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EFFECTS OF FLAXSEED OIL ON VASCULAR HEALTH IN HYPERLIPIDEMIC ADULT MALE ALBINO RATS

By

Basma Kamal Ramadan

Physiology Department, Faculty of Medicine (Girls), Al-Azhar University, Cairo

ABSTRACT

Background: Globally, the prevalence of overweight and obesity is increasing, predisposing both sexes to health hazards including cardiovascular diseases and death. **Objective:** Evaluation of the effects of flaxseed oil on vascular health in hyperlipidemia. **Material and methods:** Forty adult male albino rats of local strain between 7-8 weeks-old weighing 130-150 g were used. The rats were divided into four equal groups: Group I (control group), Group II (hyperlipidemic group), Group III (HFD-flaxseed oil prophylactic-group), Group IV (HFD-flaxseed oil treated-group). At the end of the experiment body weight, as well as serum levels of lipid profile, malondialdehyde (MDA), reduced glutathion (GSH), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), and vascular cell adhesion molecule 1 (VCAM1) were determined for all groups. **Results:** Flaxseed oils pretreatment and treatment significantly decreased body weight. Serum cholesterol, triglycerides and LDL significantly decreased, while HDL significantly increased. Furthermore, flaxseed oil suppressed the increase in MDA, serum IL-6, TNF-α, and VCAM1 level and elevated the serum GSH level significantly. **Conclusion:** Flaxseed oil possessed anti-atherogenic actions that might be mediated by their reducing effect on the lipid profile and inflammatory markers. Pretreatment was more effective than its use as a treatment. Thus, flaxseed oil may have the therapeutic potential in atherosclerotic patient and may be a novel therapeutic strategy for atherosclerosis prevention and treatment.

Key words: Flaxseed oil, Hyperlipidemia, Atherosclerosis, Cardiovascular diseases.

INTRODUCTION

Hyperlipidemia is one of the main risk factors for atherosclerosis and cardio-vascular diseases ***(Colletti et al., 2016)***. Epidemiological studies have documented that nutritional factors may affect the prevalence of cardiovascular diseases. The diet should be low in saturated fats, trans fats, cholesterol, sodium, and simple sugars with high intake of fruits, vegetables, whole grains, and monounsaturated fat ***(Esposito et al., 2007)***. Trans fats act more like saturated fats, which tend to block low density lipoprotein (LDL) receptors, thus preventing their uptake from the bloodstream. Frequent consumption of energy-dense foods, such as foods that are high in fats and sugars, promotes obesity and increases the risk of atherosclerosis and cardiovascular diseases ***(Buttar et al., 2005).***

Up to four billion people, living in the developing world, rely on medicinal plants ***(Ekor, 2014)***. Pharmacologically and biologically active compounds have been extracted from the medicinal plants. Many of these compounds have been the basis for the development of potentially therapeutic drugs, for pharmaceuticals, to

target a specific disease ***(Kong et al., 2003*** and ***Pal & Shukla, 2003).***

Flaxseed is the seed of *Linum usitatissimum* with yellow or reddish brown seeds and nutty flavor (***Rodriguez-Leyva et al., 2013).*** Flaxseed is also known as linseed and these terms are used interchangeably. Flaxseed is often used to describe flax when consumed by humans while linseed denotes when it is used specifically for industrial applications ***(Kajla, 2015).*** Flaxseed has garnered attention due to its health benefits related to the presence of the dietary ω-3 FA α-linolenic acid (ALA; 18:3n–3), which has anti-inflammatory, anti-atherogenic and antiarrhythmic characteristics ***(Ander et al., 2004***, ***Burdge & Calder, 2006, Dupasquier et al., 2006*** and ***Kaur et al. 2012)***, potent antioxidant phytoestrogen lignans, which are one of the major groups of phytoestrogens that have antitum-origenic and antioxidant properties ***(Thompson et al., 2005)*** and dietary fiber ***(Khalesi et al., 2013)***. The seeds are commonly consumed in one three ways: whole seed, ground seed or flaxseed oil. ALA has greater bioavailability in flaxseed oil than in ground or whole seed ***(Austria et al., 2008)***. Flaxseed is establishing importance in the world's food chain as a functional food (the food or food ingredients that may provide physiological benefits and helps in preventing and/or curing of diseases) ***(Kajla et al., 2015).*** It has been beneficial to health in different situations, such as preventing cardiovascular disease and reduction of total plasma cholesterol and triglycerides ***(Lucas et al., 2004)***.

The aim of the present study was to evaluate the effects of flaxseed oil on hyperlipidemia prevention and treatment induced in adult male albino rats.

MATERIAL AND METHODS

Materials:

- Commercial rat chow diet (balanced diet), containing 67% carbohydrates, 10% fat, and 23% protein as the energy sources (overall calories: 3.6 kcal/g), was purchased from El Gomhorya company (Cairo, Egypt).
- High fat diet (HFD), consisting of 88% of standard pellet animal diet, 10% natural fat and 2% cholesterol was prepared and used to induce hyperlipidemia ***(Xu et al., 2010 and Hussain et al., 2016).*** The HFD was composed of the following energy sources: 52% carbohydrates, 30% fat and 18% protein Overall calories 4.8 kcal/g ***(Hussain et al., 2016).***
- Natural cold pressed flaxseed oil was purchased from Imtenan Company, (Cairo, Egypt).

Experimental animals and design:

Forty adult male albino rats (7-8-weeks old, weighing 130-150 g) were purchased from the Nile Pharmaceuticals Company (Cairo, Egypt). They were housed in laboratory standard cages (5 rats/ 25X30X30 cm cage), under specific pathogen-free conditions in facilities maintained at controlled room temperature with a natural light/dark cycle. All animals had free access to rat chow diet (see below) and water *ad libitum* and were acclimated for one week prior to initiation of the experiment in the laboratory of Physiology, Faculty of Medicine AI-

Azhar University. All procedures were approved by the Animal Care Committee. The Principles of laboratory animal care were followed, as well as specific national laws were applicable.

The rats were divided into 4 equal groups.

Group I: Rats were assigned to control group and given normal balanced chow and supplemented with saline using a gastric gavage tube for 12 weeks.

Group II: Rats were given normal balanced chow for the first 4 weeks, then the normal diet was replaced with HFD for further 8 weeks ***(Xu et al., 2010*** and ***Hussain et al., 2016).*** The rats also were supplemented with saline using a gastric gavage tube.

Group III: Rats received flaxseed oil orally at a daily dose of 1.8 mg/kg for 4 weeks with normal balanced chow ***(Tanna et al., 2012),*** and then rats received HFD for further 8 weeks.

Group IV: Rats were kept on HFD for 8 weeks, and then were given flaxseed oil orally at a daily dose of 1.8 ml/kg for other 4 weeks with normal balanced diet.

The body weight of each rat was measured and recorded weekly for all groups.

At the end of the experiment, after overnight fasting, rats were anesthetized in the morning, and blood samples were collected from retro-orbital venous plexus by capillary tubes under light ether anesthesia. 0.2 ml of the blood was hemolyzed by addition of 1.8 ml H_2O, and the hemolysate was used for assessment of GSH level. The rest of the blood was then centrifuged at 3000 rpm for 15 minute for serum collection. Serum was separated in aliquots in Eppendorf tubes and stored frozen at -80°C until analysis.

Biochemical analysis:

1. The total serum cholesterol and HDL were measured by quantitative enzymatic colorimetric determination of total and HDL cholesterol in serum using biomed diagonstic assay kits ***(MacLachlan et al., 2000).***
2. Serum triglycerides were measured by quantitative enzymatic colorimetric determination of triglycerides in serum using Cayman colorimetric assay kit ***(Cole et al., 1997)***
3. Serum LDL cholesterol was calculated from the values of total cholesterol (TC), HDL and triglycerides using Friedewald equation: LDL (mg/dl) = TC - HDL –$(TG/5.0)^2$***(Ahmadi et al., 2008).***
4. Serum malondialdehyde (MDA) has been identified as the product of lipid peroxidation that reacts with thiobarbituric acid to give red species absorbing at 535 nm. It was measured by using free-SH groups estimation method ***(Janero, 1990).***
5. Serum reduced glutathione (GSH) was measured by the protocol described previously by, using glutathione peroxidase assay kit (Cayman Chemical, Ann Arbor, MI, USA) according to the manufacturer's instruction. Briefly, 8 ml of phosphate buffer, 3 ml of precipitating solution, and 1 ml of DTNB were added to the blood hemolysate filtrate. The optical density was measured spectrophotometrically at a wave length 410 nm ***(Ceballos-Picot et al., 1992).***

6. Serum tumor necrosis factor alpha (TNF-α) level was measured by commercial ELISA kits (Ray Bio® Rat, Ray Biotech, Norcross, GA, USA) according to manufacturer's protocol. The level of sensitivity of the kit was less than 25 pg TNF-α/ml ***(Engelmann et al., 1990).***
7. Serum interleukin-6 (IL-6) level was measured by commercial ELISA kits (Ray Bio® Rat, Ray Biotech, Norcross, GA, USA) according to manufacturer's protocol. The level of sensitivity of the kit was less than 30 pg IL-6/ml ***(Ferrari et al., 2003).***
8. Vascular cell adhesion molecule 1(VCAM1) was determined by commercially available ELISA and standards (R&D System Europe Ltd).The level of sensitivity of the kit was less than 3.9 ng/ml ***(Pigott et al., 1992).***

Statistical Analysis: All the data were expressed as mean ±standard error of mean (SEM). Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by Bonferroni post hoc multiple comparison test using the program Statistical Package for the Social Sciences (SPSS), IBM SPSS Statistics (version 18). The values of $P < 0.001$ were considered significant.

RESULTS

Effect of flaxseed oil on body weight of hyperlipidemic rats:

There were significant differences on comparing all groups with each other in body weight (Table 1).

HFD feeding for eight weeks significantly increased the body weight when compared to normal control rats. When flaxseed oil was given orally for 4 weeks before inducing hyperlipidemia as prophylactic, the body weight growth of rats significantly decreased vs hyperlipidemic rats. Notably, there was no significant difference in body weight between flaxseed prophylactic group and control group. When flaxseed oil was given after inducing hyperlipidemia, the body weight significantly decreased vs hyperlipidemic rats, but it was still significantly higher than control group.

Table (1): Effect of flaxseed oil on body weight of hyperlipidemic rats.

Groups / Parameter	Group I (Control group)	Group II Hyperlipidemic	Group III Flaxseed-prophylactic	Group IV Flaxseed-treated	ANOVA
	Mean± S.E.M	Mean± S.E.M	Mean± S.E.M	Mean± S.E.M	P value
Body weight (g)	214.9 ± 0.9	303.4 [a]± 3.4	217.7 [b] ± 2.2	244.9 [a,b] ± 3.5	P<0.001

Number of sample in each group = 10

a = Significant values versus group I (control) (P <0.001).

b = Significant values versus group II (Hyperlipidemic) (P <0.001).

Effect of flaxseed oil on lipid profile of hyperlipidemic rats:

a) Serum concentration of total cholesterol and triglycerides:

There were significant differences on comparing all groups with each other in serum concentration of total cholesterol and triglycerides respectively (Table 2).

HFD for eight weeks significantly increased the fasting serum total cholesterol level in hyperlipidemic group vs control rats. In comparison to hyperlipidemic group, flaxseed groups (prophylactic and treatment) showed significantly lower total cholesterol and triglycerides but no significant difference was observed between prophylactic flaxseed group and control group on total cholesterol and triglycerides, while its use as a treatment showed 20 - 25% higher total cholesterol and triglycerides vs control group.

b) Serum concentration of LDL and HDL:

There were significant differences on comparing all groups with each other in serum concentration of LDL and HDL respectively (Table 2).

Similar to the above results, HFD supplementation increased the serum LDL in hyperlipidemic rats compared to control rats and flaxseed both prophylactic and treatment significantly lowered LDL level. On the other hand, a 58% reduction in serum HDL was observed on the 8th week of high fat diet supplementation when compared to control rats. Flaxseed oil-pretreated and treated groups significantly elevated HDL level when compared to hyperlipidemic rats and completely returned its level back to the normal control level in case of the pretreatment but not in the flaxseed treated hyperlipidemic group.

Table (2): Effect of flaxseed oil on lipid profile of hyperlipidemic rats.

Groups / Parameters	Group I (Control group)	Group II Hyperlipidemic	Group III Flaxseed-prophylactic	Group IV Flaxseed-treated	ANOVA
Serum cholesterol (mg/ml)	100.1 ± 0.8	186.0 ^{a} ± 2.0	100.9 ^{b} ± 0.5	124.8 ^{a,b} ± 2.4	P<0.001
Serum triglycerides (mg/ml)	81.1± 0.9	150.5^{a} ± 3.4	84.8^{b} ± 1.4	98.1^{a,b} ± 1.2	P<0.001
Serum LDL (mg/ml)	51.5 ± 0.6	117.0^{a} ± 1.6	52.7^{b} ± 0.4	69.5^{a,b} ± 0.9	P<0.001
Serum HDL (mg/ml)	59.8 ± 1.0	25.1 ^{a} ± 1.2	57.4 ^{b} ± 1.1	46.1 ^{a,b} ± 1.0	P<0.001

Number of sample in each group = 10

a = Significant values versus group I (control) (P <0.001).

b = Significant values versus group II (Hyperlipidemic) (P <0.001).

Antioxidant effects of flaxseed oil on hyperlipidemic rats.

There were significant differences on comparing all groups with each other in serum concentration of ***MDA*** and GSH respectively (Table 3).

a) Serum concentration of MDA: Serum MDA level as a marker of lipid peroxidation was extremely high with HFD supplementation for eight weeks compared to normal rats. A significant decrease of serum MDA concentration was observed in flaxseed oil-pretreated and treated groups when compared to hyperlipidemic group. The increased MDA indicated enhanced lipid peroxidation in the hyperlipidemic group. When flaxseed oil was given as prophylactic, it prevented the lipid peroxidation to occur, and the MDA level was not significantly different from control animals. Yet its use as a treatment showed significant increase in MDA vs control animal.

b) Serum concentration of Glutathione (GSH): Daily feeding of HFD for 8 weeks to rats significantly decreased the level of serum GSH compared to control rats. In comparison to hyperlipidemic rats, GSH level showed significant elevation with flaxseed oil pretreatment and treatment. The GSH level was not significantly different from control animals when rats were pretreated with flaxseed before inducing hyperlipidemia. It was significantly lower in flaxseed treated group when compared to control group.

Table (3): Effect of flaxseed oil (pretreatment and treatment) on Serum Malondialdehyde (MDA) (nmol/ml), and Glutathione (GSH) (nmol/ml).

Groups / Parameters	Group I (Control group)	Group II Hyperlipidemic	Group III Flaxseed-prophylactic	Group IV Flaxseed-treated	ANOVA
	Mean± S.E.M	Mean± S.E.M	Mean± S.E.M	Mean± S.E.M	P value
Serum MDA (nmol/ml)	1.9 ± 0.1	6.7^{a} ± 0.2	2.3^{b} ± 0.2	$3.1^{a,b}$ ±0.2	P<0.001
Serum GSH (nmol/ml)	61.6 ± 1.2	32.3^{a} ± 0.9	59.6^{b} ± 1.4	$49.2^{a,b}$ ± 1.3	P<0.001

Number of sample in each group = 10
a = Significant values versus group I (control) (P <0.001).
b = Significant values versus group II (Hyperlipidemic) (P <0.001).

Anti-inflammatory effects of flaxseed oil on hyperlipidemic rats:

There were significant differences on comparing all groups with each other in serum concentration of ***TNF-α***, ***IL-6*** and ***VCAM1*** respectively (Table 4).

a) Serum TNF-α and IL-6: HFD supplementation for eight weeks up-regulated both TNF-α and IL-6 by ~3 and ~4-fold, respectively, compared to control rats. A significant down-regulation of serum TNF-α and IL-6 concentrations was observed in flaxseed oil-pretreated

and treated groups when compared to hyperlipidemic group. The flaxseed oil was better at down-regulating both TNF-α and IL-6 concentrations when used as a pretreatment before inducing hyperlipidemia. It showed no significant difference from the control rats, while its use as a treatment increased TNF-α and IL-6 concentrations compared to the normal control group.

b) Serum VCAM1: Assessment of VACM1 concentration could be useful to detect the risk for atherosclerotic lesions in hyperlipidemic rats and to estimate the effect of flaxseed supplementation. HFD supplementation for eight weeks to normal rats induced significant elevation in serum VCAM1 compared to control rats. The VACM1 level decreased when the hyperlipidemic rats received flaxseed oil before and after the HFD supplementation. When flaxseed oil was used before the HFD supplementation, there was a complete reduction of the level of VACM1, and it became not different from control rats. Its level still significantly elevated in flaxseed treated group in comparison to the control rats.

Table (4): Effect of flaxseed oil (pretreatment and treatment) on Serum Tumor Necrosis Factor Alpha (TNF- α) (pg/ml), Interlukin-6 (IL-6) (pg/ml) and Vascular Cell Adhesion Molecule 1 (VCAM1) (ng/ml).

Groups / Parameters	Group I (Control group)	Group II Hyperlipidemic	Group III Flaxseed-prophylactic	Group IV Flaxseed-treated	ANOVA
	Mean± S.E.M	Mean± S.E.M	Mean± S.E.M	Mean± S.E.M	P value
Serum TNF-α (pg/ml)	35.2 ± 0.7	101.7^{a} ± 1.3	38.5^{b} ± .8	$47.8^{a,b}$ ± 0.7	P<0.001
Serum IL-6 (pg/ml)	1.9 ± .0.1	8.1^{a} ± 0.1	2.0^{b} ± 0.1	$3.2^{a,b}$ ± 0.1	P<0.001
Serum VCAM1 (ng/ml)	37.2 ± 0.4	151.2^{a} ± 0.7	39.2^{b} ± 1.1	$51.2^{a,b}$ ± 0.9	P<0.001

Number of sample in each group = 10
a = Significant values versus group I (control) (P <0.001).
b = Significant values versus group II (Hyperlipidemic) (P <0.001).

DISCUSSION

Dietary saturated fatty acids are associated with metabolic and cardiovascular diseases. Potentially interesting strategies to reduce disease risk is rather modification of the quality of fat consumed or using medicinal plants which are rich sources of unsaturated fatty acids, antioxidants and fibers ***(Morrison et al., 2015)***. In this study, we offer a possible natural cardio-protective agent which can effectively ameliorate HFD- induced hyperlipidemia.

A diet high in saturated fats is considered to be one of main contributors to overweight and obesity. Fat is digested into monoglycerides and fatty acids by lipase and absorbed fat is accumulated in adipose tissue through excessive adipocyte differentiation ***(Yang et al.,2015).*** The significant increase of body weight with hyperlipidemic diet for eight weeks in the present study was in agreement with previous studies who attributed this increase to the high energy density of fat, since it provides ~9 kcal per gram in comparison to the carbohydrates and protein which provides only 4 kcal. Thus, increased fat intake can promote high energy consumption, increased energy density and palatability **(*Hill et al., 2000)***. The increase in body weight may also occur due to hyperphagia and consequently high energy intake induced by adipocyte-derived leptin hormone secretion ***(Dodd et al., 2015).***

Flaxseed oil administration before and after induction of hyperlipidemia significantly decreased the body weight. Our results were on line with previous studies of ***Vijaimohan et al. (2006)*** who suggested that the hypolipidemic and antioxidant effects of flaxseed oil are responsible for its beneficial action on body weight gain. Moreover, ***Baranowski et al.(2012)*** found that the effect of dietary flaxseed oil on the body weight is attributed to its content of α–linolenic acid (ALA) which reduces the adipocyte hypertrophy, protein levels inflammatory markers, monocyte chemoattractant protein-1 (MCP-1), TNF-α and T-cell infiltration in adipose tissue. In contrast, ***Deng et al. (2012)*** showed that supplementation of flaxseed oil to hyperlipidemic rats insignificantly affects the body weight gain.

Our results showed a marked increase in the lipid profile (total cholesterol, triglycerides and LDL) in the high fat diet group, while serum HDL showed significant decrease. Administration of flaxseed oil prior to and after induction of hyperlipidemia markedly improved these parameters. These results were consistent with the studies by others ***(Amin et al., 2013*** **and** ***Li et al., 2015)***. The cholesterol level in plasma and liver of hyperlipidemic rats increased due to the increased uptake of exogenous cholesterol and subsequent its deposition in addition to the decreased cholesterol catabolism as evidenced by a reduction in bile acid production and turnover of bile acids ***(Barakat and Mahmoud, 2011)***. In the present study, flaxseed oil administration improved all the lipid profile to return nearly to the normal levels. This was supported by the study of ***Hussein et al. (2014)*** who reported that flaxseed oil supplementation to rats fed high cholesterol diet decreases the serum lipid profile. They attributed this beneficial effect to ALA which results in a higher cholesterol secretion into bile leading to depletion of the intrahepatic pool of cholesterol and, therefore, to an increase in cholesterol synthesis and turnover. Moreover, diet rich in ALA reduces hepatic lipid accumulation both by stimulating β-oxidation and by inhibiting fatty acid synthesis ***(Murase et al., 2005).*** The triglycerides reducing effect of flaxseed oil is made through regulation of peroxisome proliferative-activated receptor-γ (PPARγ) and sterol regulatory element-binding protein-1 (SREBP-1), which control hepatic fatty acid

catabolism and synthesis respectively ***(Han et al., 2015).*** Conversely, ***Deng et al. (2012)*** and ***Xu et al.(2012)*** reported that flaxseed oil does not markedly affect plasma HDL-C level.

Besides hyperlipidemia, inflammation plays a crucial role in the etiology of atherosclerosis from development of fatty streaks to plaque rupture and thrombosis. Once activated by a stimulus, such as oxidized lipoproteins, vascular endothelial cells expressVCAM-1 which enhances the recruitment and adhesion of monocytes to the endothelium. TNF-α, IL-6, and IL-1β increase VCAM-1 expression and mediate localization and recruitment of monocytes into the subendothelial space ***(Libby, 2008).*** In the present study, we assessed a major compounds involved in the down regulation of substances formed during oxidative stress (MDA and GSH) and pro-inflammatory cytokines like (TNF-α and IL-6) in order to investigate the effect of flaxseed oil on hyperlipidemia-induced inflammation in rats. We showed that flaxseed oil improved the oxidative stress markers and down regulated the hyperlipidemic-induced increase in IL-6, TNF-α and the cell adhesion molecule, VCAM-1. Previous studies pointed out that acute and chronic overproduction of reactive oxygen species (ROS) under pathophysiologic conditions was integral in the development of atherosclerosis ***(Pastori et al., 2014).*** In present research, a pronounced lower concentrate of MDA and higher level of GSH was observed in flaxseed oil pretreated and treated animals than those in rats on HFD. These results suggested that flaxseed oil-mediated prevention of atherosclerosis is closely related with inhibition of oxidative stress. Also inflammatory markers have a key role in mediating inflammatory cascades and promoting atherosclerosis formation, the positive impact of flaxseed oil on plasma levels of VCAM-1, TNF-α and IL-6 observed in this research supported that better function in atherosclerosis prevention. The results with oxidative stress, inflammatory markers and endothelial dysfunctional markers were consistent with the studies of ***Peairs et al. (2011)*** and ***Herieka & Erridge (2014)*** who reported that HFD stimulates oxidative stress, impairs endothelial function and causes a rise in circulating inflammatory factors as soluble intercellular adhesion molecule-1 (ICAM-1), TNF-α and C-reactive protein (CRP). Also, ***Shi et al. (2005)*** found that the high TNF-α response, which are mainly produced by macrophages and monocytes, were the result of acute responses to the high fat diet as these cytokines normally return to baseline concentration once the acute phase response is attenuated. Finally, flaxseed oil administration before and after high fat diet treatment decreased the levels of oxidative stress and inflammatory markers significantly which was supported by the studies of ***Xu et al. (2012)*** and ***(2014)*** who reported that flaxseed oil elicit anti-inflammatory effects by inhibiting inflammatory cytokine production such as IL-6, IL-1, CRP and TNF-α via a reduction in NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells)-induced gene expression and/or an activation of PPAR-γ (Peroxisome proliferator-activated receptor gamma). Another mechanism was reported by ***Tripathi et al. (2013)*** who attribute this effect to the presence of omega-3 fatty acid which modulates the expression of adhesion proteins such as

vascular cell adhesion molecule-1, which participate in leukocyte-endothelium interactions.

The present study showed that the use of flaxseed oil as a prophylactic agent against hyperlipidemia and vascular changes exerted more significant effect on body weight with marked improvement of oxidative stress, inflammatory and vascular adhesion molecule parameters in comparison to its use after induction of hyperlipidemia. Presumably, the use of flaxseed as a treatment after induction of hyperlipidemia, in this study, was insufficient and they may need longer time to return all parameters to the normal level completely. Alternatively, HFD may induce atherosclerotic lesions which were not completely healed by administration of flaxseed oil alone and may need a combination therapy. This hypothesis is supported by a recent study of ***Han et al. (2015).*** Who demonstrated that flaxseed oil + ALA-ester of plant sterol were synergistically ameliorating atherosclerosis and optimizing overall lipid levels, inhibiting inflammation and reducing oxidative stress.

In conclusion, flaxseed oil possessed significant anti-hyperlipidemic and anti-inflammatory properties. Flaxseed oil may contribute to reduce the risk factors of cardiovascular disease by improving plasma antioxidant defenses and lipids profiles. The medicinal value of this oil may be attributed to the bioactive components established to be present in this plant. However, further studies are needed to evaluate the potential value of this oil for the management of hyperlipidemia, the most effective duration of flaxseed oil treatment to return the all parameters to the normal levels, and the adverse effects of them for being used as anti-atherogenic drugs in human being.

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تأثير زيت بذرة الكتان علي صحة الاوعية الدموية في الجرذان الذكور البيضاء البالغة عالية الدهون بالدم

بسمة كمال رمضان

قسم الفسيولوجيا- كلية طب الازهر (بنات)

خلفية البحث: علي الصعيد العالمي، يعد إنتشار زيادة الوزن والسمنة في زيادة مستمرة مهيئاً كلا الجنسين للمخاطر الصحية بما في ذلك أمراض القلب والأوعية الدموية والموت.

الهدف من البحث: دراسة تناول زيت بذرة الكتان علي صحة الأوعية الدموية كمضادات لتصلب وإلتهاب الشرايين، ومخفض لمستوي الدهون وجزيئات الإلتصاق في الفئران عالية الدهون بالدم.

مواد وطرق البحث: تم تنفيذ الدراسة الحالية على 40 من ذكور الجرذان الذكور البالغة البيضاء تم تقسيمهم إلى اربع مجموعات متساويةعلى النحو التالي :

المجموعة الأولى (المجموعة الضابطة) : تغذت علي غذاء متوازن بالإضافة إلي تناول محلول ملحي ولم تخضع لأي معالجات.

المجموعة الثانية (المجموعة عالية الدهون) : تغذت علي غذاء متوازن لمدة أربعة اسابيع ثم تم إستبدال هذا الغذاء بغذاء عالي الدهون لمدة ثمانية اسابيع بالإضافة إلي تناول محلول ملحي عن طريق أنبوبة تصل من الفم إلي المعدة.

المجموعة الثالثة (مجموعة الوقاية بزيت بذرة الكتان): تناولت هذه المجموعة زيت بذرة الكتان (1.8 مليليتر/ كجم) لمدة أربعة اسابيع عن طريق أنبوبة تصل من الفم إلي المعدة مع إستخدام غذاء متوازن. ثم تم إستبدال الغذاء المتوازن باخر عالي الدهون لمدة ثمان اسابيع.

المجموعة الرابعة (مجموعة معالجة بزيت بذرة الكتان): تغذت علي غذاء عالي الدهون لمدة ثمان أسابيع، وبعدها تم إعطائها زيت بذرة الكتان (1.8 مليليتر/ كجم) لمدة أربعة اسابيع عن طريق أنبوبة تصل من الفم إلي المعدة.

وفى نهاية التجربة تم تحديد تغيرات وزن الجسم و مستويات دهنيات الدم (نسب الكوليستيرول الكلي والكوليستيرول في البروتين الدهني منخفض الكثافة والكوليستيرول في البروتين الدهني عالي الكثافة والدهون الثلاثية)، ومضادات الاكسدة (المانولدهيد و الجلوتاثيون) هذا بالإضافة إلي دلالات الإلتهابات (عامل نخر الورم ألفا و الإنترليكون-6) وجزيئات الإلتصاق بخلايا الأوعية الدموية-1 .

النتائج: تتلخص نتائج البحث الحالي في أن الاستخدام الوقائي والعلاجي لزيت بذرة الكتان في الفئران عالية الدهون أدي إلي خفض وزن الجسم بدلالة إحصائية، وإنخفاض مستويات الكوليستيرول الكلي والدهون الثلاثية والكوليستيرول في البروتين الدهني منخفض الكثافة إنخاضا له دلالة إحصائية، بينما إرتفع الكوليستيرول في البروتين الدهني عالي الكثافة. هذا بالاضافة الي إنخفاض له دلالة إحصائية في مستويات مضادات الاكسدة (المانولدهيد)، عامل نخر الورم ألفا، الانترليكون 6 بالاضافة إلي جزيئات الإلتصاق بخلايا الأوعية الدموية-1 مع زيادة ملحوظة في مستويات عامل الاكسدة الجلوتاثيون.

الإستنتاج: إستخدام زيت بذرة الكتان قد يلعب دورا هاما في تخفيض نسبة الدهون الضارة في الجسم وبعض دلالات الإلتهاب، هذا بالإضافة الي الإقلال من إحتمالية إلتصاق خلايا الدم بجدار الأوعية الدموية. وقد كان الاستخدام الوقائي للزيت ذو تاثير أفضل من إستخدامه علي المستوي العلاجي. وعلي ذلك يمكن التوصية بإستخدام هذا الزيت لعلاج العديد من أمراض القلب والأوعية الدموية بشكل عام وتصلب الشرايين بشكل خاص.