IJMS
Vol 41, No 2, March 2016

Original Article

Effects of Sesame Butter (Ardeh) versus Sesame Oil on Metabolic and Oxidative Stress Markers in Streptozotocin-Induced Diabetic Rats

Fatemeh Haidari[1], PhD;
Majid Mohammadshahi[2], PhD;
Mehdi Zarei[3], PhD;
Zahra Gorji[4], MS

[1]Nutrition and Metabolic Diseases Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran;
[2]Hyperlipidemia Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran;
[3]Department of Food Hygiene, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran;
[4]Department of Nutritional Science, Arvand International Division of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Correspondence:
Zahra Gorji, MS;
Arvand International Division Ahvaz, Department of Nutritional Science, Jundishapur University of Medical Sciences, Golestan Square, P.O. Box: 61357-15794, Ahvaz, Iran
Tel: +98 61 33738253
Fax: +98 6 33737330
Email: ghazal.gorji@yahoo.com
Received: 10 June 2014
Revised: 9 October 2014
Accepted: 7 September 2014

Abstract

Background: Diabetes is one of the most common metabolic disorders and is related to oxidative-stress-induced diseases. Given the role of dietary antioxidants in the control and prevention of diabetes, this study aimed to examine the effects of sesame butter versus sesame oil on the serum levels of glucose, lipid profile, and oxidative stress biomarkers in diabetic rats.

Methods: Forty male albino rats of Wistar strain were randomly divided into 4 groups (i.e., nondiabetic control rats, diabetic rats, diabetic rats treated with sesame butter, and diabetic rats treated with sesame oil). Experimental diabetes was induced with an intraperitoneal injection of streptozotocin (55 mg/kg). Sesame butter (1.25 g/kg) and sesame oil (0.5 g/kg) were given by oral gavage to the diabetic rats for 6 weeks. Finally, serum glucose, lipid profile, total antioxidant capacity (TAC), and malondialdehyde (MDA) levels were measured and analyzed statistically.

Results: Our data showed that the diabetic groups treated with sesame butter and sesame oil had significantly lower levels of glucose and higher levels of high-density lipoprotein than did the diabetic control group at the end of the study ($P<0.05$). Sesame butter supplementation also increased TAC and decreased MDA concentrations significantly in the diabetic rats ($P<0.05$).

Conclusion: The antihyperglycemic, antioxidative, and partly lipid-lowering effects of sesame butter make it an excellent candidate for future human studies on diabetes, although further research is needed to determine the exact dose and duration of supplementation.

Please cite this article as: Haidari F, Mohammadshahi M, Zarei M, Gorji Z. Effects of Sesame Butter (Ardeh) versus Sesame Oil on Metabolic and Oxidative Stress Markers in Streptozotocin-Induced Diabetic Rats. Iran J Med Sci. 2016;41(2):102-109.

Keywords ● Antioxidants ● Diabetes mellitus ● Hyperglycemia ● Lipids ● Oxidative stress ● Sesame oil

What's Known

- The antihyperglycemic and antioxidant effects of sesame oil have been shown in previous studies.
- However, single-nutrient studies do not consider each nutrient's combination with other nutrients in various metabolic reactions.

What's New

- In the present study, the antioxidant effect of sesame butter versus sesame oil was more potent in diabetic rats.
- It may be because sesame butter is made with whole-grain sesame.

Introduction

Diabetes mellitus, which is characterized mainly by hyperglycemia, is rising at an alarming rate; and the number of persons with diabetes is expected to reach 370,000,000 worldwide by the year 2030.[1] Recent studies have indicated that hyperglycemia increases inflammatory mediators and oxidation agents and, thus, plays an important role in the complications of diabetes such as cardiovascular disease, nephropathy, retinopathy, and neuropathy.[2] There is evidence that oxidative stress secondary to hyperglycemia leads to many of the secondary complications

of diabetes and oxidative damage to peripheral tissues.[2,3] The high prevalence of diabetes the world over necessitates efficient new therapeutic strategies with fewer adverse effects.[4] Herbal remedies have such properties.[5]

One of the medicinal plants that have long been recognized as the traditional health food in Iran and other East Asian countries is the sesame seed and its oil.[6] Considerable quantities of sesame seeds are cultivated and used in Iran, particularly in Yazd and Khuzestan provinces. In Iran, more than 90% of the grain is used for making oil and sesame butter. Sesame butter, commonly known as "Ardeh" in Iran, is one of the natural products of sesame seeds, without any chemical and nonchemical additives, which can be prepared by grinding the whole sesame seed (roasted or non-roasted). Sesame butter and sesame oil contain substantial quantities of polyunsaturated fatty acids, monounsaturated fatty acids, and vitamin E. Sesame also consists of various lignans including sesamin, sesamol, episesamin, and sesamolin.[7,8] Sesame seeds are rich in oil (about 50%) and protein (about 20%) as well as in diverse lignins such as sesamin and sesaminol (main lignin; about 1.5%). The predominant fatty acids in sesame oil comprise oleic acid (43%), linoleic acid (35%), palmitic acid (11%), and stearic acid (7%).[9]

Several studies have shown that sesame lignans have multiple physiological functions such as antioxidant, anticarcinogen, and antihypertensive activities as well as serum lipid-lowering effects.[10-12] The synergistic effect between sesame oil and antidiabetic drugs was also demonstrated by Sankar et al.[8] in patients with type 2 diabetes mellitus. Furthermore, other studies have demonstrated that sesame oil lowers blood pressure and lipid profile in patients with hypertension medicated with calcium-channel blockers.[13] Recently, Khaneshi et al.[9] suggested that sesame might have a protective effect against oxidative-stress-induced testicular dysfunction in diabetic rats. The antioxidant and anti-inflammatory effects of sesame oil have been shown previously in patients with knee osteoarthritis.[14] However, there are limited studies evaluating the effects of sesame butter on the serum levels of glucose, lipid profile, and biomarkers of oxidative stress in diabetes. Since single-nutrient studies do not consider each nutrient's combination with other nutrients in various metabolic reactions, we hypothesized that the effects of sesame butter might be different from those of sesame oil alone because sesame butter is made from whole-grain sesame. Therefore, we sought to investigate the effects of sesame butter versus sesame oil intake on the serum levels of glucose, lipid profile, and oxidative stress biomarkers in streptozotocin (STZ)-induced diabetic rats.

Materials and Methods

Animals

In the present study, 40 male albino rats of Wistar strain (age 6–8 weeks old, body weight 200–250 g) were obtained from the Physiology Research Center of Ahvaz Jundishapur University of Medical Sciences. The animals were housed in steel cages in an air conditioned room with a controlled temperature (22±3°C), 55±5% humidity, and a 12-hour light/dark cycle (7:00–19:00 and 19:00–7:00), and were supplied with a standard pellet diet *ad libitum* and had free access to water. The study was approved by and performed under the guidelines of the Research Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, Iran (B-9205).

Induction of Diabetes

Diabetes was induced with the administration of a single intraperitoneal injection of 55 mg/kg body weight STZ (Sigma, Aldrich, U.S.A.), which was prepared freshly. Two days after the injection of STZ, fasting blood glucose levels were measured from the tail vein to confirm diabetes. Only rats with a fasting blood glucose level >250 mg/dL were selected as diabetic and included in the experiments.

Experimental Protocol

After the acclimatization period, the experimental animals were randomly divided into 4 groups (10 rats per group) and treated as follows: Group 1: nondiabetic control rats (sham), Group 2: diabetic rats, Group 3: diabetic rats treated with 1.25 g/kg of sesame butter, and Group 4: diabetic rats treated with 0.5 g/kg of sesame oil. In this study, sesame butter and sesame oil were provided by Shir Hussein Co., Yazd, Iran, and the chemical composition analysis of the sesame butter showed that it contained 40% oil. Accordingly, 1.25 g/kg of sesame butter used in this study was equal to 0.5 g/kg of sesame oil in the respective groups. Both sesame oil and sesame butter were administrated orally with gavage tubes for 6 weeks.

In the present study, the diabetic rats were not treated with insulin or other medications. During the study, the experimental animals were carefully observed daily for general well-being and weighed every other day.

Biochemical Analysis

At the end of the study, the rats were anesthetized using light ether and fasting blood samples were

collected from the heart directly. Then sera were separated and used for biochemical analysis. Serum glucose, triglyceride (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-c) levels were determined enzymatically using the standard methods with an AutoAnalyzer SA1000. The level of low-density lipoprotein cholesterol (LDL-c) was calculated using the Friedewald formula as follows:

$$LDL\text{-}c=TC–HDL\text{-}c–(TG/5)^{15}$$

The serum concentration of malondialdehyde (MDA) was assayed as a biomarker of lipid peroxidation. Briefly, 0.5 mL of serum was mixed with 2.5 mL of trichloroacetic acid (20%) in a 10 mL centrifuge tube. One mL of thiobarbituric acid (0.67%) was added to the mixture, shaken, and heated in a boiling water bath for 1 hour followed by rapid cooling. Then, it was shaken into 4 mL of n-butanol, and the serum MDA concentration was measured at 532 nm by spectrophotometer against n-butanol. The total antioxidant capacity (TAC) of the serum was also determined using commercially available kits (Glory Science Co., U.S.A.).

Statistical Analysis

The normal distribution of all the variables was checked with the Kolmogorov–Smirnov test: The distribution of all the variables was normal. Thus, parametric tests were employed for all the variables. The data are presented as mean±standard deviation. The statistical significance was evaluated via the in dependent-samples *t*-test and the analysis of covariance in the adjusted models, followed by the *post hoc* Tukey honestly significant difference (HSD) test, using the Statistical Package for the Social Sciences (SPSS), version 18.0. A P<0.05 was considered statistically significant.

Results

Body weight changes during the study in the normal and diabetic groups are presented in Figure 1. The results showed that the mean of final body weight in both the diabetic control group and the diabetic group treated with sesame butter was significantly lower than that of the normal control group (P<0.001 and P=0.004, respectively). However, the final body weight of the diabetic rats treated with sesame oil was not statistically different from that of the normal control group (P=0.059). The treatment of the diabetic rats with sesame oil restored the weight loss compared to the diabetic control group (P=0.016).

The means of the fasting blood glucose levels at the end of the study are summarized in Table 1. The results showed that the diabetic rats treated with sesame butter and sesame oil had significantly lower levels of glucose than did the diabetic control group at the end of the study (P=0.006 and P=0.013, correspondingly).

The effects of sesame butter and sesame oil administration on serum lipid profile are shown in Table 2. The present data illustrated that the serum levels of lipid profile (i.e., TG, TC, LDL-c, and HDL-c) did not alter significantly in the diabetic control group compared to the normal control group after 6 weeks. However, both sesame butter administration and sesame oil administration in the diabetic rats increased the serum levels of HDL-c compared to the diabetic control group at the end of the study (P=0.043 and P=0.037, respectively). In comparison with the diabetic control group, TG levels were also decreased after 6 weeks; however, the change was statistically significant only in the diabetic group treated with sesame oil (P=0.006).

In the present study, the serum levels of MDA — as a biomarker of lipid peroxidation — were

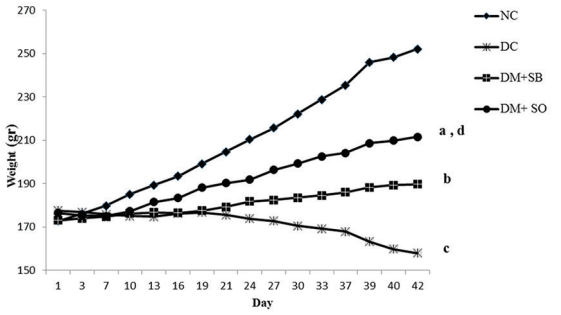

Figure 1: Effect of sesame butter and sesame oil on body weight changes. NC, normal controls; DC, diabetic controls; DM+SB, diabetic rats treated with sesame butter (1.25 g/kg); DM+SO, diabetic rats treated with sesame oil (0.5 g/kg). [a,b,c]Indicate P=0.059, P=0.004, and P<0.001 compared to the normal control group, respectively. [d]Indicates P=0.016 compared to the diabetic control group.

Table 1: Effect of sesame butter and sesame oil on serum glucose levels

Groups	FBS (mg/dL)	P1	P2
	Mean±SD		
Normal control	117.20±6.84	-	0.001
Diabetic control	303.66±175.71	0.001	-
Diabetic rats treated with sesame butter (1.25 g/kg)	150.22±94.54	0.524	0.006
Diabetic rats treated with sesame oil (0.5 g/kg)	161.87±106.14	0.405	0.013

FBS: Fasting blood glucose; All the values are expressed as mean±SD (n, 10). P1 indicates a P value between the normal controls and the other groups. P2 indicates a P value between the diabetic controls and the other groups

Table 2: Effect of sesame butter and sesame oil on lipid profile

Groups	TG (mg/dL)	TC (mg/dL)	LDL-c (mg/dL)	HDL-c (mg/dL)
Normal control	83.40±11.63	92.30±10.64	47.30±5.98	27.84±3.67
Diabetic control	89.66±14.97	85.77±11.46	44.77±6.92	25.11±4.59
Diabetic rats treated with sesame butter (1.25 g/kg)	76.60±17.48	85.22±10.68	40.01±6.98	30.22±5.69[a]
Diabetic rats treated with sesame oil (0.5 g/kg)	41.00±13.39[c]	81.12±9.34	39.25±6.62	31.03±5.80[b]

All the values are expressed as mean±SD (n, 10). [a,b,c]Indicate P=0.043, P=0.037, and P=0.006 compared to the diabetic control group, respectively. (P values were resulted from the analysis of covariance after adjusting for weight and glucose levels)
TG: Triglyceride; TC: Total cholesterol; LDL-c: Low-density lipoprotein cholesterol; HDL-c: High-density lipoprotein cholesterol

statistically higher in the diabetic control group than in the normal control group (P=0.028). The oral administration of sesame butter to the diabetic rats induced a significant reduction in serum MDA concentrations after 6 weeks (P=0.015) (Table 3).

The serum TAC levels of the experimental groups are depicted in Table 4. At the end of the study, the serum TAC levels in the diabetic control group were significantly lower than those of the normal control group (P=0.045); and following treatment with sesame butter, a significant increase in serum TAC was observed compared to the diabetic control group (P=0.004). However, TAC was not significantly changed in the diabetic group supplemented with sesame oil (P=0.405).

Table 3: Effect of sesame butter and sesame oil on the serum levels of MDA

Groups	MDA (µmol/L)	P1	P2
Normal control	2.78±0.35	-	0.028
Diabetic control	3.25±0.41	0.028	-
Diabetic rats treated with sesame butter (1.25 g/kg)	2.71±0.30	0.733	0.015
Diabetic rats treated with sesame oil (0.5 g/kg)	3.07±0.70	0.197	0.421

MDA: Malondialdehyde. All the values are expressed as mean±SD (n, 10). P1 indicates a P value between the normal controls and the other groups. P2 indicates a P value between the diabetic controls and the other groups

Table 4: Effect of sesame butter and sesame oil on serum TAC

Groups	TAC (µmol/L)	P1	P2
Normal control	0.54±0.18	-	0.045
Diabetic control	0.41±0.04	0.045	-
Diabetic rats treated with sesame butter (1.25 g/kg)	0.62±0.15	0.257	0.004
Diabetic rats treated with sesame oil (0.5 g/kg)	0.47±0.11	0.258	0.405

TAC: Total antioxidant capacity. All the values are expressed as mean±SD (n, 10). P1 indicates a P value between the normal controls and the other groups. P2 indicates a P value between the diabetic controls and the other groups

Discussion

The current study was conducted to determine whether the administration of sesame oil and sesame butter would have beneficial effects on weight and the serum levels of glucose, lipid profile, and oxidative stress biomarkers (i.e., MDA and TAC) in STZ-induced diabetic rats. Our findings clearly showed that administrating sesame oil and sesame butter improved weight loss in the diabetic rats. However, only the effect of sesame oil was significant in this respect. Weight loss in the untreated diabetic rats in this investigation was in agreement with other studies and could be due to poor glycemic control and subsequently the excessive catabolism of proteins and muscle wasting arising from insulin deficiency.[16-19] In the present study, dietary supplementation with sesame oil and sesame butter significantly improved glycemic control in the diabetic rats; consequently, the prevention of weight loss, found in the treated diabetic rats, could be partially explained by the improvement in blood glucose levels in these animals.[16] Moreover, sesame seeds are oil seeds with a chemical composition of about 44–58% oil, so they are high in energy. Sesame seeds are also a very good source of dietary proteins with fine quality amino acids, which are essential for growth. These properties could also have been responsible for the protective effect of sesame seeds against weight loss in our diabetic rats.[19]

Similar to our findings, Ramesh et al.[20] reported that their diabetic rats, fed a diet supplemented with sesame oil (6%), had a significant reduction in their levels of blood glucose compared to the diabetic control. The antihyperglycemic effect of sesame oil was also reported by Sankar et al.[7,8] in patients with hypertension and diabetes. Previous studies have suggested that a high-monounsaturated fat diet improves glycemic control by exerting protective effect against β-cell death and augmenting insulin sensitivity.[21,22] Sesame butter and sesame oil contain a great deal of monounsaturated fatty acids, which may be responsible for their antihyperglycemic effects. However, the exact mechanisms of the improved glycemic control associated with high-monounsaturated fatty acid diets remain undefined. The lignans present in sesame oil

are also thought to be responsible for many of its unique chemical and physiological properties, including its antidiabetic properties.[8]

In the present study, the diabetic rats receiving sesame oil and sesame butter had a significantly higher HDL-c concentration than did the diabetic control rats. The group treated with sesame oil also had a significantly lower level of TG than did the diabetic control group. Nevertheless, sesame had no significant effect on other lipid profiles in the diabetic rats. Numerous studies have demonstrated that oils containing high amounts of monounsaturated fatty acids and polyunsaturated fatty acids decrease TG, TC, and LDL-c levels.[23] It has also been posited that lignans present in sesame oil may play a role in the improvement of lipid profile. Sesame lignans such as sesamin and episesamin modulate cholesterol metabolism by inhibiting the synthesis and absorption of cholesterol in stroke-prone spontaneously hypertensive rats.[24] In this regard, Ide et al.[25] showed that sesamin decreased hepatic lipogenesis accompanying the downregulation of the sterol regulatory element in their study.[25] In another study, Rogi et al.[12] confirmed that the ingestion of sesamin together with α-tocopherol synergistically reduced the concentration of blood cholesterol in their study rats following a high-cholesterol diet.[12] The combined effect of sesamin and α-lipoic acid on improving serum lipid profile was recently demonstrated by Ide et al.[25] In the present study, the induction of diabetes in the rats after 6 weeks did not significantly change serum lipid profile. Therefore, some of the inconsistencies with the other relevant studies could be due to the normal values of lipid profile in our study. Moreover, it seems that this property of sesame in normal state can be considered an advantage for this medicinal plant. Although elevated levels of lipid profile in the circulation could give rise to hyperlipidemia and possibly other metabolic disorders,[26] the excessive lowering of lipid concentrations in the blood, hypolipidemia, might also contribute to several adverse effects.[27]

In the present study, we also found that a higher concentration of glucose was interrelated with higher lipid peroxidation and lower TAC. This finding denotes a direct association between diabetes and oxidative stress. Glucose oxidation, protein glycation, formation of advanced glycation end products, and polyol pathways are some of the major mechanisms involved in elevated oxidative stress biomarkers in diabetes.[28] Several studies have demonstrated that sesame and its constituent lignans (i.e., sesamin, sesamol, episesamin, and sesamolin) possess antioxidative properties as they improve TAC, suppress destructive oxygen-free radicals, and prevent oxidative stress damage.[28-30] Karatzi et al.[31] reported that sesame oil consumption (35 g/d) significantly increased plasma TAC after 2 weeks in their male subjects with hypertension. These findings are in accordance with several studies in rats showing that sesame oil may reduce oxidative stress.[29] Wichitsranoi et al.[30] demonstrated that the administration of black sesame meal capsules (2.52 g/d) for 4 weeks significantly decreased serum MDA levels in their human subjects with prehypertension. In addition, Roghani et al.[6] showed that sesamin treatment at a dose of 20 mg/kg for 7 weeks attenuated the increased MDA content and reduced the activity of superoxide dismutase in their diabetic rats. It has been suggested that dietary lignans provided through the consumption of sesame seeds or oil may protect the liver against Fe-induced oxidative damage. Antioxidant enzymes have an important role in the secondary defense mechanism during oxidative stress. Hemalatha et al.[32] showed that superoxide dismutase activity was greater in their rats following the administration of sesame oil (100 g/kg) plus sesamin (0.4 g/kg). The authors concluded that sesame lignans might enhance the ability to “mop up” superoxide radicals formed during Fe2-induced oxidative stress. Likewise, Hou et al.[33] studied the effects of sesame lignans (i.e., sesamin and sesamolin) on antioxidant enzyme activities in *in vitro* systems using cell lines and reported that the sesame antioxidants spared superoxide dismutase and catalase in hypoxia-stressed PC12 cells in a dose-dependent manner, an effect that may be related to their radical scavenging effect.

Nonetheless, the existing literature lacks evidence regarding the effect of sesame butter (Ardeh) on the markers of oxidative stress. The present study is, therefore, the first of its kind to investigate this effect. In this investigation, we found a significant increase in serum TAC and decrease in MDA concentration following the treatment of the diabetic rats with 1.25 g/kg of sesame butter. However, the administration of 0.5 g/kg of sesame oil could not significantly compensate for the reduced TAC or the elevated level of MDA concentration in the diabetic rats. It is important to note that sesame butter (Ardeh) is the product of the whole sesame seed and not merely its oil constituents. Some sesame lignans and phenolic compounds that mainly contribute to the antioxidant effect of sesame are exclusively presented in the sesame seed skin, which may explain the potent antioxidant activities of sesame butter versus sesame oil in this study.

Conclusion

The administration of sesame butter (Ardeh) conferred antihyperglycemic, antioxidative, and partly lipid-lowering effects among the diabetic rats in the present study. Although sesame oil exerted no significant effects on oxidative stress markers, it was able to compensate for weight loss and hyperglycemia in the treated group. Therefore, sesame and its products can be efficient in the prevention of diabetes complications and should be considered important candidates for human studies on diabetes in the future. Further investigations are suggested to explore the exact mechanism of sesame constituents on the complications of diabetes.

Acknowledgement

This study was derived from a master's degree thesis by Zahra Gorgi. Special thanks are due to Arvand International Division of Ahvaz Jundishapur University of Medical Sciences for its financial support (Grant # B-9205).

Conflict of Interest: None declared.

References

1. Islam MS, Choi H. Green tea, anti-diabetic or diabetogenic: a dose response study. Biofactors. 2007;29:45-53. doi: 10.1002/biof.5520290105. PubMed PMID: 17611293.
2. Zatalia SR, Sanusi H. The role of antioxidants in the pathophysiology, complications, and management of diabetes mellitus. Acta Med Indones. 2013;45:141-7. PubMed PMID: 23770795.
3. Haidari F, Keshavarz SA, Mohammad Shahi M, Mahboob SA, Rashidi MR. Effects of Parsley (Petroselinum crispum) and its Flavonol Constituents, Kaempferol and Quercetin, on Serum Uric Acid Levels, Biomarkers of Oxidative Stress and Liver Xanthine Oxidoreductase Aactivity inOxonate-Induced Hyperuricemic Rats. Iran J Pharm Res. 2011;10:811-9. PubMed PMID: 24250417; PubMed Central PMCID: PMC3813066.
4. Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006;444:840-6. doi: 10.1038/nature05482. PubMed PMID: 17167471.
5. Gupta RK, Kesari AN, Murthy PS, Chandra R, Tandon V, Watal G. Hypoglycemic and antidiabetic effect of ethanolic extract of leaves of Annona squamosa L. in experimental animals. J Ethnopharmacol. 2005;99:75-81. doi: 10.1016/j.jep.2005.01.048. PubMed PMID: 15848023.
6. Roghani M, Jalali-Nadoushan MR, Baluchnejadmojarad T, Vaez Mahdavi MR, Naderi G, Roghani Dehkordi F, et al. Endothelium-dependent Effect of Sesame Seed Feeding on Vascular Reactivity of Streptozotocin-diabetic Rats: Underlying Mechanisms. Iran J Pharm Res. 2013;12:377-85. PubMed PMID: 24250645; PubMed Central PMCID: PMC3813278.
7. Sankar D, Rao MR, Sambandam G, Pugalendi KV. A pilot study of open label sesame oil in hypertensive diabetics. J Med Food. 2006;9:408-12. doi: 10.1089/jmf.2006.9.408. PubMed PMID: 17004907.
8. Sankar D, Ali A, Sambandam G, Rao R. Sesame oil exhibits synergistic effect with anti-diabetic medication in patients with type 2 diabetes mellitus. Clin Nutr. 2011;30:351-8. doi: 10.1016/j.clnu.2010.11.005. PubMed PMID: 21163558.
9. Khaneshi F, Nasrolahi O, Azizi S, Nejati V. Sesame effects on testicular damage in streptozotocin-induced diabetes rats. Avicenna J Phytomed. 2013;3:347-55. PubMed PMID: 25050292; PubMed Central PMCID: PMC4075729.
10. Nakano D, Kurumazuka D, Nagai Y, Nishiyama A, Kiso Y, Matsumura Y. Dietary sesamin suppresses aortic NADPH oxidase in DOCA salt hypertensive rats. Clin Exp Pharmacol Physiol. 2008;35:324-6. doi: 10.1111/j.1440-1681.2007.04817.x. PubMed PMID: 17941888.
11. Miyawaki T, Aono H, Toyoda-Ono Y, Maeda H, Kiso Y, Moriyama K. Antihypertensive effects of sesamin in humans. J Nutr Sci Vitaminol (Tokyo). 2009;55:87-91. doi: 10.3177/jnsv.55.87. PubMed PMID: 19352068.
12. Rogi T, Tomimori N, Ono Y, Kiso Y. The mechanism underlying the synergetic hypocholesterolemic effect of sesamin and alpha-tocopherol in rats fed a high-cholesterol diet. J Pharmacol Sci. 2011;115:408-16. PubMed PMID: 21372506.
13. Sankar D, Sambandam G, Ramakrishna Rao M, Pugalendi KV. Modulation of blood pressure, lipid profiles and redox status in hypertensive patients taking different edible oils. Clin Chim Acta. 2005;355:97-104. doi: 10.1016/j.cccn.2004.12.009. PubMed PMID: 15820483.
14. Eftekhar Sadat B, Khadem Haghighian M, Alipoor B, Malek Mahdavi A,

Asghari Jafarabadi M, Moghaddam A. Effects of sesame seed supplementation on clinical signs and symptoms in patients with knee osteoarthritis. Int J Rheum Dis. 2013;16:578-82. doi: 10.1111/1756-185X.12133. PubMed PMID: 24164846.
15. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18:499-502. PubMed PMID: 4337382.
16. Kasetti RB, Rajasekhssar MD, Kondeti VK, Fatima SS, Kumar EG, Swapna S, et al. Antihyperglycemic and antihyperlipidemic activities of methanol: water (4:1) fraction isolated from aqueous extract of Syzygium alternifolium seeds in streptozotocin induced diabetic rats. Food Chem Toxicol. 2010;48:1078-84. doi: 10.1016/j.fct.2010.01.029. PubMed PMID: 20122979.
17. Ene A, Nwankwo E, Samdi L. Alloxan-induced diabetes in rats and the effects of black caraway (Carum carvi L.) oil on their body weight. Res J Med Med Sci. 2007;2:48-52.
18. Haidari F, Omidian K, Rafiei H, Zarei M, Mohamad Shahi M. Green Tea (Camellia sinensis) Supplementation to Diabetic Rats Improves Serum and Hepatic Oxidative Stress Markers. Iran J Pharm Res. 2013;12:109-14. PubMed PMID: 24250578; PubMed Central PMCID: PMC3813194.
19. Borchani C, Besbes S, Blecker C, Attia H. Chemical characteristics and oxidative stability of sesame seed, sesame paste, and olive oils. J Agric Sci Technol. 2010;12:585-96.
20. Ramesh B, Saravanan R, Pugalendi KV. Influence of sesame oil on blood glucose, lipid peroxidation, and antioxidant status in streptozotocin diabetic rats. J Med Food. 2005;8:377-81. doi: 10.1089/jmf.2005.8.377. PubMed PMID: 16176150.
21. Brehm BJ, Lattin BL, Summer SS, Boback JA, Gilchrist GM, Jandacek RJ, et al. One-year comparison of a high-monounsaturated fat diet with a high-carbohydrate diet in type 2 diabetes. Diabetes Care. 2009;32:215-20. doi: 10.2337/dc08-0687. PubMed PMID: 18957534; PubMed Central PMCID: PMC2628682.
22. Martin de Santa Olalla L, Sanchez Muniz FJ, Vaquero MP. N-3 fatty acids in glucose metabolism and insulin sensitivity. Nutr Hosp. 2009;24:113-27. PubMed PMID: 19593479.
23. Makni M, Fetoui H, Garoui el M, Gargouri NK, Jaber H, Makni J, et al. Hypolipidemic and hepatoprotective seeds mixture diet rich in omega-3 and omega-6 fatty acids. Food Chem Toxicol. 2010;48:2239-46. doi: 10.1016/j.fct.2010.05.055. PubMed PMID: 20510326.
24. Lim JS, Adachi Y, Takahashi Y, Ide T. Comparative analysis of sesame lignans (sesamin and sesamolin) in affecting hepatic fatty acid metabolism in rats. Br J Nutr. 2007;97:85-95. doi: 10.1017/S0007114507252699. PubMed PMID: 17217563.
25. Ide T, Azechi A, Kitade S, Kunimatsu Y, Suzuki N, Nakajima C. Combined effect of sesamin and alpha-lipoic acid on hepatic fatty acid metabolism in rats. Eur J Nutr. 2013;52:1015-27. doi: 10.1007/s00394-012-0408-3. PubMed PMID: 22752262.
26. Stone NJ. Successful control of dyslipidemia in patients with metabolic syndrome: focus on lifestyle changes. Clin Cornerstone. 2006;8:S15-20. doi: 10.1016/S1098-3597(06)80004-9. PubMed PMID: 16903165.
27. Elmehdawi R. Hypolipidemia: a word of caution. Libyan J Med. 2008;3:84-90. doi: 10.4176/071221. doi: 10.4176/071221. PubMed PMID: 21499464; PubMed Central PMCID: PMC3074286.
28. Juskiewicz J, Zdunczyk Z, Jurgonski A, Brzuzan L, Godycka-Klos I, Zary-Sikorska E. Extract of green tea leaves partially attenuates streptozotocin-induced changes in antioxidant status and gastrointestinal functioning in rats. Nutr Res. 2008;28:343-9. doi: 10.1016/j.nutres.2008.03.004. PubMed PMID: 19083430.
29. Hsu DZ, Chien SP, Li YH, Chuang YC, Chang YC, Liu MY. Sesame oil attenuates hepatic lipid peroxidation by inhibiting nitric oxide and superoxide anion generation in septic rats. JPEN J Parenter Enteral Nutr. 2008;32:154-9. doi: 10.1177/0148607108314766. PubMed PMID: 18407908.
30. Wichitsranoi J, Weerapreeyakul N, Boonsiri P, Settasatian C, Settasatian N, Komanasin N, et al. Antihypertensive and antioxidant effects of dietary black sesame meal in pre-hypertensive humans. Nutr J. 2011;10:82. doi: 10.1186/1475-2891-10-82. PubMed PMID: 21827664; PubMed Central PMCID: PMC3173298.
31. Karatzi K, Stamatelopoulos K, Lykka M, Mantzouratou P, Skalidi S, Manios E, et al. Acute and long-term hemodynamic effects of sesame oil consumption in hypertensive

men. J Clin Hypertens (Greenwich). 2012;14:630-6. doi: 10.1111/j.1751-7176.2012.00649.x. PubMed PMID: 22947362.
32. Hemalatha S, Raghunath M, Ghafoorunissa. Dietary sesame oils inhibits iron-induced oxidative stress in rats [corrected]. Br J Nutr. 2004;92:581-7. PubMed PMID: 15526409.
33. Hou RC, Huang HM, Tzen JT, Jeng KC. Protective effects of sesamin and sesamolin on hypoxic neuronal and PC12 cells. J Neurosci Res. 2003;74:123-33. doi: 10.1002/jnr.10749. PubMed PMID: 13130514.