

## Effects of Sesamin on the Glycemic Index, Lipid Profile, and Serum Malondialdehyde Level of Patients with Type II Diabetes

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### ABSTRACT

**BACKGROUND AND OBJECTIVE:** Diabetes mellitus is the most prevalent endocrine disorder associated with increased risk of cardiovascular diseases. Considering the possible effects of sesamin, the most important sesame lignan, on the prevention of metabolic disorders leading to diabetes, this study aimed to evaluate the effects of sesamin supplementation on glycemic indices, serum levels of lipid profile and Malondialdehyde (MDA) in patients with type II diabetes.

**METHODS:** This double-blind clinical trial was conducted on 44 patients with type II diabetes referring to the endocrine clinic of Golestan Hospital in Ahvaz, Iran (IRCT: 2014061818134N1). Patients were randomly divided into two groups of intervention and control. Patients of the intervention group received a daily dose of sesamin (200 mg capsules), and control subjects were administered with an equivalent dose of placebo. Anthropometric indices, fasting blood sugar (FBS), glycated hemoglobin (HbA1c), insulin level, insulin resistance (HOMA-IR) index, triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and malondialdehyde (MDA) levels were evaluated before and eight weeks after the intervention.

**FINDINGS:** Comparison of different indices before and after the intervention indicated that sesamin significantly decreased the serum levels of FBS (138.59±36.89 versus 172.50±53.9 mg/dl) (p=0.016), HbA1c (7.51±1.14% versus 8.28±1.55%) (p=0.002), TC (141.50±29.03 versus 164.54±45.96 mg/dl) (p=0.015), and LDL-C (73.86±18.34 versus 89.22±32.96 mg/dl) (p=0.008) in the intervention group compared to the control group. Moreover, after eight weeks of sesamin treatment in the intervention group, a significant reduction was observed in TG (139.04±78.46 versus 168.31±68.45 mg/dl) (p=0.021), MDA (1.93±0.30 versus 2.21±0.55 µmol/L) (p=0.023), waist circumference (101.65±9.78 versus 103.77±10.84 cm) (p=0.006), and body adiposity index (34.90±5.68 versus 36.02±5.56) (p=0.000). No significant differences were observed in the other studied variables.

**CONCLUSION:** According to the results of this study, daily administration of sesamin (200 mg) significantly improved the glycemic index, lipid profile, and serum MDA levels in type II diabetic patients. Therefore, sesamin could be effective in the prevention and control of type II diabetes complications.

**KEY WORDS:** Diabetes, Sesame, Sesamin, Glycated Hemoglobin, Lipid Profile.

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## Introduction

Diabetes is the most prevalent endocrine disorder across the world (1). According to the World Health Organization (WHO), more than 25 million people are expected to be diagnosed with diabetes by 2025 worldwide, while the prevalence rate of type II diabetes is reported to be 7.8% in Iran, with the patient population estimated at 5,125,000 (2).

Type II diabetes is associated with increased risk of cardiovascular diseases. The major risk factor for the progression of cardiovascular diseases in diabetic patients is lipid profile disorders, which could be detected with various indices, including high serum levels of triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C).

Furthermore, through the peroxidation of polyunsaturated fatty acids in LDL-C, free radicals initiate the underlying disorders that lead to the development and progression of atherosclerosis (3). Given the chronic, non-contagious and costly nature of diabetes, special attention must be paid to this disease and the subsequent complications in order to promote public health. Despite the efficacy of available anti-diabetic medications in the reduction of blood glucose, these therapeutic drugs have been shown to cause numerous side effects in the patients. As such, researchers have been concerned with finding effective substances to inhibit the mechanisms of diabetes without significant side effects (4).

In the traditional medicine, sesame has been widely used for therapeutic and medicinal purposes (5). Sesame seed contains 50% fat, 20% protein, and various lignans, such as sesamin, which constitutes 1.5% of the weight of this seed (6). This substance is one of the most abundant lignans among furfural compounds, which is phytoestrogenic and fat-soluble. Sesamin has protective effects for hepatocytes, anti-cancer properties and antioxidant features. In addition, it lowers blood pressure and cholesterol, strengthening the immune system (7, 8).

Sesamin has been used to decrease lipid and blood glucose levels, as well as the expression of vascular cell adhesion molecule-1 in the aorta of rats with metabolic syndrome (9). Although sesame is an abundant nutrient source of glycosides and other beneficial compounds, such as sesamin, few studies have evaluated the effects of this plant on the reduction of blood glucose (10). Previous studies in this regard have been performed on animal models or in vitro, and

to date, only one research has assessed the effects of sesamin on patients with type II diabetes (11). Considering the possible effects of sesamin on the prevention of metabolic disorders leading to diabetes, this study aimed to evaluate the effects of sesamin on the glycemic index, lipid profile, and serum malondialdehyde (MDA) level in type II diabetic patients.

## Methods

This double-blind clinical trial (IRCT: 2014061818134N1) was conducted on patients with type II diabetes referring to the endocrine clinic of Golestan Hospital in Ahvaz, Iran in 2013. Study protocol was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, Iran (AJUMS REC. 13/2/2013).

Sample size was estimated at 15 subjects per each group based on the findings of previous studies using the mean and standard deviation of TC (12). To increase statistical power and considering the possible sample loss, 22 patients were allocated to each group. Diagnosis of type II diabetes was confirmed by an endocrinologist based on the criteria of the American Diabetes Association (ADA) (13). Eligibility of the samples was evaluated prior to the study using a questionnaire consisting of demographic data (age, smoking habits, breastfeeding and pregnancy), medical history (presence of liver and renal diseases, cancer, allergies, hypothyroidism, hyperthyroidism, and rheumatoid arthritis), and use of medications affecting carbohydrate and lipid metabolism and blood pressure. Initial sample size was determined at 48 patients. Objectives of the study were explained to the selected subjects, and written informed consent was obtained from the patients who were willing to participate in the study. Selected patients were randomly divided into two groups of intervention (n=24) and control (placebo) (n=24). Patients in the intervention and placebo groups received 200 mg capsules daily containing sesamin and starch, respectively for 60 days. In order to control confounding factors, participants were asked to avoid consuming sesame and its products and refrain from any changes of the dietary regimen and physical activity during the study period. Before and after the intervention, a 24-hour diet recall was made in order to identify nutrient intakes of the samples, and the results were analyzed using the Nutritionist IV software. In addition,

physical activity of the participants was evaluated based on the International Physical Activity Questionnaire (14). Height and weight of the participants (with the least amount of clothing and without shoes) were calculated at the accuracy of 0.1 cm and 0.1 kg, respectively, using a Seca scale and stadiometer. Moreover, waist circumference (below the ribs) and waist-to-hip ratio (WHR) were measured using a non-elastic tape with maximum error of 0.5 cm.

In this study, body adiposity index (BAI) was measured using the following formula:

*BAI (percentage of fat): hip circumference (cm)/height (m)<sup>1.5</sup>-18*

In addition, body mass index (BMI) was calculated by dividing body weight by the square of height in meter (kg/m<sup>2</sup>). Venous blood samples were provided from the patients before and after the intervention. Moreover, levels of TC, LDL-C, HDL-C, and TG were measured using enzymatic methods, and the percentage of glycated hemoglobin (HbA1c) was calculated via chromatography. In this study, MDA level was determined using the thiobarbituric acid method, and insulin level was assessed using the DIAPLUS ELISA kit made (made in the U.S.A) and Abbott (ALCYON 300) autoanalyzer based on colorimetric evaluations. Data analysis was performed in SPSS V.17 and all data were expressed as mean and standard deviation. In case of normal distribution, independent T-test was used to evaluate the differences in the mean quantitative variables between the intervention and control groups. In addition, paired-samples T-test was applied in order to compare the mean variables before and after the study. To control the effect of confounding variables, we used the analysis of covariance (ANCOVA), and  $p < 0.05$  was considered statistically significant.

## Results

In total, 48 patients with type II diabetes were enrolled in this study, and four participants (two intervention and two control subjects) were excluded due to insulin injection, changes in the type or dose of medications, and unwillingness to cooperate with the researcher. Eventually, data of 44 subjects were recorded and analyzed. At the beginning of the study, samples were homogenous in terms of demographic data and anthropometric indices (tables 1 & 2). However, a significant difference was observed in the

mean energy level and carbohydrate intake between the groups at the beginning of the study ( $p < 0.05$ ), while other nutrient intakes and physical activity of the patients showed no significant differences (table 3). Moreover, study groups had no significant differences in the mean glycemic index, lipid profile, and MDA level before the intervention (table 4).

**Table 1. Demographic data of studied samples**

Variable	Sesamin (n=22)	Placebo (n=22)	Pvalue*
<b>Gender</b>			
Male	11	11	1
Female	11	11	1
Age (year)	50.00±12.13	51.72±12.24	0.641
Duration of Disease (year)	9.3±0.7	8.5±5.9	0.751

\*Comparison of mean and standard deviation of variables between intervention and control groups based on independent-samples T-test

After the intervention, intergroup and intragroup comparisons were indicative of no significant differences between the intervention and control groups in terms of mean weight, BMI, and WHR. After eight weeks, mean waist circumference (101.65±9.78 versus 103.77±10.84 cm) ( $P = 0.006$ ) and BAI (34.90±5.68 versus 36.02±5.56%) ( $P = 0.000$ ) showed a significant reduction in patients receiving sesamin treatment. However, differences of the study groups in this regard were not statistically significant (table 2).

On the other hand, mean carbohydrate intake had a significant decrease in the placebo group after the intervention compared to before the study; however, changes of other nutrient intakes and physical activity of the patients had no significant differences (table 3). According to the results of this study, mean fasting blood sugar (FBS) (138.59±36.89 versus 172.50±53.9 mg/dl) ( $p = 0.002$ ) and HbA1c (7.51±1.14 versus 8.28±1.55%) ( $p = 0.003$ ) significantly decreased in the sesamin group at the end of the study compared to the beginning of study. Moreover, after modifying the effects of energy level and carbohydrate intake, mean FBS and HbA1c significantly reduced in the sesamin group compared to the placebo group ( $p = 0.016$  and  $p = 0.002$ , respectively). However, no significant differences were observed between the study groups in terms of insulin level and insulin resistance (HOMA-IR) index. At the end of the study, mean serum TG

(139.04±78.46 versus 168.31±68.45 mg/dl) ( $p=0.021$ ) significantly decreased in the sesamin group. Sesamin supplementation could significantly decrease TC (141.50±29.03 versus 164.54±45.96 mg/dl) ( $p=0.004$ ) and LDL-C (73.86±18.34 versus 89.22±32.96 mg/dl) ( $p=0.007$ ) in the intervention group compared to the placebo group ( $p=0.007$  and  $p=0.002$ , respectively). This was also observed after the modification of energy level and carbohydrate intake in the

intervention and placebo groups ( $p=0.015$  and  $P=0.008$ , respectively). However, no significant difference was reported in the level of HDL-C after the intervention. After the intervention, subjects of the sesamin and placebo groups showed a significant reduction in the serum level of MDA ( $p=0.023$  and  $p=0.027$ , respectively). However, comparison of study groups revealed no significant difference in this regard ( $p=0.974$ ).

**Table 2. Mean anthropometric indices of studied samples**

Variable	Sesamin(n=22) Mean±SD	Placebo(n=22) Mean±SD	P <sub>a</sub>	P <sub>b</sub>
<b>Weight (kg)</b>				
Before Intervention	75.42±14.68	75.06±14.55	0.935	0.918
After Intervention	75.30±14.54	74.51±14.44	0.857	0.950
P <sub>c</sub>	0.820	0.372		
<b>Body Mass Index (kg/m<sup>2</sup>)</b>				
Before Intervention	29.53±6.68	28.76±5.62	0.625	0.958
After Intervention	29.67±4.87	28.51±5.83	0.481	0.966
P <sub>c</sub>	0.619	0.351		
<b>Waist Circumference (cm)</b>				
Before Intervention	103.77±10.84	98.79±13.02	0.176	0.264
After Intervention	101.65±9.78	98.52±12.83	0.378	0.52
P <sub>c</sub>	0.006	0.694		
<b>Waist-to-hip Ratio</b>				
Before Intervention	0.95±0.06	0.94±0.07	0.704	0.756
After Intervention	0.95±0.07	0.94±0.06	0.637	0.347
P <sub>c</sub>	0.895	0.895		
<b>Body Adiposity Index (%)</b>				
Before Intervention	36.02±5.56	33.56±7.29	0.215	0.291
After Intervention	34.90±5.68	33.33±7.16	0.428	0.865
P <sub>c</sub>	0.000	0.235		

P<sub>a</sub>: Comparison of mean variables in two groups based on independent-samples T-test;

P<sub>b</sub>: Comparison of mean variables in two groups after modification of effect of energy level and carbohydrate intake;

P<sub>c</sub>: Comparison of mean variables in two groups before and after study based on paired-samples T-test

**Table 3. Mean nutrient intake and physical activity of studied samples**

Variable		Sesamin (n=22) Mean±SD	Placebo (n=22) Mean±SD	P <sub>a</sub>
Energy (kcal)	Before Intervention	1424.63±393.63	1820.18±505.55	0.006
	After Intervention	1390.26±428.37	1598.02±520.91	0.156
	P <sub>b</sub>	0.716	0.074	
Carbohydrate (g)	Before Intervention	220.20±84.78	282.77±57.15	0.006
	After Intervention	191.76±56.80	232.68±86.15	0.070
	P <sub>b</sub>	0.121	0.009	
Protein (g)	Before Intervention	62.94±19.16	81.82±49.70	0.104
	After Intervention	61.70±28.05	73.69±27.62	0.161
	P <sub>b</sub>	0.835	0.415	
Lipids (g)	Before Intervention	34.52±18.03	47.67±37.51	0.146
	After Intervention	13.29±15.74	47.66±28.71	0.574
	P <sub>b</sub>	0.161	0.999	
Physical Activity	Before Intervention	2626.47±1684.32	2774.52±1706.24	0.790
	After Intervention	2397.97±2162.44	2466.56±2078.22	0.915
	P <sub>b</sub>	0.395	0.060	

P<sub>a</sub>: Comparison of mean variables between groups based on independent samples T-test;

P<sub>b</sub>: Comparison of mean variables between groups before and after intervention based on paired-samples T-test

**Table 4. Mean glycemic index, lipid profile and malondialdehyde (MDA) in studied samples**

Variable		Sesamin (n=22)	Placebo (n=22)	P <sub>a</sub>	P <sub>b</sub>
		Mean±SD	Mean±SD		
Fasting Blood Sugar (mg/dl)	Before Intervention	172.50±53.09	145.40±49.53	0.087	0.255
	After Intervention	138.59±36.89	147.13±54.97	0.548	0.016
	P <sub>c</sub>	0.002	0.801		
Glycated Hemoglobin (HbA1c)	Before Intervention	8.28±1.55	7.76±1.77	0.305	0.401
	After Intervention	7.51±1.14	7.83±1.85	0.503	0.002
	P <sub>c</sub>	0.003	0.537		
Insulin Level (mg/l)	Before Intervention	32.99±9.71	40.56±25.35	0.198	0.262
	After Intervention	36.78±18.57	37.28±18.61	0.929	0.826
	P <sub>c</sub>	0.383	0.469		
Insulin Resistance (HOMA-IR)	Before Intervention	13.24±6.11	12.72±6.97	0.799	0.944
	After Intervention	12.73±6.32	12.19±7.06	0.791	0.613
	P <sub>c</sub>	0.746	0.741		
Triglyceride (mg/dl)	Before Intervention	168.31±68.45	181.81±100.44	0.605	0.451
	After Intervention	139.04±78.46	136.45±66.7	0.907	0.761
	P <sub>c</sub>	0.021	0.005		
Total Cholesterol (mg/dl)	Before Intervention	164.54±45.96	174.45±39.94	0.450	0.372
	After Intervention	141.5±29.03	170.94±39.61	0.007	0.015
	P <sub>c</sub>	0.004	0.480		
Low-density lipoprotein cholesterol (mg/dl)	Before Intervention	89.22±32.96	92.77±24.65	0.688	0.489
	After Intervention	73.86±18.34	96.77±24.65	0.002	0.008
	P <sub>c</sub>	0.007	0.558		
High-density lipoprotein cholesterol (mg/dl)	Before Intervention	47.59±11.52	49.77±9.34	0.494	0.172
	After Intervention	46.00±10.10	48.09±10.56	0.506	0.378
	P <sub>c</sub>	0.308	0.228		
MDA (μmol/L)	Before Intervention	2.21±0.55	2.19±0.83	0.922	0.837
	After Intervention	1.93±0.3	1.93±0.58	0.974	0.866
	P <sub>c</sub>	0.023	0.037		

P<sub>a</sub>: Comparison of mean variables between groups based on independent samples T-test;

P<sub>b</sub>: Comparison of mean variables between groups after modification of effects of energy level and carbohydrate intake based on ANCOVA;

P<sub>c</sub>: Comparison of mean variables between groups before and after intervention based on paired-samples T-test

## Discussion

According to the results of the present study, daily administration of 200 mg sesamin significantly decreased FBS, HbA1c, MDA, and several lipid profile indices in patients with type II diabetes, which is in line with the findings of previous studies performed on animal models (8, 9, 11, 15). However, few studies have been conducted to evaluate the effects of sesamin on patients with type II diabetes. In the current research, sesamin supplementation significantly reduced waist circumference and BAI in the participants. It has been well established that type II diabetes is associated with excessive weight gain, especially abdominal obesity (16, 17). One of the most common methods to assess general and abdominal obesity in diabetic patients involves the measurement of waist circumference and body fat percentage (BFP), which has been shown to be associated with a high risk of progressive cardiometabolic complications in type II diabetes (18). Findings of the present study are in

congruence with the results obtained by Helli et al., who reported that use of 200 mg of sesamin daily for six weeks significantly reduced BFP in women with rheumatoid arthritis (19). Furthermore, the study by Fujiwara et al. demonstrated that consumption of sesamin supplement effectively decreased BFP in diabetic rats (20). In the current clinical trial, sesamin supplementation was observed to significantly lower the levels of FBS and HbA1c in patients with type II diabetes. In this regard, only one research by Ryu et al. has investigated the effects of sesamin on the blood glucose of type II diabetic patients. In the mentioned study, daily consumption of 8.7 mg sesamin for eight weeks was reported to have no effect on the blood glucose level of patients with type II diabetes and hyperlipidemia (11). This discrepancy in the results might be due to the very low dosage of sesamin used in the study by Ryu et al. For the most part, previous experimental studies have suggested that sesamin

prescription could significantly decrease the level of FBS in rats (9, 11, 15). According to the literature, dose-dependent treatment with sesamin causes a significant reduction in the levels of FBS and HbA1c in diabetic rats, while inhibiting the elevation of blood glucose level through glycogen production in the liver (8). In a study by Bigonya et al., use of sesame seed supplementation was shown to reduce blood glucose levels and enhance glucose tolerance in rats.

With this background in mind, it seems that sesame lignans are able to regulate the expression of the genes involved in glucose uptake, insulin signaling pathways, and carbohydrate metabolism in rats with type II diabetes (21). Although the exact function of sesamin in reducing HbA1c remains unclear, these effects might be associated with the antioxidant properties of this lignan (22). According to the results of the present study, sesamin treatment could significantly decrease the levels of LDL-C, TC, and TG, while it had no significant effect on HDL-C levels of diabetic patients. This is consistent with the results of previous studies in this regard. For instance, in the research by Hirata et al., consumption of 65 mg sesamin daily for four weeks was reported to cause a significant reduction in the levels of LDL-C and TC in patients with high cholesterol, while no significant differences were observed in TG and HDL-C levels (12). In another study by Wu et al., daily consumption of powdered sesame seed (50 grams) for five weeks led to a significant decrease in the plasma levels of TC in menopausal women. In addition to the lipid profile, LDL-C and HDL-C levels were observed to improve by 5% and 10%, respectively (23).

In this regard, the study by Chan et al. was conducted on 21 patients with normal weight and high blood cholesterol. According to the findings, partial substitution of daily calorie intake with 40 grams of sesame seed for four weeks, followed by four weeks of sesame-free dietary regimen, significantly decreased TC and LDL-C levels (6.4% and 9.5%, respectively), while it had no significant effect on TG and HDL-C (16). According to another research by Hong et al., dose-dependent treatment with sesamin could improve insulin resistance in diabetic patients. In the mentioned study, doses of 50 and 100 mg/kg of sesamin caused a significant reduction in serum levels of FBS, HbA1c, insulin, TG, and TC (8). Sesamin lowers serum and liver cholesterol levels through reducing intestinal cholesterol absorption, increasing the excretion of

cholesterol through the bile, and enhancing the activities of HMG-CoA and 7-alpha hydroxylase enzymes (24). Furthermore, sesamin significantly increases the activity of liver enzymes involved in fat oxidation, including acyl-CoA oxidase, carnitine palmitoyltransferase, 3-hydroxyacyl-CoA, and 3-ketoacyl-thiolase. On the other hand, sesamin intensifies the activity of enzymes involved in fatty acid synthesis, such as fatty-acid synthase, glucose-6-phosphate dehydrogenase, ATP citrate lyase, and pyruvate kinase. Consequently, sesamin lowers serum lipid levels through increasing fatty acid beta-oxidation and reducing lipogenic enzyme activities in the liver (25, 26). In the current research, a significant decrease was observed in the mean serum level of MDA in the intervention and control groups. In a previous study conducted *in vitro*, sesamin significantly reduced lipoprotein peroxidation potential through copper, as well as the MDA level and peroxidation of erythrocyte membrane lipids (27). Furthermore, daily consumption of powdered sesame seed (50 grams) for five weeks has been shown to decrease MDA levels in postmenopausal women by 18% (23). Remarkable antioxidant effects of sesamin have been demonstrated *in vitro*, and this lignan could play a pivotal role in the prevention of coronary artery disease in diabetic patients *in vivo* (27). According to the literature, sesamin is able to increase serum vitamin E and reduce lipid peroxidation through improving the bioavailability of vitamin E and reducing its metabolism by cytochrome P450 (22).

In conclusion, the results of this study indicated that daily consumption of sesamin supplement (200 mg) could effectively control plasma levels of glucose and lipids, as well as lipid peroxidation. Therefore, it is recommended that supplementary sesamin be used for the prevention and monitoring of the complications associated with type II diabetes. Further investigations on larger sample sizes with longer durations are required as to confirm the beneficial effects of sesamin.

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