105.014 [*]			109.546 [*]			236.918 [*]			103.331 [*]	
	†P		<0.001 [*]			<0.001 [*]			<0.001 [*]			<0.001 [*]			<0.001 [*]	
	LSD 5%		5.723			4.832			1.331			3.112			0.973	

No. of rats = 8. †HDL: high-density lipoproteins, LDL: low density lipoprotein and VLDL: very low density lipoprotein. Data was expressed by using mean ± SD. Means in the same column with common small letters are not significant. §F for ANOVA test, pairwise comparison between each 2 groups was done using Post Hoc Test (LSD). †P value for comparing between the different studied groups. *:

Statistically significant at $P \leq 0.05$.

Table (5): The protective effect of L-carnitine and garlic oil against high cholesterol diet on blood serum free fatty acid, malondialdehyde, glucose, insulin and insulin resistance

	Free fatty acid (mg/dL)			Malondialdehyde ($\mu\text{mol/L}$)			Glucose (mg/dL)			Insulin ($\mu\text{IU/ml}$)			Insulin Resistance (HOMA-IR)		
	2 Weeks	4 weeks	8 weeks	2 weeks	4 weeks	8 weeks	2 weeks	4 weeks	8 weeks	2 weeks	4 weeks	8 weeks	2 weeks	4 weeks	8 weeks
Control	11.81 ^p ± 0.57	12.20 ^p ± 0.40	12.14 ^p ± 0.77	1.76 ^{lmn} ± 0.4 9	1.64 ⁿ ± 0.63	1.78 ^{lmn} ± 0.5 5	72.0 ^o \pm 2.98	76.38 ⁿ \pm 3.70	78.88 ^{mn} \pm 4.26	0.77 ^p \pm 0.11	0.81 ^p \pm 0.15	0.83 ^p \pm 0.13	0.14 ⁿ \pm 0.03	0.15 ⁿ \pm 0.04	0.16 ⁿ \pm 0.04
High cholesterol diet															
1g/Kg	14.26 ^{no} ± 0.18	16.83 ^{gh} ± 0.27	17.98 ^{de} ± 0.51	2.11 ^{klm} ± 0.64	2.16 ^{klm} ± 0.57	3.03 ^{efg} ± 0.63	84.25 ^{kl} \pm 1.98	94.38 ^{gh} \pm 1.77	102.9 ^d \pm 5.19	1.09 ^o \pm 0.14	2.23 ^{hi} \pm 0.14	3.15 ^{ef} \pm 0.37	0.23 ^{mn} \pm 0.04	0.52 ^{gh} \pm 0.04	0.80 ^e \pm 0.14
2g/Kg	15.48 ^k ± 0.37	17.70 ^{ef} ± 0.45	21.64 ^b ± 0.67	3.06 ^{efg} ± 0.32	3.30 ^o ± 0.49	4.25 ^d ± 0.38	93.25 ^{ghi} \pm 3.85	101.9 ^{de} \pm 1.55	112.0 ^b \pm 4.34	1.94 ^{jk} \pm 0.18	3.16 ^{ef} \pm 0.34	4.76 ^b \pm 0.37	0.45 ^{hi} \pm 0.06	0.80 ^o \pm 0.09	1.32 ^b \pm 0.15
3g/Kg	17.43 ^{ef} ± 0.42	21.99 ^b ± 0.79	25.51 ^a ± 1.06	4.88 ^c ± 0.57	5.78 ^b ± 0.47	6.46 ^a ± 0.49	102.6 ^d \pm 2.88	107.6 ^c \pm 4.72	133.4 ^a \pm 11.61	2.61 ^g \pm 0.22	4.14 ^e \pm 0.21	5.88 ^a \pm 0.56	0.66 ^f \pm 0.08	1.10 ^c \pm 0.11	1.96 ^a \pm 0.34
L-carnitine															
1g/Kg	14.0 ^o \pm 0.13	15.24 ^{klm} ± 0.22	15.60 ^{jk} ± 0.39	1.94 ^{klmn} $\pm 0.$ 54	2.05 ^{klmn} $\pm 0.$ 41	2.21 ^{ijkl} ± 0.52	81.75 ^{lm} \pm 1.98	84.88 ^{kl} \pm 1.55	90.63 ^{hij} \pm 5.24	0.83 ^p \pm 0.09	1.56 ^{mn} \pm 0.22	1.84 ^{kl} \pm 0.16	0.17 ⁿ \pm 0.02	0.30 ^{klm} \pm 0.05	0.41 ^{ij} \pm 0.06
2g/Kg	14.68 ^{mn} $\pm 0.$ 31	15.15 ^{klm} ± 0.20	19.63 ^c ± 0.92	2.29 ^{ijk} ± 0.38	2.56 ^{hij} ± 0.42	3.25 ^{ef} ± 0.38	84.63 ^{kl} \pm 0.92	89.75 ^{ij} \pm 3.37	103.1 ^d \pm 4.70	1.68 ^{lm} \pm 0.16	2.48 ^{gh} \pm 0.20	3.75 ^d \pm 0.70	0.35 ^{ijkl} \pm 0.04	0.55 ^g \pm 0.05	1.08 ^c \pm 0.17
3g/Kg	16.35 ^{hi} ± 0.32	16.26 ^{hi} ± 0.63	18.49 ^d ± 1.31	3.14 ^{ef} ± 0.36	3.35 ^e ± 0.34	3.41 ^e ± 0.43	95.75 ^{fg} \pm 3.58	91.0 ^{hij} \pm 3.55	104.0 ^{cd} \pm 3.59	2.26 ^{hi} \pm 0.23	3.25 ^e \pm 0.20	3.60 ^d \pm 0.18	0.53 ^{gh} \pm 0.07	0.73 ^{ef} \pm 0.07	0.93 ^d \pm 0.08
Garlic oil															
1g/Kg	14.0 ^o ± 0.39	14.70 ^{mn} ± 0.13	15.41 ^{kl} ± 0.38	1.73 ^{mn} ± 0.55	1.94 ^{klmn} $\pm 0.$ 42	1.95 ^{klmn} $\pm 0.$ 53	78.63 ^{mn} \pm 1.77	82.13 ^{lm} \pm 1.55	87.88 ^{jk} \pm 5.82	0.76 ^p \pm 0.08	1.41 ⁿ \pm 0.16	1.80 ^{klm} \pm 0.27	0.15 ⁿ \pm 0.02	0.29 ^{lm} \pm 0.03	0.39 ^{ijk} \pm 0.09
2g/Kg	13.95 ^o ± 0.20	14.90 ^{lm} ± 0.25	17.54 ^{ef} ± 1.04	2.03 ^{klmn} $\pm 0.$ 38	2.29 ^{ijk} ± 0.40	2.65 ^{ghi} ± 0.32	80.88 ^{lm} \pm 1.55	84.25 ^{kl} \pm 3.88	96.75 ^{fg} \pm 6.02	1.34 ^{no} \pm 0.09	2.21 ⁱ \pm 0.16	2.98 ^f \pm 0.23	0.27 ^{lm} \pm 0.02	0.46 ^{ghi} \pm 0.05	0.72 ^{ef} \pm 0.10
3g/Kg	16.05 ^{ij} ± 0.22	15.41 ^{kl} ± 0.36	17.30 ^{fg} ± 0.91	2.81 ^{fgh} ± 0.31	3.10 ^{efg} ± 0.26	3.20 ^{ef} ± 0.25	90.25 ^{ij} \pm 3.41	84.38 ^{kl} \pm 1.77	97.88 ^{ef} \pm 3.76	2.13 ^{ij} \pm 0.18	3.10 ^{ef} \pm 0.13	3.01 ^{ef} \pm 0.25	0.47 ^{ghi} \pm 0.06	0.65 ^f \pm 0.04	0.73 ^{ef} \pm 0.09
§F		210.985 [*]			51.774 [*]			76.488 [*]			191.889 [*]			137.061 [*]	
†P		<0.001 [*]			<0.001 [*]			<0.001 [*]			<0.001 [*]			<0.001 [*]	
LSD 5%		0.572			0.455			4.042			0.253			0.096	

No. of rats = 8. Data was expressed by using mean \pm SD. Means in the same column with common small letters are not significant. §F for ANOVA test, pairwise comparison between each 2 groups was done using Post Hoc Test (LSD). †P value for comparing between the different studied groups.

*: Statistically significant at $P \leq 0.05$.

Table (6): Protective effect of L-carnitine against high cholesterol diet (1, 2, and 3 g cholesterol /kg of Paddy feed) on hepatic glutathione state (μ mol/gm protein)

	High cholesterol diet									L-Carnitine (250 mg/Kg. BW)								
	1 g cholesterol /Kg			2 g cholesterol /Kg			3 g cholesterol /Kg			1 g cholesterol /Kg			2 g cholesterol /Kg			3 g cholesterol /Kg		
	2 ws	4 ws	8 ws	2 ws	4 ws	8 ws	2 ws	4 ws	8 ws	2 ws	4 ws	8 ws	2 ws	4 ws	8 ws	2 ws	4 ws	8 ws
Total glutathione	63.95 \pm 3.99 ^b	64.12 \pm 4.06 ^b	64.19 \pm 4.12 ^b	46.08 \pm 3.96 ^b	64.13 \pm 3.98 ^b	64.17 \pm 4.01 ^b	64.22 \pm 4.03 ^b	64.29 \pm 4.11 ^b	64.32 \pm 4.23 ^b	64.11 \pm 4.01 ^a	64.15 \pm 3.99 ^a	64.26 \pm 4.12 ^a	64.11 \pm 4.3 ^a	64.25 \pm 3.63 ^a	64.24 \pm 3.92 ^a	64.78 \pm 4.08 ^a	64.25 \pm 3.94 ^a	64.31 \pm 3.98 ^a
Reduced glutathione	48.06 \pm 3.06 ^b	48.41 \pm 3.12 ^a	48.05 \pm 3.21 ^a	48.22 \pm 3.18 ^b	48.09 \pm 3.19 ^b	48.03 \pm 3.08 ^b	48.07 \pm 3.13 ^b	47.39 \pm 3.06 ^b	47.21 \pm 3.13 ^b	48.91 \pm 3.12 ^a	49.14 \pm 3.21 ^a	49.23 \pm 2.99 ^a	49.3 \pm 3.19 ^a	49.34 \pm 3.17 ^a	49.52 \pm 3.15 ^a	49.4 \pm 3.21 ^a	49.65 \pm 3.25 ^a	49.72 \pm 3.51 ^a
Oxidized glutathione	15.89 \pm 1.15 ^b	15.71 \pm 0.98 ^b	16.14 \pm 1.06 ^b	18.86 \pm 1.19 ^a	16.04 \pm 1.21 ^b	16.16 \pm 1.07 ^b	16.21 \pm 0.96 ^b	16.9 \pm 0.92 ^b	17.11 \pm 1.03 ^b	15.20 \pm 0.97 ^c	15.01 \pm 1.05 ^c	15.03 \pm 1.09 ^c	14.31 \pm 0.97 ^d	14.91 \pm 1.08 ^c	14.72 \pm 1.03 ^d	14.53 \pm 0.93 ^d	14.60 \pm 0.95 ^d	14.59 \pm 0.01 ^d
Glutathione Quotient (GSH/GS.S)	3.02	3.08	2.98	3.04	2.98	2.97	2.96	2.80	2.76	3.22	3.27	3.28	3.33	3.31	3.36	3.4	3.4	3.41

L.S.D for total glutathione =1.88, L.S.D for reduced glutathione =0.93, L.S.D for oxidized glutathione = 0.61.

Table (7): Protective effect of Garlic oil against high cholesterol diet (1, 2, and 3 g cholesterol /kg of Paddy feed) on hepatic glutathione state (μ mol/gm protein)

	High cholesterol diet									Garlic oil (28 mg/Kg BW)								
	1 g cholesterol /Kg			2 g cholesterol /Kg			3 g cholesterol /Kg			1 g cholesterol /Kg			2 g cholesterol /Kg			3 g cholesterol /Kg		
	2 ws	4 ws	8 ws	2 ws	4 ws	8 ws	2 ws	4 ws	8 ws	2 ws	4 ws	8 ws	2 ws	4 ws	8 ws	2 ws	4 ws	8 ws
Total glutathione	63.95 \pm 3.99 ^b	64.12 \pm 4.06 ^b	64.19 \pm 4.12 ^b	46.08 \pm 3.96 ^b	64.13 \pm 3.98 ^b	64.17 \pm 4.01 ^b	64.22 \pm 4.03 ^b	64.29 \pm 4.11 ^b	64.32 \pm 4.23 ^b	64.2 \pm 4.13 ^a	64.35 \pm 4.26 ^a	64.45 \pm 4.05 ^a	64.21 \pm 4.21 ^a	64.32 \pm 4.09 ^a	64.46 \pm 4.29 ^a	64.82 \pm 4.23 ^a	64.85 \pm 4.35 ^a	64.99 \pm 4.39 ^a
Reduced glutathione	48.06 \pm 3.06 ^b	48.41 \pm 3.12 ^a	48.05 \pm 3.21 ^a	48.22 \pm 3.18 ^b	48.09 \pm 3.19 ^b	48.03 \pm 3.08 ^b	48.07 \pm 3.13 ^b	47.39 \pm 3.06 ^b	47.21 \pm 3.13 ^b	48.96 \pm 2.86 ^a	49.35 \pm 2.92 ^a	49.39 \pm 3.11 ^a	49.51 \pm 2.91 ^a	49.62 \pm 3.01 ^a	49.72 \pm 3.11 ^a	49.53 \pm 3.17 ^a	49.62 \pm 3.05 ^a	49.78 \pm 3.13 ^a
Oxidized glutathione	15.89 \pm 1.15 ^b	15.71 \pm 0.98 ^b	16.14 \pm 1.06 ^b	18.86 \pm 1.19 ^a	16.04 \pm 1.21 ^b	16.16 \pm 1.07 ^b	16.21 \pm 0.96 ^b	16.9 \pm 0.92 ^b	17.11 \pm 1.03 ^b	15.24 \pm 1.12 ^c	15.00 \pm 1.11 ^d	15.06 \pm 0.98 ^d	14.70 \pm 1.1 ^d	14.70 \pm 1.11 ^d	14.74 \pm 1.03 ^d	15.29 \pm 1.05 ^c	15.23 \pm 0.97 ^c	15.21 \pm 1.03 ^c
Glutathione Quotient (GSH/GS.SG)	3.02	3.08	2.98	3.04	2.98	2.97	2.96	2.80	2.76	3.28	3.29	3.28	3.37	3.38	3.37	3.24	3.26	3.27

L.S.D for total Glutathione = 1.86, L.S.D for Reduced Glutathione = 0.92, L.S.D for Oxidized Glutathione =0.61.

Table (8): Consequence of high cholesterol diet (1, 2, and 3 g cholesterol /kg of Paddy feed) on hepatic fat %, protective and treated effect of L-carnitine (250 mg/Kg. BW) and garlic oil (28 mg/Kg. BW)

		Control	High cholesterol diet			L-Carnitine (250 mg/Kg)			Garlic oil (28 mg/Kg)		
			1g cholesterol	2g cholesterol	3g cholesterol	1g cholesterol	2g cholesterol	3g cholesterol	1g cholesterol	2g cholesterol	3gm cholesterol
Protective effect	2 Ws	5.11 ±0.6 ^b	5.56 ±0.34 ^a	5.71 ±0.38 ^a	5.78 ±0.32 ^a	5.26 ±0.29 ^b	5.42 ±0.32 ^{ab}	5.56 ±0.34 ^a	5.35 ±0.19 ^b	5.58 ±0.28 ^a	5.69 ±0.4 ^a
	4 Ws	5.06 ±0.19 ^b	5.74 ±0.22 ^a	5.89 ±0.31 ^a	5.99 ±0.32 ^a	5.39 ±0.28 ^b	5.59 ±0.26 ^a	5.74 ±0.25 ^a	5.49 ±0.32 ^b	5.73 ±0.33 ^a	5.82 ±0.29 ^a
	8 Ws	5.10 ±0.22 ^c	5.82 ±0.29 ^a	6.05 ±0.31 ^a	6.21 ±0.35 ^a	5.47 ±0.32 ^b	5.63 ±0.38 ^b	5.99 ±0.28 ^a	5.53 ±0.26 ^b	5.81 ±0.27 ^b	5.89 ±0.31 ^a
Treated effect	4 Ws	5.06 ±0.19 ^c	5.74 ±0.23 ^a	5.89 ±0.19 ^a	5.99±0.31 ^a	5.62 ±0.26 ^b	5.73 ±0.36 ^a	5.91 ±0.31 ^a	5.59 ±0.28 ^b	5.71 ±0.28 ^a	5.81 ±0.29 ^a

L.S.D = 0.34 for protective effect and 0.35 for treated effect.

Table (9): Effect of L-carnitine and Garlic oil treatment for 4 weeks following expose of the rats to high cholesterol diet (1, 2, and 3 g cholesterol /kg of Paddy feed) for 4 weeks on blood serum cholesterol, triglyceride, low density lipoprotein, very low density lipoprotein, high-density lipoproteins (mg/dL).

		Cholesterol (mg/dL)	Triglyceride (mg/dL)	HDL-cholesterol (mg/dL)	LDL-cholesterol (mg/dL)	VLDL-cholesterol (mg/dL)
Control for 4 weeks		108.5 ^f ± 4.50	73.0 ^f ± 3.59	49.88 ^a ± 1.13	50.25 ^g ± 4.74	14.60 ^f ± 0.72
High cholesterol diet for 4 weeks	1g/Kg	145.1 ^e ± 4.02	94.75 ^e ± 1.83	39.50 ^{bc} ± 1.20	65.25 ^f ± 1.39	18.95 ^e ± 0.37
	2g/Kg	169.4 ^b ± 4.93	101.9 ^d ± 1.55	36.0 ^e ± 1.31	82.25 ^d ± 4.83	20.38 ^d ± 0.31
	3g/Kg	189.6 ^a ± 9.18	122.6 ^a ± 10.28	33.0 ^f ± 1.31	95.13 ^{bc} ± 3.44	24.53 ^a ± 2.06
Treatment L-carnitine for another 4 weeks	1g/Kg	152.5 ^d ± 5.76	105.3 ^{cd} ± 6.61	37.50 ^d ± 1.20	71.38 ^e ± 7.61	21.03 ^{cd} ± 1.36
	2g/Kg	161.1 ^c ± 6.88	128.8 ^a ± 7.09	37.38 ^{de} ± 0.92	105.6 ^a ± 5.34	25.75 ^f ± 1.42
	3g/Kg	167.5 ^b ± 5.83	111.8 ^{bc} ± 4.56	33.13 ^f ± 1.55	103.9 ^a ± 3.31	22.33 ^{bc} ± 0.97
Treatment Garlic oil for another 4 weeks	1g/Kg	145.3 ^e ± 5.68	90.88 ^e ± 4.36	40.75 ^b ± 1.98	66.75 ^{ef} ± 5.95	18.13 ^e ± 0.77
	2g/Kg	149.9 ^{de} ± 6.69	114.0 ^b ± 12.46	39.63 ^{bc} ± 1.77	100.8 ^{ab} ± 9.32	22.80 ^b ± 2.49
	3g/Kg	153.5 ^d ± 6.19	102.8 ^d ± 5.80	39.0 ^c ± 1.77	94.25 ^c ± 6.86	20.55 ^d ± 1.16
	§F	94.526 [*]	46.616 [*]	86.590 [*]	90.444 [*]	46.584 [*]
	†P	<0.001 [*]				
	LSD 5%	6.103	6.665	1.445	5.697	1.335

No. of rats = 8. [†]HDL: high-density lipoproteins, LDL: low density lipoprotein and VLDL: very low density lipoprotein. Data was expressed by using mean ± SD. Means in the same column with common small letters are not significant. [§]F for ANOVA test, pairwise comparison between each 2 groups was done using Post Hoc Test (LSD). [†]P value for comparing between the different studied groups. * Statistically significant at $P \leq 0.05$.

Table (10): Effect of L-carnitine and Garlic oil treatment for 4 weeks following expose of the rats to high cholesterol diet (1, 2 and 3 g cholesterol /kg of Paddy feed) for 4 weeks on blood serum free fatty acid, malaonaldhide, glucose, insulin and insulin resistance

N	Free fatty acid (mg/dL)	Malondialdehyde (μ mol/L)	Glucose (mg/dL)	Insulin (μ IU/ml)	Insulin Resistance (HOMA-IR)	
Control for 4 weeks	12.20 ^f \pm 0.40	1.64 ^f \pm 0.63	76.38 ^f \pm 3.70	0.81 ^f \pm 0.15	0.15 ^e \pm 0.04	
High cholesterol diet for 4 weeks	1g/Kg	16.83 ^c \pm 0.27	2.16 ^e \pm 0.57	94.38 ^e \pm 1.77	2.23 ^{de} \pm 0.14	0.52 ^d \pm 0.04
	2g/Kg	17.70 ^d \pm 0.45	3.30 ^d \pm 0.49	101.9 ^d \pm 1.55	3.16 ^c \pm 0.34	0.80 ^c \pm 0.09
	3g/Kg	21.99 ^a \pm 0.79	5.78 ^a \pm 0.47	107.6 ^{abc} \pm 4.72	4.14 ^a \pm 0.21	1.10 ^a \pm 0.11
Treatment L-carnitinefor another 4weeks	1g/Kg	16.60 ^e \pm 0.39	3.28 ^d \pm 0.45	95.63 ^e \pm 4.47	2.48 ^d \pm 0.27	0.53 ^d \pm 0.11
	2g/Kg	20.33 ^b \pm 1.09	4.05 ^{bc} \pm 0.27	111.8 ^a \pm 2.31	4.11 ^a \pm 0.42	1.13 ^a \pm 0.13
	3g/Kg	20.30 ^b \pm 0.87	4.41 ^b \pm 0.43	108.6 ^{ab} \pm 3.85	4.11 ^a \pm 0.22	1.11 ^a \pm 0.10
Treatment Garlic oil for another 4weeks	1g/Kg	16.16 ^e \pm 0.44	3.58 ^{cd} \pm 0.46	93.38 ^e \pm 7.69	2.16 ^e \pm 0.31	0.50 ^d \pm 0.12
	2g/Kg	18.46 ^c \pm 1.03	3.75 ^{cd} \pm 0.33	103.4 ^{cd} \pm 7.48	3.60 ^b \pm 0.33	1.02 ^{ab} \pm 0.29
	3g/Kg	19.13 ^c \pm 0.94	3.85 ^c \pm 0.60	105.9 ^{bcd} \pm 3.52	3.50 ^b \pm 0.33	0.92 ^{bc} \pm 0.12
§F	114.995*	45.077*	41.331*	117.091*	51.889*	
†P	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	
LSD 5%	0.726	0.481	4.561	0.285	0.131	

No. of rats = 8. Data was expressed by using mean \pm SD.

Means in the same column with common small letters are not significant.

§F for ANOVA test, pairwise comparison between each 2 groups was done using Post Hoc Test (LSD). †P value for comparing between the different studied groups.

*: Statistically significant at $P \leq 0.05$.

Table (11): The consequence of treated group by using L-carnitine (250 mg/Kg. BW) and Garlic oil (28 mg/Kg. BW) for 4 weeks following exposure of the rats to high cholesterol diet (1, 2 and 3 g /Kg diet) for 4 weeks on hepatic glutathione state (μ mol/gm protein)

	High cholesterol diet			L-Carnitine (250 mg/Kg)			Garlic oil (28 mg/Kg)		
	1g cholesterol	2g cholesterol	3g cholesterol	1g cholesterol	2g cholesterol	3g cholesterol	1g cholesterol	2g cholesterol	3gm cholesterol
Total glutathione	64.12 \pm 4.06 ^a	64.13 \pm 3.98 ^a	64.29 \pm 4.11 ^a	63.83 \pm 4.19 ^a	63.92 \pm 4.12 ^a	64.08 \pm 3.99 ^a	64.22 \pm 4.08 ^a	64.35 \pm 4.13 ^a	64.42 \pm 3.92 ^a
Reduced glutathione	48.41 \pm 3.12 ^a	48.09 \pm 3.19 ^{ab}	47.39 \pm 3.06 ^b	49.13 \pm 2.99 ^a	49.26 \pm 2.85 ^a	49.27 \pm 3.06 ^a	49.36 \pm 3.16 ^a	49.55 \pm 3.11 ^a	49.72 \pm 2.98 ^a
Oxidized glutathione	15.71 \pm 0.97 ^b	16.04 \pm 1.03 ^b	16.90 \pm 0.96 ^a	14.70 \pm 0.95 ^c	14.66 \pm 1.11 ^c	14.81 \pm 1.12 ^c	14.86 \pm 0.95 ^c	14.80 \pm 0.99 ^c	14.70 \pm 1.06 ^c
Glutathione Quotient (GSH/GS.SG)	3.08	3.00	2.95	3.34	3.36	3.33	3.33	3.35	3.38

BW.: body weight, L.S.D for total glutathione = 1.88, L.S.D for reduced Glutathione = 0.91, and L.S.D for oxidized glutathione = 0.59.

Discussion

Hypercholesterolemia is a metabolic abnormality identified by elevated levels of serum TC and LDL-C. Hypercholesterolemia is considered one of the most crucial risk factors in the development and progression of atherosclerosis that causes cardiovascular diseases (CVDs) [35].

In the current study, there was significant increase in the levels of TC, TG, LDL-C, VLDL-C, FFAs, hepatic fat %, glucose, insulin, insulin resistance, and MDA in the experimental groups with different HCD regimens (1g/Kg, 2g/Kg, and 3g/Kg of Paddy feed). Also, the levels of HDL-C groups with HCD regimens are significantly decreased by increasing the amount of cholesterol in their diet. These findings are confirmed by El-Rabey *et al.* [36] who reported that rats feeding with 2% cholesterol in the fat rich diet for two months produce hypercholesterolemia causing elevated TC, LDL, VLDL, and decreased HDL. Mohamed *et al.* [37] reported that high fat diet (HFD) administration resulted in dyslipidemic changes as described by elevating serum total lipids (TL), serum TG, TC, LDL-C, and low level of serum HDL-C. Also, Yang *et al.* [38] declared the elevation of MDA concentrations which is the final result of polyunsaturated fatty acid peroxidation in higher lipid group. Many of oxygenated compounds, particularly aldehydes such as MDA and conjugated dienes, are produced during the attack of free radicals to membrane lipoproteins and polyunsaturated fatty acids [39]. Our findings are supported by the results of Zhang *et al.* [40] who found that an increased fat diet leads to serious elevation in serum glucose, insulin level, and insulin resistance. Reduction of glucose uptake by hepatic and muscular tissues resulted in hyperlipidemia because of the high fat mobilization from adipose tissue and resistance to the antilipolytic behavior of insulin. Moreover, the total and reduced glutathione concentrations decreased

significantly in rats administered HCD at a dose of 3g/kg for 4 and 8 weeks as compared with other groups. In contrast the levels of oxidized glutathione increased in rats administered high cholesterol at a dose of 2 and 3 g/kg for 2, 4, and 8 weeks as compared with other groups. This result is settled by Mutaf *et al.* [41] who reported that blood cholesterol, MDA, and oxidized glutathione (GSSG) were elevated and the reduced glutathione (GSH) was reduced in white male rabbits which was fed chow supplemented with 1% cholesterol. The obesity produced by high fat diet is accompanied by increased tissues oxidative stress, which is characterized by reduction in the antioxidant enzymes activities and glutathione levels that correlate with the increase in MDA levels in most tissues [42].

The obtained results revealed that the rats co-administered L- carnitine or garlic oil with HCD showed significant decrease in serum TC, TG, VLDL-C, FFAs, LDL-C, MDA, glucose, insulin and insulin resistance and significantly increase in serum HDL-C. Also, revealed a serious decrease in liver lipid percent and oxidized glutathione and significantly increase in the liver total glutathione and reduced glutathione.

The hypercholesterolemic rats that received L-carnitine and garlic oil supplementations after 4 weeks from beginning administration HCD for another 4 weeks, showed a highly decline in serum TC, TG, FFAs, HDL-C, MDA, liver lipid percent and oxidized glutathione. In addition, our results showed a significant increase in the liver reduced glutathione, serum LDL-C, VLDL-C, glucose, insulin, and insulin resistance. These findings are in agreement with previous studies. Many of researches have shown that L-carnitine supplementation is efficient for normalizing the blood concentrations of cholesterol and TGs [43]. González-Ortiz *et al.* [44] described that L-carnitine supplementation induce marked decrease in serum TG,

VLDL, and TC, LDL-C. On another hand, there was marked elevation in HDL-C in obese rats. Furthermore, oral administration of L-carnitine is accompanied by hypoglycemia because it encourages insulin sensitivity. As a result, it decreases insulin resistance in obese rats may be due to the management of cell energy metabolism or decreasing FFAs [44].

Rajasekar and Anuradha [45] found that L-carnitine provoked a marked suppression of MDA release and a marked elevation in GSH and action of catalase. L-carnitine addition to the HCD produce a significant decrease in thiobarbituric acid reactive substances (TBARS) and a significant increase in GSH, superoxide dismutase (SOD) levels compared to high cholesterol group. Therefore, L-carnitine may be a useful antioxidant in hypercholesterolemic case [46]. L-carnitine protective role might result directly from antioxidant impacts against oxygen radicals or from increased biosynthesis of enzymatic antioxidants such as GSH and catalase [47]. The protective effect of L-carnitine on lipid peroxidation was induced by diminishing hydrogen peroxide formation [48].

Some studies have shown that the impact of L-carnitine supplementation on lipid profiles is conflicting. Huang *et al.* [49] revealed that L-carnitine supplementation can markedly reduce LDL-C concentrations, whereas, it does not highly influence concentrations of TC, HDL-C, and serum TG in patients needing hemodialysis. A recent meta-analysis, that involved trials made on adults with cardiovascular risk factors, revealed that L-carnitine supplementation markedly declines concentrations of TC, LDL-C, and HDL-C. However, it does not highly influence concentrations of TG [50].

The results of garlic oil administration are in accordance with results reported by Ragab *et al.* [51] who stated that garlic extract supplementation highly enhanced serum lipid profile as demonstrated by a significant elevation in HDL-C level and

lowering of serum TC, TG, and LDL-C level. These results are closely comparable to these reported by Karthikesan *et al.* [52]. Other studies have reported that ingestion of garlic caused suppression of hepatic fatty acid synthesis by decreasing key enzymes action in supplying substrates, thus diminishing lipid aggregation in the liver and TG level in plasma [53]. Garlic oil has cardio-protective impacts as it may aid to decline TC, LDL-C and blood pressure while elevating high HDL [54]. Arivazhagan *et al.* [55] declared that oral administration of garlic extract in rats kept on HCD showed significantly increase of total antioxidant potential and antioxidant enzyme activities SOD and glutathione peroxidase (GSH-Px), but reduce plasma MDA concentration. The inhibition of lipid peroxidation resulted in prominent decrease in MDA level [56]. In addition, Gardner *et al.* [57] stated that garlic extract supplementation enhances blood lipid profile, improves blood antioxidant capacity and reduces the level of MDA in blood samples. Garlic oil reduces the level of cholesterol by decreasing the synthesis and absorption of cholesterol and fatty acid [58].

The GSH: GSSG ratio is a good indicator of oxidative stress in cells and tissues [59]. Inhye *et al.* [59] reported that serum and hepatic tissue of the aged black garlic (ABG) extract-administered groups shows increased GSH and decreased GSSG levels so, GSH: GSSG ratio was higher than obese group. *In vivo* and *in vitro* studies showed that garlic has cholesterol and triglyceride-lowering, antibacterial, hypoglycemic, hypotensive capacity and anti-aggregatory effects [60]. Mohammadi and Oshaghi [61] found that HDL-C level was significantly increased and also fasting blood glucose levels was significantly decreased in garlic group compared with hypercholesterolemic group.

It is evident from our results of experiments that L-carnitine and garlic oil have a stronger effect when they are

administrated with food that contains a high percentage of cholesterol from the beginning of experiments as a protective group when compared with the treated groups, in which L-carnitine and garlic oil administrated for 4 weeks after rats taking food that contains a high percentage of cholesterol for 4 weeks. It is cleared that garlic oil is more effective than L-carnitine because garlic oil decreased the level of TC, TG, LDL-C, VLDL-C, FFAs, MDA, glucose, insulin, insulin resistance, liver lipid percent, and oxidized glutathione in hypercholesterolemic rats more than L-carnitine. Also, garlic oil increased levels of HDL-C, reduced glutathione, and total glutathione.

Conclusion

From the obtained results, it can be concluded that feeding HCD disrupts the normal metabolic state in the body and resulted in a significant increase in the serum lipid profile, FFAs, MDA, glucose, insulin, insulin resistance, liver lipid percent, and oxidized glutathione. Besides, a marked decrease in serum HDL-C, liver total glutathione, and reduced glutathione. Furthermore, both L-carnitine and garlic oil have a stronger hypolipidemic effect when they are administrated with HCD for 4 weeks than after 4 weeks from feeding HCD. Moreover, garlic oil is more effective than L-carnitine.

Conflict of interest

The authors have no conflict of interest to declare.

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المخلص العربي

تأثير الكارنتين وزيت الثوم علي زيادة كولسترول الدم في الجرذان البيضاء التي تم تغذيتها علي النظام الغذائي عالي الكوليسترول

مدحت محمد فوزي محمود وأحمد محسن محمد حسن

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أجريت هذه الدراسة لفحص فرط كولسترول الدم نتيجة لارتفاع الكوليسترول الغذائي ولتقدير تأثير ل-كارنتين وزيت الثوم علي معدلات الدهون في الدم، الأحماض الدهنية الحرة، الجلوكوز، أنسولين، مقاومة الأنسولين، مالونديالديهيد ومتجانسات الكبد لقياس الجلوتاثيون ونسب الدهون في الكبد. تم تقسيم مانئين وثمانية وثمانين ذكر من الجرذان البيضاء إلى أربع مجموعات علي النحو التالي: المجموعة الضابطة، مجموعة النظام الغذائي عالي الكوليسترول (1جم، 2 جم، و3 جم كولسترول / كجم من علف الأرز لمدة 8 أسابيع)، المجموعة الوقائية (تتغذي علي نظام غذائي عالي الكوليسترول 1 جم، 2 جم، 3 / كجم من علف الأرز مع ل-كارنتين 200 مجم / كجم من وزن الجسم أو زيت الثوم 28 ملجم / كجم من وزن الجسم لمدة 8 أسابيع، المجموعة المعالجة تتغذي علي نظام غذائي عالي الكوليسترول لمدة 4 أسابيع، ثم بعد ذلك تمت معالجتها بواسطة ل-كارنتين أو زيت الثوم لمدة 4 أسابيع أخرى. أظهرت النتائج في المجموعات الوقائية (إضافة ل-كارنتين أو زيت الثوم مع الغذاء عالي الكوليسترول) انخفاضاً ذو دلالة إحصائية لمعدلات الكوليسترول الكلي، الدهون الثلاثية، كولسترول البروتين الدهني منخفض الكثافة، كولسترول البروتين الدهني منخفض الكثافة جداً، الأحماض الدهنية الحرة، مالونديالديهيد، الجلوكوز، الأنسولين ومقاومة الأنسولين وزيادة ذو دلالة إحصائية في كولسترول البروتين الدهني عالي الكثافة. وأيضاً، أظهرت النتائج انخفاضاً ذو دلالة إحصائية في (نسبة دهون الكبد والجلوتاثيون المؤكسد) وزيادة ذو دلالة إحصائية في الجلوتاثيون الكلي والمختزل). أظهرت النتائج في المجموعات المعالجة انخفاضاً ذو دلالة إحصائية لمعدلات الكوليسترول الكلي، الدهون الثلاثية، كولسترول البروتين الدهني عالي الكثافة، الأحماض الدهنية الحرة، مالونديالديهيد، نسبة الدهون في الكبد والجلوتاثيون المؤكسد، وزيادة ذو دلالة إحصائية في الجلوتاثيون المختزل. بالإضافة إلى ذلك، أظهرت نتائجنا زيادة ذو دلالة إحصائية في كولسترول البروتين الدهني منخفض الكثافة، وكوليسترول البروتين الدهني منخفض الكثافة جداً، الجلوكوز، الأنسولين ومقاومة الأنسولين. بناءً علي نتائج التجارب، يتضح أن زيت الثوم أكثر فعالية من ل-كارنتين..