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

Fatemeh Haidari¹, PhD; Majid Mohammadshahi², PhD; Mehdi Zarei³, PhD; Zahra Gorji⁴, MS

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

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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.

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

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...
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of diabetes and oxidative damage to peripheral tissues.²³ 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.⁷⁸ 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.¹⁰¹² 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:

\[
LDL-c = TC - HDL-c - \frac{TG}{5}
\]

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 thiorbituric 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.).

\[\text{Statistical Analysis}\]

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.

\[\text{Results}\]

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
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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    |
| Diabetic rats treated with sesame oil (0.5 g/kg) | 41.00±13.39 | 81.12±9.34  | 39.25±6.62    | 31.03±5.80    |

All the values are expressed as mean±SD (n, 10). abcIndicate 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

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 administering 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. 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).

Our findings clearly showed that administrating sesame oil and sesame butter improved weight loss in our 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. 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. 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.

Similar to our findings, Ramesh et al. 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. 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. 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.  

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. 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. In this regard, Ide et al. showed that sesamin decreased hepatic lipogenesis accompanying the downregulation of the sterol regulatory element in their study. In another study, Roghi et al. 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. The combined effect of sesamin and α-lipoic acid on improving serum lipid profile was recently demonstrated by Ide et al. 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, the excessive lowering of lipid concentrations in the blood, hypolipidemia, might also contribute to several adverse effects.

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. 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. Karatzi et al. 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. Wichitsranoei et al. 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. 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. 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. 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.

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Conflict of Interest: None declared.

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