Int J Pharm Bio Sci 2015 July; 6(3): (B) 177 - 189

Research Article **Biochemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

POTENCY OF SESAME OIL AS ANTIHYPERCHOLESTEROLEMIC AGENT IN RATS FED HIGH-FAT DIET

FAROUK K. EL-BAZ *[1], ZEINAB A. SALAMA[1], HANAN F. ALY[2] AND HANAN A. TAIE[1]

[1]Plant Biochemistry Department, National Research Centre (NRC), 33 EL Bohouth st. (former EL Tahrir st.), Dokki, Giza, Egypt, P.O.12622.
[2]Therapeutic Chemistry Department, National Research Centre (NRC), 33 EL Bohouth St. (Former EL Tahrir st.), Dokki, Giza, Egypt, P.O.12622.

ABSTRACT

The present study aims to investigate the anti-hypercholesterolemic effects of sesame oil in a high-fat fed rat's model for ninety days. Black sesame oil (BSO) rich in linoleic acid (*omega* 6 and 9) was tested to evaluate prophylactic, protective and therapeutic hypolipidemic effects in comparison with evening primrose oil (rich in linoleic acid and γ-linolenic acid, *omega* 6) and with olive oil (rich in oleic acid and *omega* 9). The serum total lipid (TL), total cholesterol (TC), triglycerides (TG), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), risk ratio (RR), and liver function enzyme activities; aspartate and alanine aminotransferases (AST and ALT) as well as alkaline phosphatase (ALP) were investigated. Hypercholesterolemic feeding rats resulted in significant elevation of TC, TG, LDL-C, HDL-C, AST and ALT as compared to the rats feeding normal diet ($P \leq 0.05$). Supplementation of hyperlipidemic rats with sesame oil was found to have lower circulating concentrations of TC, LDL-C, HDL-C, AST and ALT ($P \leq 0.05$), and normalized TG level in therapeutic rats supplemented with sesame oil as well as ameliorate serum levels of total lipid and hepatic enzyme activities in rats under a high-fat diet.

KEYWORDS: ***Sesamum indicum L.; antihyperlipidemic; liver function; kidney function; liver fatty acids and hyperlipidemia***

*Corresponding author

FAROUK K. EL-BAZ
Plant Biochemistry Department, National Research Centre (NRC), 33 EL Bohouth st. (former EL Tahrir st.), Dokki, Giza, Egypt, P.O.12622.

INTRODUCTION

Recent decades have seen a rapid rise in reports indicating that botanical dietary supplements can improve cardiovascular health and prevent from atherosclerosis disease at several steps [1]. Current research into free radicals has confirmed that foods rich in antioxidants play an essential role in the prevention of cardiovascular disease and cancer [2,3]. Therefore, plant derived antioxidants are now receiving special attention [4-6]. *Sesamum indicum* Linn. (Sesame) belongs to the family Pedaliaceae. Sesame is an ancient oil seeds and is one of the oldest cultivated plants in the world. It is a highly prized oil crop of Babylon and Assyria at least 4,000 years before .and has been routinely used for culinary purposes in the oriental cuisine. In addition, several lines of evidence from traditional as well as modern medicine have confirmed various medicinal properties of sesame [7-9]. This plant possesses significant amounts of diverse phytochemicals, most importantly phenolic acids and lignans [10]. Oils and phytochemicals obtained from sesame have been shown to serve as promising natural antioxidants for both food preservation and medicinal applications [8,11]. Sesame seeds contain moisture, crude oil, crude proteins, carbohydrates, crude fiber, and ash. Sesame oil (constituting~50% of total seed content) is a rich source of mono and polyunsaturated fatty acids [12]. Previous studies have reported that, high antioxidant properties of sesame seeds appear to be related to its main lignans namely sesamol, sesamolinol, pinoresinol, and sesaminol as well as vitamin E [12,13]. Oil is considered the major component of black sesame seeds. The fatty acids composition grown organically and conventionally of sesame crops by using GC were identified [14]. The highest value of fatty acids was recorded by linoleic acid (43.89% - 47.60%) followed by oleic acid (39.41% - 41.30%), palmitic acid (7.67% - 8.01%) and stearic acid (4.28% - 5.92%). They also found that the organic sesame oils grown organically contained lower stearic acid and lower total saturated fatty acids content and more α-linolenic acid compared with conventional sesame oils and did not affect the *omega* 6: *omega* 3 ratio. The sesame oil was found to increase cell resistance to lipid peroxidation [15]. The potential of sesame oil could be used to attenuate oxidative stress and relieve hepatic disorder after intoxication in rats. In addition, the effect of sesame seeds on lowering serum lipids and enhancing antioxidant capacity in 21 hyperlipidemic patients were investigated [16]. They found that, the diet with sesame significantly decreased the levels of serum TC and LDL-C. However, only a few studies have been conducted to clarify these pharmacological effects in hypercholesterolemic models supplemented with sesame oil [17,18]. Therefore, the present work is designed to study the anti-hypercholesterolemic effect of sesame oil in a high-fat fed rats model. The effect on apolipoproteins, liver function, and kidney function were also investigated.

MATERIALS AND METHODS

(i) Oils extraction [19]

The air-dried sample (black sesame seeds) was crushed twice-using a grinder. The crushed samples were pressed with laboratory- type of carver hydraulic press under 10000 lb/in^2, pressure for one hour at room temperature.

(ii) Biological experiment

Black sesame oil (BSO) rich in linoleic acid (*omega* 6&9) was tested to evaluate its prophylactic, curative and protective hypolipidemic effects in comparison with primrose oil (rich in linoleic acid ,γ- linolenic acid and *omega* 6) and with olive oil (rich in oleic acid and *omega* 9).

1. Experimental animals [20,21]

Eighty rats of ninety days-old male albino rats with an average weight of (80-100 g) were obtained from animal house lab, National Research Centre, Dokki, Giza and were used in this study. Animals were housed under normal laboratory condition for two weeks before the initiation of the biological experiments (adaptation period), housed in a well-ventilated box (22 ± 20° C) on a twelve hours light and dark cycle. Diets and water were supplied

adlibitum and had free access of water. The animals were divided randomly into three main groups as given in the experimental design below. Animals were fed with natural basal diet (NBD) and hyperlipidemic diet (HCD). Evening primrose seed oil (without chemical fertilizers), and virgin olive oil (OO) was purchased from the local market and used as a reference oils. Black sesame seed oil (BSO), were extracted from the treated BS as a substituted material. The salt mixture and vitamin mixture requirements were given. The present study is approved by the Ethical Committee of the National Research Centre (NRC), Egypt, provided that the animals will not suffer at any stage of the experiment.

2. Induction of Hypercholesterolemia [22]

Hypercholesterolemia was induced in rats, by feeding rats high-fat diet (cholesterol), cholesterol was orally administrated at a dose of 30 mg/0.3 ml olive oil/0.5% bile salts/ kg body weight five times/week for twelve consecutive weeks, lard fat was mixed with normal diet (One kilogram of animal lard was added to 5 Kgs of normal diet), the occurrence of hypercholesterolemia was determined by measuring the lipid profile (TL, TG, TC, LDL-C, HDL-C), the hypercholesterolemic rats were only used.

3. Experimental design

Eighty male rats were divided into eight groups of ten rats each as follows

Group (1): Served as normal control rats feeding normal basal diet during all the experimental period (four months).

Group (2): Is considered as hyperlipidemic rats.

Group (3): Is considered as prophylactic group, where rats were fed with basal diet substituted with 5% BSO for one month then hypercholesterolemia was induced.

Group (4): Hyperlipidemic diet co-administered with basal diet substituted with 5% BSO for three months.

Group (5): Curative (BSO 5%): Hyperlipidemic rats were fed with basal diet substituted with 5% BSO for one month.

Group (6): Curative (BSO 10%): Hyperlipidemic rats were fed with basal diet substituted with 10 % BSO for one month.

Group (7): EPO 5%: Hyperlipidemic rats were fed with basal diet substituted with 5% EPO for one month (as reference oil).

Group (8): Olive oil 5%: Hyperlipidemic rats were fed with basal diet substituted with 5% olive oil for one month (as second reference oil).

4. Blood sampling periods

After an overnight fasting blood samples were withdrawn from the orbital plexus by means of hypernaized fine capillary glass tubes after 12 and 16 weeks of the experimental period.

5. Biochemical analysis

Biochemical parameters were determined in serum at the specific intervals using Biodiagnostic kits (Bio diagnostics Co., Egypt) as follows

5.1. Determination of serum lipid profile [23-27]

Serum total lipid (TL), total cholesterol (TC) and triglycerides (TG) were determined. The chylomicrons and lipoproteins of very low density (VLDL-C) and low density (LDL-C) in serum sample were precipitated by the addition of phosphotungstic acid in the presence of magnesium ions. The supernatant obtained after centrifugation contained high-density lipoproteins (HDL-C). The cholesterol fraction was determined using the enzymatic method. Low-density lipoproteins esterified with cholesterol (LDL-C), risk ratio (RR) and atherogenic index (HTR) were calculated by Friedewald's equations.

5.2. Determination of liver function [28,29]

AST, ALT and ALP enzyme activities were determined by colorimetric method in serum samples

5.3. Determination of kidney function [30-32]

Creatinine, urea and uric acid levels were determined in seum samples.

5.4. Determination of blood glucose level [33]

Serum glucose level was determined in fasting rats and the blood glucose level was calculated as follows:

Glucose concentration in the serum (mg/dl) = $(A_{sample} / A_{standard}) \times 100$.

5.5. Determination of liver fatty acids [34-36]

Liver of different groups were removed, rinsed from blood and homogenized in chloroform – methanol mixture (2:1) to extract liver lipids. The fatty acid contents in different liver samples were separated and methylated. GLC was used for identification of fatty acids profile.

Statistical analysis [37]

The experiment data were analyzed using Analysis of Variance (ANOVA) combined with co-state computer program, where unshared letter is significant at $p \leq 0.05$.

RESULTS AND DISCUSSION

1. Lipid profile, lipoprotein fraction and risk ratio in hyperlipidemic and different therapeutic groups

Results given in Table (1) showed the blood total lipid (TL), total cholesterol (TC) and triglycerides (TG) levels in different therapeutic groups. The present results reveal a significant increase in TL, TC and TG in hyperlipidemic rats with percentages increase reached to 80.95, 212.16 and 128.61%, respectively as compared to normal control rats. However, marked amelioration was noticed in TL level in hyperlipidemic rats co-administered with 5% BSO (59.46%) and treated with 5 and 10% BSO (52.79 and 59.41%, respectively) as compared to hyperlipidemic rats treated with olive oil and EPO (64.49 and 67.85%, respectively). Also, TC showed a significant decrease with prophylactic, co-administered and therapeutic treated with BSO (5 and 10%) with percentages of improvement reached to 158.20, 162.97, 196.31 and 206.15%, respectively as compared to standard olive oil and EPO (222.27 and 224.18%, respectively). In addition, a significant decrease in TG level in hyperlipidemic rat's prophylactic treated, co-administered as well as treated with BSO with marked amelioration percentages reached to 128.52%, for hyperlipidemic rats treated with 10% BSO as compared to reference olive oil (124.77%) and EPO (130.57%). Hyperlipidemia was induced in albino male rats, by feeding on excess mixture of cholesterol, bile salt (cholic acid) in diet substituted with fats for three months. High cholesterol diet is the predominant factor resulting in hyperlipidemia [38,39]. Because rats are generally hypo-responsive to dietary cholesterol and cholic acid was found to increase the absorption of cholesterol *via* increasing enormously the surface area of lipid molecules exposed to pancreatic lipase [40]. The results in Table (2) demonstrated significant decrease in HDL-C level with percentage increase 27.79 % .While, significant increase in LDL-C level and risk ratio (316.04 and 500%, respectively). In addition, a significant increase in HDL-C level with different types of treatment, although prophylactic treatment recorded percentages of improvement reached to 35.24%, as compared to references oil (34.27 and 40.96%, respectively for olive oil and EPO). Moreover, LDL-C level exhibited the highest percentage of amelioration with 10% BSO treatment (243.75%), as compared to olive oil (308.18%) and EPO (315.91%). However, risk ratio showed percentage of improvement reached to 523.52% with hyperlipidemic diet co-administered with 5% BSO followed by therapeutic 10% BSO (419.60%) as compared to olive oil and EPO (496.07 and 507.07%, respectively). The obtained results concerning the effect of *Omega* 3 fatty acids on lowering serum triglyceride are in harmony with those obtained by Asgary et al. [39,41]. The authors showed that *Omega* 3 fatty acids reduce serum TG by three general ways: reduction of substrate (fatty acids) availability, which could be increased in β-oxidation, decreasing free fatty acids delivery to the liver, decreasing hepatic fatty acids synthesis; increasing phospholipid synthesis; or decreasing activity of TG- synthesizing enzymes. However, data of the present study show that, total cholesterol level was scrimped by substitution of 5% EPO followed by 5% olive oil, 10% BSO and 5% BSO treated hyperlipidemic rats as compared to normal and untreated hyperlipidemic one. In addition, the current .

Table 1
Lipid profile levels in normal, hyperlipidemic and different therapeutic groups

Groups / Parameters	Normal control	Hyperlipidemia	Prophylactic 5%BSO	Co-administration	Therapeutic 5%BSO	Therapeutic 10%BSO	Therapeutic 5%Olive Oil	Therapeutic 5%EPO
TL (mg/dl) % Change % Improvement	333.33[a]±67.80[a]	603.17±15.80[b] 80.95 -----	593.86±22.5[b] 78.15 2.79	404.95±43.50[c] 21.48 59.46	427.19±59.4[c] 28.15 52.79	405.11±47.30[c] 21.53 59.41	388.201±18.2[d] 16.46 64.49	377.0 ±25.3[d] 13.10 67.85
TC (mg/dl) % Change % Improvement	98.19 ±10.85a	306.51±23.42[b] 212.16 ---	151.17±13.31[c] 53.95 158.20	146.48 ± 4.57[c] 49.18 162.97	113.75±6.90[d] 15.84 196.31	104.09±7.09[a] 6.00 206.15	88.26±10.28[e] 10.11 222.27	86.38±11.99 [e] 12.02 224.18
TG (mg/dl) % Change % Improvement	166.45±9.55[a]	380.53 ±20.84[b] 128.61 --	236.11±5.33c 41.85 86.76	180.53±2.84[d] 8.45 120.15	188.63±16.90[d] 13.32 115.28	166.60±18.11[a] 0.09 128.52	172.85±6.84[a] 3.84 124.77	163.18±6.61[a] 1.96 130.57

-All values are means±SD of 10 rats in each group
-Data were analyzed using analysis of variance (ANOVA) combined with co –state computer program, where unshared letter is significant at p≤0.05
-BSO: Black Sesame oil
-EPO: Evening Primrose Oil
-TL: Total Lipids
-TC: Total Cholesterol
-TG: Triglycerides

Table 2
Lipoprotein fraction and risk ratio in normal, hyperlipidemic and different therapeutic groups

Groups / Parameters	Normal control	Hyperlipidemia	Prophylactic 5%BSO	Co-administration	Therapeutic 5%BSO	Therapeutic 10%BSO	Therapeutic 5%Olive oil	Therapeutic 5%EPO
HDL (mg/dl) % Change %Improvement	46.45 ±3.30[a]	33.541 ± 1.50[b] 27.79 -----	49.91 ± 5.33[c] 7.44 35.24	41.47 ± 3.02[a] 10.72 17.06	42.82±11.90[a] 7.81 19.97	45.95 ±3.47[a] 1.07 26.71	49.46±13.50[a] 6.48 34.27	52.57 ±1.86[a] 13.17 40.96
LDL (mg/dl) % Change %Improvement	24.57±2.12 [a]	102.22 ± 12.55[b] 316.04 ---	49.12 ± 8.20[c] 99.91 216.10	70.58 ±10.20[d] 187.28 128.77	51.99 ±12.10[c] 111.59 205.43	42.33±10.11[c] 72.28 243.75	26.50 ±2.20[a] 7.85 308.18	24.6 ±1.02[a] 0.12 315.91
Risk ratio % Change %Improvement	0.51 ± 0.01[a]	3.06 ± 0.05[b] 500.00 -----	1.71 ± 0.15[c] 235.29 264.70	0.39 ± 0.06[d] 23.52 523.52	1.32 ± 0.05[c] 158.82 341.17	0.92 ±0.09[e] 80.39 419.60	0.53 ±0.002[a] 3.92 496.07	0.479 ±0.001[a] 6.07 507.07

All values are means±SD of 10 rats in each group
-Data were analyzed using analysis of variance (ANOVA) combined with co –state computer program, where unshared letter is significant at p≤0.05
-BSO: Black Sesame oil
-EPO: Evening Primrose Oil
-HDL: High Density Lipoprotein
-LDL: Low Density Lipoprotein

results show that lipoproteins esterifies with cholesterol (HDL-C and LDL-C) and risk ratio in hyperlipidemic rats were improved in all curative groups as compared to the corresponding normal control and hyperlipidemic one. The effect of oils as hypolipidemic materials may be

due to the different unsaturated fatty acid composition of these oils. Rafael et al. [42] suggested that linoleic acid reduces the levels of LDL-C more than oleic acid. The reduction in total cholesterol level in oils treated rats may be explained on the basis of lipid esters containing PUFAs require more space in lipoproteins and thereby satirically exclude cholesterol. Both of monounsaturated and polyunsaturated fatty acids could affect the lipoprotein metabolism in hypocholesterolemic models. Thus, the linoleic acid reduces the levels of LDL-C more than oleic acid [42]. Also; HDL-C levels are anti- atherogenic, while low levels are associated with increasing risk for coronary heart diseases [16]. Findings of the present study suggest that dietary supplementation with sesame oil significantly reduces TC and LDL-C concentrations in rats under lipogenic diet. These findings are consistent with those of previous study of Visavadiya and Narasimhacharya [11]. They examined the effects of 5% sesame oil supplemented with hypercholesterolemic diet for a period of 4 weeks. Administration of sesame seed oil to hypercholesterolemic rats resulted in a significant decline in serum total lipid ,cholesterol, and LDL- C while increasing HDL-C concentrations.

2. Liver function enzyme activities in hyperlipidemic and different therapeutic groups

Table (3), demonstrated a significant increase in AST, ALT and ALP enzyme activities in hyperlipidemic rats with percentages increase of 66.26, 103.38 and 47.53%, respectively. Significant decrease in liver enzyme activities with different treatment types as they exhibited the highest level of amelioration with prophylactic, co-administered and post treated with 10% BSO, recorded 39.87, 71.50 and 39.06%, respectively for AST enzyme activity as compared to olive oil and EPO (68.50 and 51.48%, respectively). However, ALT demonstrated percentages of improvements amounting to 92.94, 75.08 and 88.10%, with 5% BSO co-administered with hyperlipidemic diet, treated with 5 and 10% BSO, respectively as compared to olive oil and EPO (88.08 and 81.77%,respectively). Furthermore, ALP recorded the highest percentages of enhancement with prophylactic treatment (28.80), co-administered (45.69) and therapeutic treated with 10% BSO (23.17%), as compared to standard olive and EP oils (24.47 and 19.25%, respectively). Data given in Table (3) revealed significant decrease in the activities of liver enzymes in hyperlipidemic rats supplemented with 5% EPO, 5% olive oil, 10% BSO and 5% BSO respectively. Thus, BSO provide a positive ameliorative effect on liver function enzyme activities. The supplementation of basal diet substituted with 5 and 10 % BSO and either co -administered with or post treated high fat diet showed the highest percentages of amelioration in liver function enzyme activities followed by the diet substituted with 5 % EPO and 5% olive oil. The hypolipidamic effects of *omega* 3 fatty acids are similar to those *omega* 6. These effects may be provided the unsaturated fatty acids, which replaced saturated fats in the diet. An added benefit is shown by *omega* 3 PUFAs that in hypertriglyceridemia patients' consistently have lower serum triglycerides than *omega* 6 fatty acids. In addition, *omega* 3 has several beneficial properties in human. This effect may be attributed to the *omega* 3 is incorporated in membrane phospholipids [41,43,44]. Also, the current results are in agreement with Azonov et al. [45], as they showed that the induction of hyperlipidemia for 12 weeks caused significant elevation in ALT, AST and ALP enzyme activities. In prophylactic treatment, the administration of 5% BSO prior the induction of high cholesterol diet could provide protective way, preventing the elevation of liver function enzymes. In this concern, the reduction of blood cholesterol in response to unsaturated fatty acids treatments may be due to changes in several parameters of cholesterol metabolism including fecal extraction of steroids and desaturases activities [46]. Similar findings have been found by Mararet et al. [47], Paul et al. [48] and Tricia et al. [49] as they reported that the main sources of plant-derived *omega* 3 fatty acids are including flaxseed oil, walnuts, canola oil, and soybean oil which reduce the risk of cardiovascular disease. The manipulated results show distinctly good defense for hyperlipidemia and liver enzyme activities when rats fed with basal diet substituted with 5 %, BSO for one month before induction of hyperlipidemia. The Committee on

the Medical Aspects of food Policy (COMA) recommended that, the consumption of fat and particularly saturated fatty acids should be decreased in the world in order to reduce mortality from cardiovascular disease, the major cause of death [50]. WHO and National Advisory Committee on Nutrition (NACNE) demonstrated similar recommendations [51]. Essentially the lipid theory stated that, high concentrations of plasma cholesterol are associated with an increased risk of Cardio Heart Disease (CHD). The concentration of plasma cholesterol depends, in part, upon the quantity and type of fatty acids present in the diet. The saturated fatty acids (lauric, myristic and palmatic) were decreased. Oleic acid, the major dietary mono-unsaturated fatty acids are shown to decrease LDL-C like PUFAs but without their decrease in HDL-C, a form protecting against Cardio Heart Disease (CHD). Thus, the old ratio of polyunsaturated to saturated fatty acids (TU: TS ratio) is inappropriate as an index of diet atherogenicity.

3. Kidney function and glucose level in hyperlipidemic and different therapeutic groups

The results manipulated in Table (4) clearly demonstrated an insignificant change in total urea and blood glucose levels in hyperlipidemic and therapeutic treated rats as compared to normal control one. While, hyperlipidemic rats showed a significant increase in uric acid and creatinine levels with percentage increase of 32.75 and 50.55%, respectively. However, co-administration of hyperlipidemic diet with 5% BSO showed the highest percentages of improvement in uric acid and creatinine levels (33.62 and 37.91%,respectively) as compared to references oils; olive and EP (41.92, 24.01%, for uric acid and 43.41 and 73.62%, for creatinine respectively). These results added support to the beneficial treatments of BSO as compared to the both standard oils. The results revealed that sesame supplementation is associated with enhancement in liver and kidney function. Kumar et al. [52] reported that the ameliorative effects of sesame oil could be attributed to the induction of cholesterol turnover *via* increasing fecal sterol excretion and hepatic bile acid production. Moreover, supplementation with sesame has been shown to improve antioxidant capacity through promoting hepatic catalase and superoxide dismutase activities [53]. Sesame contains a diversity of phytochemicals including lignans, polyphenolic and flavonoid compounds, dietary fibers, PUFA, and lecithin, as they all possess documented antihyperlipidemic functions [54,55]. Anbu et al. [56] concluded that, the antihyperlipidemic activity may be due to the presence of tannins, triterpenes, alkaloids, inulin, and essential oil present in the roots of *Saussurae Lappa*. Different lignin derivatives of sesame such as sesamin, sesamol, sesaminol, sesaminolinol, and pinoresinol possess antioxidant functions thus could be prevent against membrane lipid peroxidation, induced microsomal lipid peroxidation. Furthermore, vitamin E and flavonoids as they naturally occur in sesame have been reported to possess antioxidant and lipid-lowering properties [57,58]. Sesamin is considered as one of the most important lignan components of sesame seeds. This phytochemical has been reported to exert hypocholesterolemic effects through inhibition of the intestinal absorption of cholesterol, increase of biliary cholesterol excretion, and down regulation of 3-hydroxy-3-methylglutaryl coenzyme A reductase activity [59]. Sesamin has promising antioxidant property which is, at least in part, due to the inhibition of tocopherol catabolism and enhancement of circulating as well as tissue concentrations of tocopherols [60].

4. Fatty acid composition in rat's liver in hyperlipidemic and different therapeutic groups

Table 3
Liver function enzyme activities in normal, hyperlipidemic and different therapeutic groups

Groups / Parameters	Normal control	Hyperlipidemia	Prophylactic 5%BSO	Co-administration	Therapeutic 5%BSO	Therapeutic 10%BSO	Therapeutic 5%Olive Oil	Therapeutic 5%EPO
AST(U/L) **% Change** **%Improvement**	47.72 ±10.1[a]	79.34 ±16.60[b] 66.26 ---	60.31 ±18.95[c] 26.38 39.87	45.22 ±11.10[a] 5.23 71.50	61.41±10.83[c] 28.68 37.57	60.70 ±7.82[c] 28.70 39.06	46.65 ±1.31[a] 27.20 68.50	54.77±19.67[d] 14.77 51.48
ALT(U/L) **% Change** **%Improvement**	38.69±8.03[a]	78.69 ±5.87[b] 103.40 -----	63.43 ±9.82[c] 63.94 39.44	42.73 ±6.35[a] 10.44 92.94	49.64±10.14[d] 28.30 75.08	44.61 ±4.14[d] 15.30 88.08	41.66±10.33[a] 7.67 88.08	47.05±8.37[d] 21.60 81.77
ALP(U/L) **% Change** **%Improvement**	49.96 ±1.53 [a]	73.71 ±4.47[b] 47.53 ------	59.32 ±12.61[c] 18.73 28.80	50.88 ±4.53[a] 1.84 45.69	65.46 ±6.87[d] 31.02 16.51	62.13 ±4.27[d] 24.35 23.17	61.48±9.03[d] 23.05 24.47	64.09±7.66[d] 28.28 19.25

-All values are means±SD of 10 rats in each group
-Data were analyzed using analysis of variance (ANOVA) combined with co –state computer program, where unshared letter is significant at p≤0.05
-BSO: Black Sesame oil
-EPO: Evening Primrose Oil
-AST: Aspartate aminotransferase
-ALT: Alanine aminotransferase
-ALP: Alkaline phosphatase

Table 4
Kidney function tests in normal, hyperlipidemic and different therapeutic groups

Groups / Parameters	Normal control	Hyperlipidemia	Prophylactic 5%BSO	Co-administration	Therapeutic 5%BSO	Therapeutic 10%BSO	Therapeutic 5%Olive Oil	Therapeutic 5%EPO
Urea (mg/dL) **% Change** **%Improvement**	26.12 ±0.08[a]	28.20 ±0.023[a] 7.96 ----	28.10 ±0.025[a] 7.58 0.38	27.70 ± 0.025[a] 6.04 1.91	27.10 ±0.055[a] 3.75 4.21	29.90 ±0.026[a] 14.47 6.50	27.60 ±0.015[a] 5.66 2.29	31.00 ±0.13[a] 18.68 10.71
Uric acid (mg/dL) **% Change** **%Improvement**	2.29 ±0.15[a]	3.04 ±0.30[b] 32.75 -----	2.43 ±0.04[a] 6.11 26.63	2.27 ±0.08[a] 0.87 33.62	2.31 ±0.11[a] 0.87 31.87	2.29 ±0.16[a] 0 32.75	2.08 ± 0.21[a] 9.17 41.92	2.49 ±0.17[a] 8.73 24.02
Creatinine (mg/dL) **% Change** **%Improvement**	1.82 ±0.20[a]	2.74 ±0.31[b] 50.55 -----	2.15 ± 0.27[c] 18.13 32.42	2.05 ±0.24[c] 12.63 37.91	2.18 ± 0.70[c] 19.78 30.77	2.09 ±0.70[a] 14.83 35.71	1.95 ±0.49[a] 7.14 43.41	1.40 ± 0.17[d] 23.07 73.62
Glucose (mg/dL) **% Change** **%Improvement**	58.96 ±0.12[a]	59.92 ±1.89[a] 1.63 ------	57.93 ± 7.97[a] 1.74 2.37	61.50 ±5.13 [a] 4.31 2.67	60.23 ±3.66[a] 2.15. 0.53	57.54 ±12[a] 2.41 4.04	61.27 ±6.13[a] 3.91 2.29	55.55 ± 5.36[a] 5.78 7.41

-All values are means±SD of 10 rats in each group
-Data were analyzed using analysis of variance (ANOVA) combined with co –state computer program, where unshared letter is significant at p≤0.05
-BSO: Black Sesame oil
-EPO: Evening Primrose Oil

Changes in fatty acids composition in rat's liver for the different feeding groups were illustrated in Table (5). As expected, rats fed with basal diet substituted with 5% olive oil treatment produced less amount of linoleic acid (13.37%) and minor content of α-linolenic acid (0.247%) whereas substituted basal diet with 10 % BSO produced linoleic acids by 25.15%. In parallel, there was a significant increase (30.3%) in the content of liver oleic acid in rats fed with basal diet substituted with 5 % olive oil, while reached to 29.01 % in rats fed with basal diet substituted with 10 % BSO. In contrast, γ-linolenic acid was observed (5.41 %) in rats fed with basal diet substituted with 10 % BSO. The above mentioned results are in agreement with those showed by Javier and Gutikrez [61] as they obtained a higher monounsaturated fatty acids proportion in animal's fed virgin olive oil. Nevertheless, olive oil intake resulted in a high amount of oleic acid in tissues [47, 61]. The previous data reflected a higher amount of polyunsaturated fatty acids in substituted 10% BSO (31.47%) and substituted 5 % olive oil group (14.59 %). On contrary, the monounsaturated fatty acids showed highest significant increase in rats liver fed with 5 % olive oil (36.35%) followed by 10% BSO group (29.01%). This may due to oleic acid *omega* 9 in both of olive oil and BSO. The predominant *omega* 6 fatty acids are linoleic and arachidonic acids, as they converted to prostaglandins, those products are important regulators of cellular functions with inflammatory. Typical *omega* 3 fatty acids are α-linolenic, docosahexaenoic and eicosapentaenoic acids, as they competitive substrates for the enzymes and products of arachidonic acids metabolism. *Omega* 3 fatty acids derived eicosanoids antagonize the pro-inflammatory effects of *omega* 6 fatty acids [62]. On the contrary, Arja et al. [63] observed that both *omega* 6 and *omega* 3 polyunsaturated fatty acids had been associated with lower cardiovascular risk. Supplementation with lignan-rich sesame has a remarkable ntial effect on hepatic fatty acid oxidation while down regulating the activity of lipogenic enzymes [9,64].

Table 5

Fatty acid composition (%) in rat's liver in normal, hyperlipidemic and different therapeutic groups

Fatty Acids	Normal control	Hyperlipidemia	Prophylactic 5%BSO	Co-administration	Therapeutic 5%BSO	Therapeutic 10%BSO	Therapeutic 5%Olive Oil
Lauric acid 12:0	ND.	ND.	2.37	2.35	ND.	0.87	0.89
Myristic acid 14:0	ND.	ND.	5.37	5.00	1.72	1.015	1.00
Palmitic acid 16:0	25.62	27.74	37.39	36.90	40.0	27.33	26.90
Palmitoleic 16: 1	ND.	ND.	8.00	7.56	6.056	ND.	ND.
Stearic acid 18:0	18.19	5.55	5.80	6.00	4.115	5.31	5.00
Oleic acid 18:1 *omega 9*	15.69	20.80	26.18	26.00	30.3	29.01	30.0
linoleic acid 18:2 *omega 6*	17.5	40.40	12.01	12.88	13.37	25.15	24.87
α-linolenic acid 18:3 *omega 3*	1.59	3.131	0.654	0.60	0.247	0.296	0.29
γ-linolenic acid 18:3 *omega 6*	ND.	ND.	ND.	ND.	ND.	5.41	5.60
Arachidic 20:0	13.71	1.82	1.59	1.77	2.12	3.61	3.77
Arachidonic 20:4 *omega 6*	1.46	0.564	0.683	0.70	0.97	0.620	0.68
Total saturated (TS) fatty acids	57.52	37.02	52.25	52.00	47.52	38.13	39.00
Total monounsaturated fatty acids	15.69	20.80	34.18	35.20	36.35	29.01	30.00
Total polyunsaturated fatty acids	20.55	44.1	13.35	12.89	14.59	31.47	31.00
Total unsaturated (TU) fatty acids	36.24	64.9	47.53	50.00	50.94	60.48	60.00
TU / TS	0.630	1.753	0.910	0.90	1.072	1.586	1.50

CONCLUSION

It could be concluded that, amelioration of lipid profile and hepato-renal function as well as fatty acid composition were detected in response to sesame oil supplementation. These positive effects of sesame oil need further study to estimate the potential therapeutic role as a safe and effective supplement for patients with of high risk ratio , hypercholesterolemia and/or non-alcoholic fatty liver disease. In addition to, postulate the exact mechanisms underlying the antihyperlipidemic effects to explore whether these effects are exerted by a single constituent or are due to a synergism between different phytochemical.

CONFLICT OF INTEREST

Conflict of Interest declared none.

REFERENCES

1. Mahmood ZA, Sualeh M, Mahmood SB and Karim MA, Herbal treatment for cardiovascular disease the evidence based therapy. Pakistan Journal of Pharmaceutical Sciences, 23(1): 119-124, (2010).
2. Kris-Etherton PM, Hecker KD, Bonanome A, Coval SM, Binkoski AE, Hilpert KF, Griel AE and Etherton TD, Bioactive compounds in foods: their role in the prevention of cardiovascular disease and cancer. American Journal of Medicine, 113(9): 71s-88s, (2002).
3. Blazovics A, Lugasi A, Hagymasi K, Szentmihalyi K and Kery A, Ed. Natural antioxidants and tissue regenerations: Curative effect and reaction mechanism. In Phytochemistry and Pharmacology II. In Majumdar DK, Govil JN and Singh VK Edn. Recent Progress in Medicinal Plants series. SCI TECH Pub. USA, 115-156, (2002).
4. Ghosal S, Bhattacharya A and Bhattacharya SK, Antioxidant effects of *Emblica officinalis* and their biological consequences, in Recent Progress in Medicinal Plants, DK. Majumdar, JN. Govil, and VK. Singh, Eds., 8, 149, (2003).
5. Wenli Y, Yaping Z and Bo S, Theradical scavenging activities of *radix puerariae* iso flavonoids: a chemilum inescence study. Food Chemistry, 86(4): 525-529, (2004).
6. Hernandez-Ortega M, Ortiz-Moreno A, Hernandez-Navarro MD, hamorro-Cevallos, G, Dorantes-Alvarez, L and Necoechea-Mondrag´on, H, Antioxidant, antinociceptive, and anti- inflammatory effects of carotenoids extracted from dried pepper (*Capsicum annuum* L.). Journal of Biomedicine and Biotechnology, 2012, 1-10, (2012).
7. Kapoor LD, Ed. Hand book of ayurvedic medicinal plants, 1st Edn, CRC Press, New York, NY, US, A124-125, (2001).
8. Namiki M, A review, Critical reviews in food science and nutrition. 47, 651-673, (2007).
9. Gauthaman K and Saleem, TSM, Nutraceutical value of sesame oil. Pharmacognosy Reviews, 3, 264-269, (2009).
10. Suja KP, Jayalekshmy A and Arumughan C, *In vitro* studies on antioxidant activity of lignans isolated from sesame cake extract, Journal of the Science of Food and Agriculture, 85, 1779-1783, (2005).
11. Visavadiya NP and Narasimhacharya AVR, Sesame as a hypocholesteraemic and antioxidant dietary component. Food and Chemical Toxicology, 46, 1889-1895, (2008).
12. Roma RB, Tabekhia MM and Williams JD, Phytate and oxalate contents in sesame seed (*Sesam umindicum* L.). Nutrition Reports International, 20, 25-31, (1979).
13. Lemcke-Norojarvi M, Kamal-Eldin A, Appelqvist LA, Dimberg LH, Ohrvall M and Vessby B, Corn and sesame oils increase serumγ-tocopherol concentrations in healthy Swedish women. Journal of Nutrition, 131, 1195-1201, (2001).

14. Samman S, Chow, MJJ, Foster WY, Ahmad ZI, Phuyal JL and Petocz P, Fatty acid composition of edible oils derived from certified organic and conventional agricultural methods. Food Chemistry, 109, 670-674, (2008).
15. Dur-Zong H, Chiang P, Chien S and Huang B, Parenteral sesame oil attenuates oxidative stress after endotoxin intoxication in rats. Toxicology, 196, 147-153, (2004).
16. Chen PR, Chien KL, Su TC, Chang CJ, Liu TL, Cheng H and Tsai C, Dietary sesame reduces serum cholesterol and enhances antioxidant capacity in hypercholesterolemia. Nutrition Research, 25, 559-567, (2005).
17. Bhaskaran S, Santanam N, Penumetcha M and Parthasarathy S, Inhibition of atherosclerosis in low-density lipoprotein receptor-negative mice by sesame oil. Journal of Medicinal Food, 9, 487-490, (2006).
18. Hirata F, Fujita K, Ishikura Y, Hosoda K, Ishikawa T and Nakamura H, Hypocholesterolemic effect of sesame lignan in humans, Atherosclerosis, 122, 135-136, (1996).
19. Ustum G, Kent L, Cekin, N and Civelekoglu H, Investigation of the technological properties of *Nigellaq sativa* (black cumin) seed oil. Journal of the American Oil chemist's Socity, 67, 958-960, (1990).
20. Hubbell RB, Mendel LB and Wakeman AJ, A new salt mixture for use in experimental diets Journal of Nutrition, 14, 273-285, (1937)
21. Campbell JA, Ed. Methodology of protein evaluation P.A.G10th Edn, 370, Nutrition Document Press: New York, (1961).
22. Deepa PR and Varalakshmi P, Favourble modulation of inflammatory changes in hypercholesterolemic atherogenesis by low molecular weight heparin derivtive. International Journal of Cardiology, 106, 338-347, (2006).
23. Zollner N and Kirsch K, Determination of total lipids (TL) concentration. Zeitschrift for die Gesampte Experimentelle Medizin, 135, 545-548, (1962).
24. Richmond W, Preparation and properties of cholesterol oxidase from *Nacardia* sp. and its application to enzymatic assay of total cholesterol in serum. Clinical Chemistry, 19, 1350-1360. (1973).
25. Fossati P and Prencipe L, Enzymatic determination of triglycerides in serum. Clinical Chemistry, 15, 2028-2077, (1982).
26. Lopez–Virella MF, Methods of high-density lipoproteins (HDL-C) separation. Clinical Chemistry, 23, 882-889, (1977).
27. Friedewald WT, Levy RI and Fredrickson DS, Estimation of the concentration of low-density lipoproteins cholesterol in plasma, whitout use of the preparative ultracentrifuge. Clinical Chemistry, 18, 499-505, (1972).
28. Reitman A and Frankel S, A colorimetric method for the determination of serum glutamate - oxaloacetate and glutamate pyruvate transaminase. American Journal of clinical Pathology, 28, 56-61, (1957).
29. Belfield A and Goldberg DM, Determination of alkaline phosphatase activity (ALP). Enzyme, 12, 561-266, (1971).
30. Bartles H, Bohrnes M and Heirlis C, Determination of creatinine methods; Clinical Chemistry Acta, 37, 193-196, (1972).
31. Fawcett JK and Soctt JE, Determination of urea concentration methods. Journal of Clinical pathology, 13, 156-159, (1960).
32. Barham D and Trinder P, Determination of uric acid concentration methods. Analyst, 97, 142-145, (1972).
33. Trinder P, Glucose (GOD), method enzymatic and calorimetric method. Annals of Clinical Biochemistry, 6, 24-26, (1969).
34. Bligh EG and Dyer WJ, A rapid method of total extraction and purification. Canadian Journal of Biochemistry and Physiology, 37, 91 l-920, (1959).
35. Stahl E, Ed. Thin layer hand book, Springer Verloag, Berlin, 359. Heidelberg, New York. (1967).

36. Farag RS, Hallabo SAS, Hewedi FM and Basyony AE, Chemical evolution of rape seed. Fette-Seifen Anstrichmittel, 88, 391-397, (1986).
37. Freud RJ and Wilson WJ, Ed. Design of experiments in statistical methods, (revised Edn). Academic Press: 461-507, (1997).
38. Miller W, Janosz K, Zalesin K and McCullough P, Optimal dietary intake for cardiovascular risk reduction. Current Cardiovascular Risk Reports, 3, 95-101, (2009).
39. Asgary S, Rafieian-Kopaei M, Najafi S, Heidarian E and Sahebkar A, Antihyperlipidemic Effects of *Sesamum indicum* L. in rabbits fed a high-fat diet. The Scientific World Journal, 2013, 1-5, (2013).
40. Moghadasian MH, Experimental atherosclerosis: historical overview. Life Science, 70, 855-865, (2002).
41. Asgary S, Setorki M and Rafieian-kopaei M, Postprandial hypolipidemic and hypoglycemic effects of *Allium hertifolium* and *Sesamum indicum* on hypercholesterolemic rabbits. African Journal of Pharmacy and Pharmacology, 6, 1131-1135, (2012).
42. Rafael C, Ascaso JF, Camejob G, Varelad G, Camejo EH, Ordovas M, Valls M, Bergst M and Wallin B, Effect of olive and sunflower oils on low-density lipoprotein level, composition, size, oxidation and interaction with arterial proteoglycans. Atherosclerosis, 125, 243-255, (1996).
43. Muriana FJG and Ruiz-Gutierrez V, Effect of n-6 and n-3 polyunsaturated fatty acids ingestion on rat liver membrane - associated enzymes and fluidity. Journal of Nutritional Biochemistry, 3, 659-663, (1992)
44. Wiesenfeld PW, Babu, US, Collins TF, Sprando R, O'Donnell MW, Flynn TJ, Black T and Olejnik, N, Flaxseed increased α-linolenic and eicosapentaenoic acid and decreased arachidonic acid in serum and tissues of rat dams and offspring. Food and Chemical Toxicology, 41, 841-855, (2003).
45. Azonov J, Khorshid H, Novitsky Y, Farhadi M, Ghorbanoghli Z and Shahosseiny M, Protective effects of setrud (IMODTM) on development of diet induced hypercholesterolami in rabbits. Drugs, 16, 218-222, (2008).
46. Sunitha T, Manorama R and Rukmini C, Lipid profile of rats fed blends of rice bran oil in combination with sunflower and safflower oil. Plant Foods for Human Nutrition, 51, 219-230, (1997).
47. Margaret AA, Hall D, Kingham K, Pang D, Petocz P, Engler MM and Mary BE, The effects of dietary evening primrose, black current, borage and fungal oils on plasma, hepatic and vascular tissue fatty acid composition in the spontaneously hypertensive rat. Nutrition Research, 18, 1533-1544, (1998).
48. Paul W, Leach C, Ah-Sing EE, Hussain N, Miller GJ, Millward DJ.and Griffin BA, Influence of α-linolenic acid and fish-oil on markers of cardiovascular risk in subjects with an atherogenic lipoprotein phenotype. Atherosclerosis, 181, 115-124, (2005).
49. Tricia L, Sarah P, Gebauer K and PK, Etherton Dietary *omega* 3 fatty acid intake and cardiovascular risk. The American Journal of Cardiology, 98, 4-18, (2006).
50. Committee on the Medical Aspects of food Policy (COMA), Department of Health London.http://www.actiononsalt.org.uk/about/40596.html# sthash.KkZSsVCe.dpuf, (1994).
51. WHO, Education recommendations for the composition of a healthful diet proposed by a working party of the National Advisory Committee for Nutrition Education (NACNE), (1985).
52. Kumar M, Kamboj A and Sisodia SS, Hepatoprotective activity of *Sesamum indicum* Linn. against CCl4-induced hepatic damage in rats. International Journal of Pharmaceutical and Biological Archive, 2, 710-715, (2011).
53. Saleem TSM, Chetty CM and Kavimani S, Sesame oil enhances endogenous antioxidants in ischemic myocardium of rat. RevistaBrasileira de Farmacognosia, 22, 669-675, (2012).

54. Babio N, Balanza R, Basulto J, Bull´o M and Salas-Salvad´o J, Dietary fibre: influence on body weight, glycemic control and plasma cholesterol profile, Nutricion Hospitalaria, 25, 327-340, (2010).
55. Biswas A, Dhar P and Ghosh S, Antihyperlipidemic effect of sesame (*Sesam umindicum* L.) Protein isolate in rats fed a normal and high cholesterol diet, Journal of Food Science, 75, H274-H279, (2010).
56. Anbu J, Anjana A, Purushothaman K, Sumithra M, Suganya S, Bathula NK and Modak S, evaluation of antihyperlipidemic activity of ethanolic extract of *saussurae lappa* in rats, International Journal of Pharma and Biosciences, 2, 550-556, (2011).
57. Nakano D, Itoh C and Ishii F, Effects of sesamin on aortic oxidative stress and endothelial dysfunction in deoxycorticosterone acetate-salt hypertensive rats. Biological and Pharmaceutical Bulletin, 26, 1701-1705, (2003).
58. Hu Y, Wang M and Ye HWC, Flavones from flowers of *Sesamum indicum*, China Journal of Chinese Materia Medica, 32, 603-605, (2007).
59. Hirose N, Inoue T and Nishihara K, Inhibition of cholesterol absorption and synthesis in rats by sesamin. Journal of Lipid Research, 32, 629-638, (1991).
60. Parker R, Sontag STJ and Swanson JE, Cytochrome P4503A-dependent metabolism of tocopherols and inhibition by sesamin, Biochemical and Biophysical Research Communications, 277, 531-534, (2000).
61. Javier SP and Gutikrez VR, Two highly monounsaturated oils, olive oil and high-oleic sunflower oil induce different triglycerol molecular species distribution in rat liver. Nutrition Research, 18, 1723-1732, (1995).
62. Gerd S and Ecker J, The opposing effects of *n*-3 and *n*-6 fatty acids. Progress in Lipid Research, 47, 147-155, (2008).
63. Arja E, Vanessa DF, Ulf R and Laaksonen DE, Dietary fatty acids and cardiovascular disease: An epidemiological approach. Progress in Lipid Research, 47, 172-187, (2008).
64. Sirato-Yasumoto S, Katsuta M, Okuyama Y, Takahashi Y and Ide T, Effect of sesame seeds rich in sesamin and sesamolin on fatty acid oxidation in rat liver, Journal of Agricultural and Food Chemistry, 49, 2647-2651, (2001).