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Beneficial effect of flaxseed oil on lipid metabolism in high cholesterol diet fed rats

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A B S T R A C T

Hypercholesterolemia is one of the major risk factors that precipitate coronary heart disease and atherosclerosis. In the present study, the effect of flaxseed oil supplementation on serum lipid profile, apolipoprotein A (apo A), apolipoprotein B (apo B), Lipoprotein a Lp(a), homocysteine and endotheline-1 (ET-1) in high cholesterol diet-induced hypercholesterolemia in rats have been evaluated. This study was carried out on 60 male rats. The rats were divided into four equal groups of 15 rats each. Group I :(Control group): rats fed on normal diet. Group Π: Rats fed with hypercholesterolemic diet (HCD) [4% cholesterol (w/w) and 1% cholic acid] and received no drug all over the period of the experiment. Group III: Rats fed with HCD + administrated flaxseed oil (270 mg/kg, body weight/day orally) after two weeks from induction of hypercholesterolemia. Group IV: Rats fed with normal diet + administrated with flaxseed oil (270 mg/kg, body weight/day orally) after two weeks from the onset of the experiment. Blood samples were collected from all animal groups three times at 2, 4 and 6 weeks from the onset of treatment with flaxseed oil. The obtained results showed that, cholesterol-induced hypercholesterolemia caused a marked increase in serum total cholesterol, triacylglycerols, LDL-C, VLDL-C, phospholipids, lipoprotein A, Apo B, endothelin-1 and homocysteine. On the other hand, a significant decrease in serum HDL–C and Apo A were observed in high cholesterol diet-induced hypercholesterolemia in rats. Treatment with flaxseed oil to high cholesterol diet-induced hypercholesterolemia rats lowered serum total cholesterol, triacylglycerols, LDL-C, VLDL-C, phospholipid, endothelin-1 and homocysteine concentration in addition to increasing HDL-C and Apo A. These results suggest that, flaxseed oil may be effective in controlling cholesterolemic status and improving dyslipidemia and has the potential in reducing cardiovascular complications due to hypercholesterolemia.

Keywords: Flaxseed oil; Hypercholesterolemia; lipid profile; Endothelin-1; Homocysteine

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1. INTRODUCTION

American heart association (AHA) defined hyperlipidemia is a high level of fats in the blood. These fats, called lipids include cholesterol and triglycerides. There are different types of hyperlipidemia depending on which lipid levels are high in the blood (Jain et al., 2007). Elevated levels of plasma total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triacylglycerol (TAG) as well as reduced levels of plasma high density lipoprotein cholesterol (HDL-C) are often associated with an increased risk of coronary heart disease (Smith et al., 2004).

Hypercholesterolemia has been associated with enhanced oxidative stress related to increased lipid peroxidation. Increased generation of oxidized LDL is a major factor in the vascular damage associated with high cholesterol levels. Hence, the inhibition of oxidative stress under hypercholesterolemic conditions is considered to be an important

therapeutic approach and efforts have been made to identify the antioxidative functions of various medicinal plants (Adaramoye et al., 2008). Hypercholesterolemia is one of the most important risk factors for atherosclerosis and subsequent cardiovascular disease (Steinberg, 2002). Hypercholesterolemia and Hyperlipidemia has been ranked as one of the greatest risk factors contributing to the prevalence and severity of coronary heart diseases. In developing countries, the incidence of cardiovascular disease is increasing alarmingly especially; India is on the verge of a cardiovascular epidemic (Okrainec et al., 2004). Feeding animals with cholesterol has often been used to elevate serum or tissue cholesterol levels to study the etiology of hypercholesterolemia-related metabolic disturbances (Bocan, 1998). Exogenous hypercholesterolemia causes fat deposition in the liver and depletion of the hepatocyte population; it can also cause malfunctioning of the liver, which apparently follows micro vesicular stenosis due to the intracellular accumulation of lipids (Assy et al., 2000). In addition, feeding cholesterol-rich diets induces free radical production (ROS), followed by oxidative stress and hypercholesterolemia (Bulur et al., 1995).

Flaxseed (Linum usitatissimum) is the richest dietary source of omega-3 fatty acids among plant sources. Flaxseed is widely used for its edible oil in many parts of the world. A number of investigations have demonstrated that diet supplemented with flaxseed oil has profound beneficial health effects in various pathologies. Flaxseed is also the richest source of lignans, which have been reported to have antioxidant and hypolipidemic effects (Newairy and Abdou, 2009). Flaxseed in the diet in animal studies has shown inhibit atherogenesis (Prasad, 2005) and protect during hyper-cholesterolemic conditions (Dupasquier et al., 2006). Accordingly, the purpose of the present study was to investigate the effect of flaxseed oil against high cholesterol diet induced hypercholesterolemia in rats. Also, to determine whether flaxseed when administered to hypercholesterolemic induced-rats beneficial for prevention and treatment of hypercholesterolemia complications.

2. MATERIALS AND METHODS

2.1. Experimental animals:

Sixty male albino rats, 12-16 weeks old and average body weight 180-220 g were used in the experimental investigation of this study. Rats were obtained from Laboratory Animals Research Center, Faculty of Veterinary Medicine, Moshtohor, Benha University. Animals were housed in separate metal cages, fresh and clean drinking water was supplied ad-libitum. Rats were kept at constant environmental and nutritional conditions throughout the period of experiment. The animals were left 14 days for acclimatization before the beginning of the experiment.

2.2. Flaxseed oil:

Flaxseed oil manufactured by (South Egypt Drug Industries Co. (SEDICO), 6 October City-Egypt) and it had a light yellow color. The concentration of flaxseed oil 1000mg and present in the soft gelatine capsulated form. Flaxseed oil was dissolved in propylene glycol and was administered orally in a daily dose of 270 mg/kg body weight using stomach tube. Dose of flaxseed oil was chosen to be within the therapeutic range levels reported in the pamphlet according to Paget and Barnes, (1964).

2.3. Induction of Hypercholesterolemia:

Hypercholesterolemia was induced in rat by feeding high cholesterol diet [4% cholesterol (w/w) and 1% cholic acid (w/w)] for 8-weeks (Kamesh and Sumathi, 2012).

2.4. Design of the experimental work:

Rats were randomly divided into four main equal groups, 15 rats each, placed in individual cages and classified as follow:-
Group 1: Control Normal group: Rats fed an ordinary diet only. *Group 2*: High cholesterol diet (HCD) group: Rats fed with hypercholesterolemic diet (HCD) [4% cholesterol (w/w) and 1% cholic acid] and received no drug all over the period of the experiment. *Group 3*: High cholesterol diet (HCD) + flaxseed oil treated group: Rats fed with HCD + administrated flaxseed oil (270 mg/kg, body weight/day orally) after two weeks from the onset of the experiment (induction of hypercholesterolemia).
Group 4: Normal flaxseed oil group: Rats fed with normal diet + administrated with flaxseed oil (270 mg/kg, body weight/day orally) after two weeks from the onset of the experiment.

2.5. Sampling:

Random blood sample specimens were collected from all animals groups (control and experimental groups) three times along the duration of experiment after 2 weeks, 4 weeks and 6 weeks from the onset of treatment with flaxseed oil.

2.5.1. Blood samples:

Blood samples for serum separation were collected by ocular vein puncture in dry, clean, and screw capped tubes and serum were separated by centrifugation at 2500 r.p.m for 15 minutes. Serum was separated by automatic pipette and received in dry sterile samples tube and kept in a deep freeze at -20ºC until used for subsequent biochemical analysis .All sera were analyzed for total cholesterol (TC), triacylglycerol (TAG), high density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), phospholipid, apolipoprotein A (apo A), apolipoprotein B (apo B), Lipoprotein a Lp(a), homocysteine and endotheline-1 (ET-1).

2.6. Biochemical analysis:

Serum total cholesterol (TC), triacylglycerol (TAG), high density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), phospholipid, apolipoprotein A (apo A), apolipoprotein B (apo B), Lipoprotein a Lp(a), homocysteine and endotheline-1 (ET-1) concentration were analyzed according to the methods described by Ellefson and Caraway, (1976); Stein, (1987); National cholesterol Education program Recommendation for measurement of High –density Lipoprotein Cholesterol, (1995); Friedewald et al., (1972); Bauer, (1982); Takayama et al., (1977); Rat Apolipoprotein A1 (APOA1) ELISA (Kamiya Biomedical Company, Cat. No. KT-7354); Rat Apolipoprotein B (APO B) ELISA (Kamiya Biomedical Company, Cat. No. KT- 7394); Rat Lp-a (Lipoprotein a) ELISA Kit (Elabscience, Catalog No: E-EL-R0591); Rat Homocysteine (Hcy) ELISA Kit (Catalog No.CSB-E13376r); Rat Endothelin-1 (EDN1) ELISA (Kamiya Biomedical Company.Cat.No.KT-14033).

2.7. Statistical analysis:

The obtained data were statistically analyzed by one-way analysis of variance (ANOVA) followed by the Duncan multiple test. All analyses were performed using the statistical package for social science (SPSS, 13.0 software, 2009), values of $P<0.05$ were considered to be significant.

3. RESULTS

3.1. Effect of flaxseed oil administration on serum total cholesterol, triacylglycerol and phospholipids concentration in normal and high cholesterol fed male rats (mg/dl):

The obtained results in table (1) revealed, a non-significant increase in serum TC concentration after 2 week this increase became significant after 4,6 week, associated with a significant increase in serum TAC and phospholipids concentration was observed in cholesterol fed rats all over the period of the experiments when compared with rats fed normal control diet.
Flaxseed oil treatment to rats fed high cholesterol diet associated with non-significant decrease in serum TC level after two weeks. This decrease became significant after four and six weeks of the experiments. In addition to, a significant decrease in serum TAC all over the periods of the experiments as compared to untreated cholesterol -fed rats. Flaxseed oil treatment in rats fed high cholesterol diet resulted in a non-significant decrease in serum phospholipids level after two and four weeks of the experiments as compared to untreated cholesterol -fed rats, this non-significant decrease became significant after six weeks of the experiments as compared to untreated cholesterol -fed rats.

3.2. Effect of flax seed oil administration on serum HDL-c, LDL-c and VLDL-c concentration in normal and high cholesterol fed male rats (mg/dl):

The obtained results in table (2) revealed a significant increase in serum LDL-c and VLDL-c concentration. On the other hand, a significant decrease in serum HDL-c concentration was observed in cholesterol fed rats all over the period of the experiments when compared with rats fed normal control diet. Flaxseed oil treatment resulted in a significant decrease in serum LDL-c and VLDL-c level all over the periods of the experiments as compared to untreated cholesterol -fed rats. On the other hand, flaxseed oil treatment resulted in a non-significant increase in serum HDL-c level all over the period of the experiments as compared to untreated cholesterol -fed rats.

3.3. Effect of flaxseed oil administration on serum Lipo A, Apo A and Apo B concentration in normal and high cholesterol fed male rats (mg/dl):

The obtained results in table (3) revealed, a significant increase in serum lipoprotein A and Apo B concentration, meanwhile, a significant decrease in serum Apo A was observed in cholesterol fed rats all over the period of the experiments when compared with rats fed normal control diet.
Flaxseed oil treatment in rats fed high cholesterol diet resulted in a significant decrease in serum Lipoprotein A and Apo B level, meanwhile, a non-significant increase in serum Apo A all over the period of the experiments as compared to untreated cholesterol -fed rats.

3.4. Effect of flaxseed oil administration on serum Endothelin-1 and Homocysteine concentration in normal and high cholesterol fed male rats (mg/dl):

The obtained results in table (4) revealed, a non-significant increase in serum endothelin-1 and homocysteine concentration in cholesterol fed rats after two weeks when compared with rats fed normal control diet. This increase became significant after four and six weeks of experiment.
Flaxseed oil treatment in rats fed high cholesterol diet resulted in a significant decrease in serum Endothelin-1 level all over the period of the experiment when compared to untreated cholesterol -fed rats. While a non-significant decrease in serum Homocysteine level was showed after two weeks of the experiment then it became significant decrease after four and six weeks of the experiment when compared to untreated cholesterol-fed rats.

Table (1): Effect of flax seed oil administration on serum total cholesterol, triglycerides and phospholipids concentration in normal and high cholesterol fed male rats (mg/dl)

Experimental groups	Total Cholesterol (mg/dl)			Triacylglycerols (mg/dl)			phospholipids (mg/dl)		
	2 weeks	4 weeks	6 weeks	2 weeks	4 weeks	6 weeks	2 weeks	4 weeks	6 weeks
Normal control	67.04 ±8.27 a	78.42 ±0.42 b	85.77 ±2.43 b	85.89 ±2.65 b	88.14 ±2.45 b,c	76.52 ±11.95 b	66.56 ±1.07 c	67.95 ±5.42 b	79.13 ±6.31 c
High cholesterol diet	74.94 ±3.70 a	96.89 ±10.39 a	111.68±5.98 a	117.62±6.00 a	121.01±9.09 a	111.59±7.71 a	111.82±15.74 a	98.47 ±11.67 a	120.59±1.67 a
Flax seed Oil treated	66.69 ±3.34 a	64.23 ±3.68 b,c	73.46 ±5.11 b,c	80.28 ±5.61 b	71.12 ±9.91 c	86.93 ±4.45 b	96.57 ±4.14 a,b	97.27 ±10.46 a,b	97.77 ±5.34 b
Flax seed Oil Normal	79.20 ±7.85 a	77.91 ±3.68 b	65.29 ±4.97 c	87.59 ±4.58 b	98.23 ±8.12 b	62.55 ±4.41 b	80.51 ±0.58 b,c	83.37 ±8.75 a,b	78.49 ±4.86 c

Data are presented as (Mean ± S.E). S.E = Standard error. Mean values with different superscript letters in the same column are significantly different at ($P \leq 0.05$).

Table (2): Effect of flaxseed oil administration on serum HDL-c, LDL-c and VLDL-c concentration in normal and high cholesterol fed male rats (mg/dl)

Experimental groups	VLDL-C (mg/dl)			LDL-C (mg/dl)			HDL-C (mg/dl)		
	2 weeks	4 weeks	6 weeks	2 weeks	4 weeks	6 weeks	2 weeks	4 weeks	6 weeks
Normal control	39.62 ±0.75 a,b	47.29 ±1.05 a	49.95 ±2.44 a	7.05± 2.09 c	13.51 ±0.81 b	20.51 ±2.29 b	17.18 ±0.35 b	17.63 ±0.49 b,c	15.31 ±2.39 b
High cholesterol diet	32.93 ±1.43 b	34.14 ±0.94 b	37.18 ±0.21 b	35.21 ±8.65 a	38.55 ±8.29 a	51.94 ±4.67 a	23.52 ±1.20 a	24.20 ±1.82 a	22.32 ±1.54 a
High CHL + Flaxseed Oil	38.74 ±3.72 a,b	35.68 ±3.19 b	41.32 ±1.82 b	11.89 ±2.68 b,c	14.33 ±1.17 b	17.52 ±2.43 b	16.06 ±1.12 b	14.23 ±1.98 c	17.39 ±0.89 b
Flax seed Oil Normal	41.62 ±1.88 a	40.71 ±3.02 a,b	33.59 ±3.72 b	20.07 ±7.18 a,b,c	17.55 ±0.35 b	19.18 ±2.34 b	17.51 ±0.92 b	19.64 ±1.63 b	12.51 ±0.88 b

Data are presented as (Mean ± S.E). S.E = Standard error. Mean values with different superscript letters in the same column are significantly different at ($P \leq 0.05$).

Table (3): Effect of flaxseed oil administration on serum Lipo A, Apo A and Apo B concentration in normal and high cholesterol fed male rats (mg/dl)

Experimental groups	Lipo a			ApoA1			Apo B		
	2 weeks	4 weeks	6 weeks	2 weeks	4 weeks	6 weeks	2 weeks	4 weeks	6 weeks
Normal control	3.03± 0.25 ^{b,c}	3.09± 0.07 ^{b}	2.26± 0.24 ^{b}	17.74 ±1.50 ^{a}	20.45 ±1.38 ^{a}	16.68 ±1.01 ^{a}	0.71± 0.10^{b}	0.74± 0.09^{b}	0.64± 0.03^{b,c}
High cholesterol diet	4.02± 0.18 ^{a}	4.12± 0.39 ^{a}	4.79± 0.30 ^{a}	10.56 ±1.23 1^{b}	13.97 ±1.88 ^{b}	12.37 ±1.22 ^{c}	1.13± 0.09^{a}	1.16± 0.05^{a}	1.05± 0.08^{a}
High CHL + Flaxseed Oil	2.50± 0.15^{b,c,d}	2.22± 0.49 ^{b}	3.15± 0.44 ^{b}	14.11 ±0.66 ^{a,b}	14.07 ±0.38 ^{b}	13.66 ±0.20 ^{b,c}	0.65± 0.03^{b}	0.58± 0.07^{b}	0.49± 0.05^{c}
Flax seed Oil Normal	3.00± 0.15^{c,d}	2.62± 0.14 ^{b}	2.98± 0.16 ^{b}	17.18 ±0.53 ^{a}	18.50 ±0.36 ^{a}	15.87 ±0.32 ^{a,b}	0.67± 0.05^{b}	0.54± 0.05^{b}	0.84± 0.18^{a,b}

Data are presented as (Mean ± S.E). S.E = Standard error. Mean values with different superscript letters in the same column are significantly different at *(P*≤0.05)

Table (4): Effect of flaxseed oil administration on serum Endothelin-1 and Homocysteine concentration in normal and high cholesterol fed male rats (mg/dl)

Experimental groups	Endothelin-1			Homocysteine		
	2 weeks	4 weeks	6 weeks	2 weeks	4 weeks	6 weeks
Normal control	21.61±0.64^{a}	18.17±0.64^{b}	20.79±0.64^{b,c}	0.88±0.08 ^{a}	1.09±0.34 ^{c}	0.67±0.16 ^{c}
High cholesterol diet	22.73±0.64^{a}	25.73±0.64^{a}	25.35±0.64^{a}	1.42±0.09 ^{a}	2.20±0.11 ^{a}	1.68±0.14 ^{a}
High CHL + Flaxseed Oil	7.51±0.64^{e}	8.59±0.64^{c}	19.12±0.64^{c,d}	1.32±0.34 ^{a}	1.13±0.21 ^{c}	1.16±0.12 ^{b,c}
Flax seed Oil Normal	14.39±0.64^{c}	16.02±1.17^{b}	18.78±0.64^{c,d}	0.86±0.12 ^{a}	1.14±0.04 ^{c}	0.92±0.17 ^{b,c}

Data are presented as (Mean ± S.E). S.E = Standard error. Mean values with different superscript letters in the same column are significantly different at *(P*≤0.05).

4. DISCUSSION

The obtained results demonstrated in (Table 1, 2) revealed that, a significant increase in lipid profile in high cholesterol diet group. Cholesterol-cholic acid feeding has often been used to raise cholesterol levels in plasma and tissues of experimental animals (Chen et al., 2004). It has been shown by other investigators that an increase in dietary cholesterol intake in animals led to hypercholesterolemia (Kishida et al., 2002). The high levels of TAG in the present study may be due to inhibition of 7a-hydroxylase activity (Beigneux et al., 2002). Also, the high levels of LDL-C found in hyper-cholesterolemic rats, may be attributed to a down regulation in LDL receptors by cholesterol and saturated fatty acids included in the diet (Mustad et al., 1997), moreover, this increase in LDL-c level after high fat diet

consumption might be explained via involvement of two enzymes namely cholesterol ester hydrolase and cholesterol ester synthetase. These enzymes balance the cholesterol levels in the blood. Hence, it is logical to assume that the elevation in plasma cholesterol is mediated through increased cholesterol turnover and influenced by the relative balance between cholesterol ester hydrolase and cholesterol ester synthetase activity. With increased esterifying activity (when cholesterol ester hydrolase: cholesterol ester synthetase is lowered) cholesterol will be predominantly in its ester form (as in LDL-c) and can lead to the development and progression of atherosclerosis (Shanmugasundaram et al., 1986). The obtained results demonstrated in (Table 1,2) revealed that, flaxseed oil in rats fed high cholesterol diet resulted in decrease of TC, TAC, LDL-c, VLDL-c and phospholipid. Alpha-linolenic acid (ALA) rich flaxseed oil (FO) results in a higher cholesterol secretion into bile leading to, a depletion of the intra-hepatic pool of cholesterol, and thus to an increase in cholesterol synthesis and turnover (Morise et al., 2004). Moreover, ALA rich diet reduces hepatic lipid accumulation both by stimulating β-oxidation and by suppressing fatty acid synthesis (Murase et al., 2005). Furthermore, Ide et al., (2000) reported that, FO could have exerted its protective effect probably as a better substrate for mitochondrial and peroxisomal β-oxidation. All these mechanism may account for the better regulation of hepatic lipid metabolism by FO. The present results indicate that hepatic cholesterol lowering effect resulted from the reduction of cholesterol synthesis in liver tissues. Thus, the reduction of esterified cholesterol level by FO may indicate that the cholesterol was used for the synthesis of vital molecules in tissues, including the liver. Dietary ALA results in higher cholesterol secretion into bile, leading to a depletion of the intra-hepatic pool of cholesterol, which indicated reduced cholesterol content of the liver (Kim et al., 1999). Supplementation with ALA significantly inhibited the hepatic triglyceride accumulation and fatty liver formation (Murase et al., 2005). There was a consistent reduction of TG and PL concentrations in HFD+FO rats in comparison with HFD rats which might be due to hypocholesterolemic activity of ALA in FO. These observations may be suggest that FO is incorporated into the liver cells and influence metabolism of serum and liver lipids. The obtained results demonstrated in (Table 3) revealed that, a significant increase in serum lipoprotein A and Apo B was observed in cholesterol fed rats all over the period of the experiments. In present study, increased level of Apo B on high cholesterol feeding diet may be due to decreased expression of LDL-receptor during hyper-cholesterolemia. Decreased level of LDL-receptor is responsible for decreased clearance of Apo B along with LDL, so these apolipoproteins are accumulated in the body (Ouguerram et al., 2004). However, most of the studies suggested that one molecule of Apo B exists per lipoprotein particle, thus the quantity of Apo B in fasting plasma predicts the number of LDL and VLDL particles (Levinson and Wagner, 1992). Therefore, plasma apoB levels maybe a better assay of the concentration of atherogenic lipoprotein particles than total or LDL cholesterol levels (Sniderman and Silberberg, 1990). Abnormalities in the apoB metabolism are responsible for the generation of hypercholesterolemia and increased risk of coronary heart disease (Whitfield et al., 2004). Several mechanisms of Lp(a) participation in atherogenesis have been proposed. One of them consists in the direct deposition of that lipoprotein on arterial wall, similarly to that which happens with LDL and oxidized LDL. The fact that Lp(a) is more likely to undergo oxidation than LDL itself might facilitate uptake by macrophages via scavenger receptors (Argraves et al., 1997). That is the most universal mechanism of

atherogenesis, in which macrophages 'indulge themselves' in the cholesterol from LDL, and eventually from Lp(a), transforming themselves into foam cells, precursors of atherosclerosis. Another pro-atherogenic mechanism of Lp(a) would relate to the inverse correlation between that lipoprotein levels and vascular reactivity, in which case the increase in Lp(a) plasma levels would induce endothelial dysfunction (Wu et al., 2004). Apo A plays a key role in the metabolism of HDL-cholesterol, which is esterified in the bloodstream by lecithin cholesterol acetyltransferase, using Apo A as a cofactor, and then returns to the liver for excretion as bile acids or redistribution to other tissues, since high levels of Apo A are accompanied by high concentrations of the oxidation-resistant HDL, Apo A is thought to be a marker of adequate anti-atherogenic defense. By contrast, Apo B is associated with the LDL, which plays a central role in the uptake of cholesterol-rich LDL particles by peripheral tissues and liver. A high concentration of LDL (and therefore of Apo B), is atherogenic, since it is ingested by macrophages, thus producing foamy cells (Hashimoto et al., 2000). LDL is also involved in other pathological processes such as up-regulation of adhesion molecule expression, attachment to endothelial cells, migration and subendothelial localization of macrophages, recruitment of smooth muscle cells and platelet activation, with resulting risk of thrombosis (Witting et al., 1999). As pointed out by Martens et al., (1999), oxidatively modified Apo B plays a central role in the above mechanisms, since it is the main macrophage proliferation inducing factor. The obtained results demonstrated in (Table 4) revealed that, a marked increase in serum endothelin-1 and homocysteine concentration was observed in cholesterol fed rats. Horio et al., (1991) reported that, animal studies in rats fed a high-cholesterol diet have shown that circulating ET-1 levels and ET-1 immunoreactivity are increased in the epicardial coronary arteries and aortas of these animals before the development of atherosclerotic plaques. Oxidized LDLs have also been shown to increase ET-1 mRNA expression in cultured porcine and human aortic endothelial cells (Boulanger et al., 1992). Studies have indicated that LDL and oxLDL cholesterol stimulate the production of ET-1(Niemann et al., 2005). It has also been indicated that ET-1 stimulates the uptake of oxLDL in endothelial cells via stimulation of LDL receptor 1(LOX-1), mediated by ETB receptor (Morawietz et al., 2001). Similarly, ET-1 levels are elevated in patients with hypercholesterolemia, even in the absence of clinical cardiovascular disease (Mangiafico et al., 1996). Chronic homocysteinaemia also activates production of protein-1-mediated deregulation of endothelin-1 (ET-1), which is a strong vasoconstrictor and a key molecule involved in atherogenesis. Pro-oxidative states and hyperhomocysteinaemia also induce oxidation of LDL particles and the expression of lectin-type oxidized LDL receptor 1(LOX-1) on endothelial cell surfaces (Antoniades et al., 2009). These events induce foam cell formation and further promote atherogenesis. High plasma homocysteine levels have been linked to coronary artery disease (CAD) (Nygard et al., 1997). In present study, flaxseed oil decrease the level of Apo B and lipoprotein a meanwhile, increase the level of Apo A. This inhibition of the Apo B and lipoprotein a may possibly help to decrease the hypercholesterolemia and cardiac vascular dieses.

Conclusion: The flaxseed oil administration produces potent anti-atherogenic and an effective treatment against hyper-cholesterolemia induced by high cholesterol diet in rats, since flaxseed oil was able to ameliorate serum biochemical parameters, lipid profile, and endothelial function. We recommended that, administration of diet rich in the natural antioxidant is very important for

protection of different body tissue, against oxidative stress or hypercholesterolemia and cardiac vascular disease and may be beneficial for patients who suffer from hyper-lipidemia, hypercholesterolemia and/or arteriosclerosis.

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التأثير المفيد لزيت بذرة الكتان علي أيض الدهون في الفئران المغذاه علي غذاء عالي الكوليستيرول.

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الملخص العربي

في هذه الدراسة تم تقييم التأثير العلاجي لزيت بذره الكتان على التغيرات في مستوي الدهون في الدم، أبوليبوبرتين-أ ،أبوليبوبروتين–ب ، الليبوبرتين–أ ، اندوسيلين-1، هيموسيستين-1في دم الفئران المستحدث فيها زياده الكوليسترول بالدم عن طريق تغذيتها على مدى طويل بعليقة غنية بالكوليسترول. هذا وقد أستخدم لأجراء هذه الدراسة عدد 60 من ذكور الفئران البيضاء أعمارهم تتراوح من 12-16 أسبوع وأوزانها من180-220جرام وقد قسمت إلى أربع مجموعات متساوية اشتملت كل مجموعة على عدد خمسه عشرة فأرا وتم توزيعها كالآتي: المجموعة الأولى: (المجموعة الضابطة): تم تغذيتها على العليقة الأساسية ولم يتم تجريعها أدوية واستخدمت كمجموعة ضابطة للمجموعات الأخرى. المجموعة الثانية: (المجموعة المحدث بها زيادة الكوليسترول بالدم): تم تغذيتها بغذاء عالي الكولستيرول (4% كولستيرول + 1% حمض الكوليك) لمده 8 أسابيع وأستخدمت كمجموعة ضابطة إيجابية لكل المجموعات التجريبية. المجموعة الثالثة:(المجموعة المحدث بها زيادة الكولستيرول بالدم + زيت بذره الكتان): تم تغذيتهم بالعليقة عالية الكولسترول مع تجريعها بزيت بذرة الكتان بجرعه 270 مجم لكل 1كجم من وزن الفئران بعد مُضى اسبوعين منذ بداية التجربة. المجموعة الرابعة:(مجموعه زيت بذرة الكتان الطبيعه): تم تغذيتها على العليقة الأساسية ثم تم تجريعها بالكركومين بجرعه 270 مجم لكل 1كجم من وزن الفئران بعد مُضى اسبوعين منذ بداية التجربة. جمعت عينات الدم من جميع الفئران على ثلاث فترات بعد 2، 4، 6 أسابيع من بداية العلاج لإجراء التحاليل البيوكيميائية للكوليستيرول و الجليسريدات الثلاثية و البروتينات الدهنية عالية الكثافة ومنخفضة الكثافة و شديدة إنخفاض الكثافة و الفوسفوليبد و أبوليبوبرتين-أ و أبوليبوبروتين–ب و الليبوبرتين–أ و اندوسيلين-1 بالاضافه الي هيموسيستين-1. وقد أسفرت نتائج التحليل البيوكيميائى عن وجود زيادة معنويه فى كلا من الكوليسترول والجليسريدات الثلاثية ومنخفضة الكثافة و شديدة إنخفاض الكثافة و الفوسفوليبد و أبوليبوبروتين –ب و الليبوبرتين –أ و اندوسيلين-1 و هيموسيستين-1، من جهة اخرى اظهرت النتائج نقص معنوي في البروتينات الدهنية عالية الكثافة و أبوليبوبرتين -أ فى المجموعه المحدث بها زياده الكوليستيرول. كما أن نتائج مجاميع الفئران المحدث بها زيادة الكوليسترول بالدم والتي تم علاجها بزيت بذرة الكتان أظهرت نقص في كلا من الكوليستيرول و الجليسريدات الثلاثية ومنخفضة الكثافة و شديدة إنخفاض الكثافة و الفوسفوليبد و أبوليبوبروتين–ب و الليبوبرتين–أ و اندوسيلين-1 و هيموسيستين-1. كما ادي زيت بذرة الكتان الي حدوث زيادة في البروتينات الدهنية عالية الكثافة و أبوليبوبرتين-أ عند مقارنتها بتللك الفئران التى تغذت على عليقة غنية بالكوليستيرول. أوضحت هذه الدراسة بأن زيت بذرة الكتان يلعب دوراً هاماً كعلاج لإرتفاع الدهون والكوليسترول بالدم وقدرته على حماية الأوعية الدموية من الآثار الضارة والخطيرة التى يسببها ارتفاع الكوليسترول بالدم. لذلك توصى الدراسة بأن تناول الغذاء الغني بزيت بذرة الكتان قد يكون مفيدا للمرضى الذين يعانون من ارتفاع الكولسترول والجليسريدات الثلاثية بالدم وكذلك في حالات الإجهاد التأكسدي وتصلب الشرايين.

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