Effects of Sesame Oil on the Reproductive Parameters of Diabetes Mellitus-Induced Male Rats

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Purpose: The purpose of the present study was to investigate the effect of sesame oil on the reproductive parameters of diabetic male Wistar rats.

Materials and Methods: The adult male rats in a split plot design were divided into normal (n=10), normal 5% (n=5; 5% sesame oil enriched diet), diabetic (Streptozocin induced diabetes; n=9), diabetic 5% (n=9; 5% sesame oil enriched diet), and diabetic 10% (n=9; 10% sesame oil enriched diet) groups. Diet supplementation continued for 56 days.

Results: Sesame oil supplementation did not reduce the plasma glucose concentration of rats in the diabetic groups (p > 0.05). The total spermatogonia, spermatocytes, Leydig cells/tubule, and the germ cell to Sertoli cell ratio were lower in the diabetic rats than the normal ones (p < 0.05), and with the exception of spermatogonia counts, these values improved by the addition of sesame oil to the diet (p < 0.05). The sperm progressive motility and viability were lower in the diabetic rats (p < 0.05) and sesame oil supplementation did not improve them. Incorporation of sesame oil into the diet improved the plasma testosterone concentration of the diabetic rats in a dose-dependent manner (p < 0.05).

Conclusions: In summary, sesame oil supplementation improved the reproductive parameters of diabetic rats at the levels of the testicular microstructure and function, but was not effective in protecting the epididymal sperm.

Key Words: Rats; Diabetes mellitus; Spermatozoa; Testis; Testosterone; Sesame oil

INTRODUCTION

The effects of diabetes on male reproduction have been documented. Impairment of sexual behavior, semen quality, and ejaculation are the most common reproductive consequences in diabetic men. Disrupted spermatogenesis and oligozoospermic cases of diabetes have also been reported. Decreased sperm motility and disturbance in gonadal and gonadotropin hormones were reported in diabetics as well. Two different mechanisms have been suggested for the reproductive complications of diabetes: endocrine neuropathies and metabolic disturbances leading to oxidative stress. Diabetes mellitus is usually accompanied by extensive disturbances in the metabolism of glucose and fatty acids. The extensive impacts of lipid peroxidation in the testis and epididymal...
sperm of streptozocin (STZ)-induced diabetic rats have been demonstrated previously.14

Different drugs and compounds may reduce the reproductive consequences of diabetes. Ginseng extract supplementation,15 nano-structures,16 *Zingiber officinale* root,17 rosiglitazone,18 metformin,19 and insulin supplementation20 improved the reproductive performance and sperm quality of diabetics. *Sesamum radiatum* leaves improved the testicular structures of normo-glycemic adult males.21 It has been suggested that the effects of sesame leaves can be mediated through the antioxidative properties of their lignans.22-24 Sesame oil is beneficial in improving the blood glucose, glycosylated hemoglobin, lipid-peroxidation, and antioxidative levels in female STZ-induced diabetic rats.21,22,25

The aim of the present study was to investigate whether sesame oil supplementation can reduce the impact of diabetes on testicular structures and function, specifically the testicular micro-structures, sperm parameters, and hormone profile, of STZ-induced diabetic rats.

**MATERIALS AND METHODS**

Male Wistar rats were purchased from the animal facility of Shahid Chamran University of Ahvaz. STZ was acquired from Pharmacia and Upjohn (Germany). All chemicals were from Merck (Germany). The sources of other materials have been specified throughout the text.

**1. Animals and the induction of diabetes mellitus**

The animals were harbored in stainless steel cages under standard laboratory conditions of a 12 hours light/dark cycle throughout the experimental period with *ad libitum* access to food and water. Supplementation of the diet with sesame oil (v/w) in the respective groups was performed by mixing an adequate volume of oil and powdered food. The rats were housed at a controlled temperature of 23 ± 2°C schedule and their health was carefully monitored every day. For the animal care, the ethics guidelines for using laboratory animals in experiments published by Tehran University of Medical Sciences was followed throughout the study (http://mehr.tums.ac.ir/ShowCode.aspx?CodeID=104&lang=en).

Diabetes was induced by intravenous administration of citrate buffered (0.1 M, pH = 4.5) STZ (50 mg/kg; body weight). One week after induction, the concentration of blood glucose was measured by a glucometer (Glucose assay tape; Bayonim, Berneck, the Netherlands), and the rats with a glucose concentration greater than 300 mg/dl were classified as diabetic. A similar volume of only citrate buffer (0.5 ml/kg; body weight) was intravenously infused in the rats assigned to the non-diabetic groups.

**2. Plasma collection and analysis**

At the end of the experiment, the animals were euthanized and blood samples were collected in EDTA-coated glass tubes, centrifuged at 3,500 rpm for 15 minutes, and the separated plasma was stored at −20°C until the glucose and hormone assays. The samples were assayed for glucose by the glucose oxidase method using a commercially available kit (glucose assay kit, Pars Azmun, Iran). The plasma testosterone and estradiol concentrations were measured using enzyme-linked immunosorbent assay (ELISA; DRG Instruments GmbH, Marburg, Germany). The intra- and inter-assay coefficients of variation for testosterone were 4.16 and 9.94, and for estradiol were 6.81 and 7.25, respectively.

**3. Organ sample collection**

The scrotum was cut with fine scissors and the testis-epididymis was removed. The testes and epididymides were dissected and weighed using a digital electronic balance. The testis and epididymis length and width were measured using a plastic tape. The testis was fixed in buffered-formalin (10%) and embedded within paraffin. The paraffin sections (5-μm thickness) were prepared and stained with H&E. The specimens were examined under light microscopy (Olympus/3H, Tokyo, Japan).

**4. Sperm collection and evaluation**

The left caudal epididymis was separated and the total recovered sperm during 4 h of incubation in normal saline (volume = 1 ml, 35–37°C) was calculated. The sperm concentration was determined by the conventional method using a hemocytometer chamber for the red blood cell count. The right epididymis was finely minced by anatomical scissors in 1 ml of warmed isotonic saline in a petri dish. The sperm progressive motility (SPM) was estimated
by evaluating 4 fields of a sperm droplet under a cover-slip on a warm glass slide (35 ~ 37°C) under light microscopy (×40). The sperm vitality was assayed using a conventional procedure of eosin B-nigrosin stain (1.67% eosin, 10% nigrosin, and 0.1 M sodium citrate) under ×100 magnification and 100 sperm were counted. Later, the morphological abnormalities of sperm were considered and recorded. All of the sperm evaluation procedures were carried out based on the World Health Organization manual for human sperm analysis26 with some modifications.

5. Histological study

Five slides were selected from each group and 5 seminiferous tubules within each slide were evaluated for spermatogonia (spermatogonia A, intermediate, and B), spermatocytes (primary and secondary spermatocytes) and the Sertoli cell counts, and the Leydig cell numbers were evaluated in the interstitial tissue.27 The average of the different cell counts of each slide was used for the analysis. The evaluation of all of the samples was performed at a constant magnification of 40× with light microscopy. The ratio of the germ cell to the Sertoli cell number was calculated by dividing the sum of the counted spermatogonia and spermatocytes by the Sertoli cell numbers per tubule.

6. Experimental design

Forty-two diabetic and non-diabetic rats (190 ± 10 g) were assigned into five groups; normal (n=10): the non-diabetic rats without any treatment, diabetic (n=9): the diabetic rats with no treatment, diabetic 5% (n=9): the diabetic rats that received a diet with 5% sesame oil (Saman, Tehran, Iran), diabetic 10% (n=9): the diabetic rats that received a diet with 10% sesame oil, and normal 5% (n=5): the non-diabetic rats that received a diet with 5% sesame oil. The experimental period lasted for 56 days to cover the period of a complete pathway of spermatogenesis in the rat.28

7. Statistical analysis

The univariate normal plot procedure was used for normality of data. Except SPM, the other parameters had a normal distribution. The arcsine transformation was used for normalizing the data on the SPM. The main effects of diabetes (diabetics and normal) and diet supplementation (with sesame oil or not) on the general parameters, serum glucose, T2 and cortisol concentrations, and testicular parameters were analyzed by one way analysis of variance using

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**Table 1.** The effects of sesame oil on general and sperm parameters and endocrine assays in male diabetic Wistar rats*

|                         | Normal (n=10) | Diabetic (n=9) | Diabetic 5% oil (n=9) | Diabetic 10% oil (n=9) | Normal 5% oil (n=5) |
|-------------------------|--------------|----------------|-----------------------|------------------------|-------------------|
| **General parameters**  |              |                |                       |                        |                   |
| Body weight (g)         | 300.8±11.0§  | 220.3±9.4†     | 220.3±14.7†           | 237.3±14.6†           | 299.6±17.2§      |
| Testis weight (g)       | 1.4±0.05†    | 1.2±0.06†      | 1.3±0.06†             | 1.4±0.06†             | 1.3±0.08†        |
| Testis volume (mm³)     | 1.39±0.14†   | 1.35±0.13†     | 1.4±0.11†             | 1.4±0.13†             | 1.42±0.13†       |
| Testis length (mm)      | 19.5±0.42†   | 19.3±0.54†     | 20.0±0.39†            | 20.7±0.27†            | 19.5±0.45†       |
| Testis width (mm)       | 11.6±0.24†   | 10.9±0.32†     | 11.2±0.18†            | 11.2±0.17†            | 11.4±0.05†       |
| Epididymis weight (g)   | 0.48±0.02§   | 0.37±0.03†     | 0.395±0.03†           | 0.41±0.03†            | 0.44±0.02§       |
| Testis to body weight   | 0.005±0.0002†| 0.006±0.0003§  | 0.006±0.0003§         | 0.006±0.0003§         | 0.004±0.0003‡    |
| Epididymis to testis weight | 0.35±0.02† | 0.3±0.02§      | 0.3±0.02§             | 0.3±0.02§             | 0.34±0.02‡       |
| **Sperm parameters**    |              |                |                       |                        |                   |
| Concentration (×10⁹/ml) | 261.1±18.05† | 212.7±31.74†  | 215.9±16.48†          | 199.7±19.47†          | 344.6±11.07§     |
| Motility†               | 63.9±4.44†   | 22.77±3.91†    | 41.1±4.62§            | 21.9±2.97†            | 79.20±1.80†      |
| Abnormality†            | 6.8±1.83§    | 23.5±2.90†     | 9.9±1.68§             | 13.8±2.49§            | 1.4±0.50‡        |
| Viability†              | 89.6±2.38§   | 74.2±4.24†     | 87.9±2.70‖            | 81.5±4.61‖            | 95.8±0.58‖       |
| **Endocrine and glucose assay** |         |                |                       |                        |                   |
| Estradiol (pg/ml)       | 13.1±0.91†   | 13.05±1.12†    | 10.5±1.43†            | 10.05±0.66†           | 9.9±2.40†        |
| Testosterone (ng/ml)    | 2.5±0.28†    | 1.4±0.26†      | 1.9±0.52†             | 5.1±1.51‡             | 2.7±0.42‡        |
| Glucose (mg/dl)         | 135.4±15.1†  | 411.6±50.49§   | 416.9±75.28§          | 467.7±76.71§          | 107.5±5.66 §     |

*Values are presented as least square mean±standard mean; and †percentage. †, ‡, §, † Values with a common mark within rows are not significantly different (p>0.05).
a Generalized Linear Model (GLM) procedure in SAS software (Statistical Analysis System 9.1.3; SAS Institute, Cary, NC, USA). The Duncann’s multiple range test was used to make all possible pairwise comparisons. The results were expressed as least square mean (L.S. Mean) and the standard error of the means.

RESULTS

Table 1 shows the effects of sesame oil supplementation and diabetes on the general parameters, sperm parameters, and hormone and glucose assays in the experimental groups.

1. Body weight and testicular and morphologic parameters

Diabetes (220.3 ± 9.4) reduced the body weight (g) compared to the normal group (300.8 ± 11.0; p < 0.05). Sesame oil supplementation did not improve the body weight gain (Table 1). Testis weight (g), volume (mm³), and length and width (mm) did not differ between the groups (p > 0.05). Diabetes (0.37 ± 0.03) reduced the weight (g) of the epididymis compared to the normal (0.48 ± 0.02) animals (p < 0.05), and diet supplementation of diabetic rats with sesame oil (0.395 ± 0.03 and 0.41 ± 0.03; for 5% and 10% oil, respectively) improved the weight of the epididymis compared with normal rats (Table 1; p > 0.05). The testis to body weight ratio in the diabetic animals was higher than in the normal ones (p < 0.05) and oil supplementation did not affect it (p < 0.05). The ratio of epididymis to testis weight was higher in the diabetic rats than the normal group (p < 0.05), and oil supplementation did not improve it in the diabetic animals (p > 0.05).

2. Sperm evaluation

The total sperm count was not significantly affected in the diabetic and sesame oil supplemented diabetic rats compared to the normal animals (p > 0.05). However, supplementation of the normal rats’ diet with 5% sesame oil significantly increased the total sperm count compared to the other groups (Table 1; p < 0.05). Diabetes significantly decreased the SPM (p < 0.05). Supplementation of the diet with 5% sesame oil improved the SPM in both the diabetic (p < 0.05) and normal animals (p < 0.05), while it was not statistically different in the diabetic 10% compared to the non-treated diabetic group (p > 0.05). Diabetes reduced the sperm vitality (p < 0.05) and 5% oil supplementation increased the percentage of live sperm compared with the non-treated diabetic rats (p < 0.05). The high oil supplementation diet reduced the live sperm percentage to a similar level as the non-supplemented diabetic rats (p > 0.05). The most obvious sperm abnormality was detached heads, which was significantly higher (p < 0.05) in the diabetic rats, and oil supplementation did not influence it (p < 0.05).

3. Testicular microstructure

Fig. 1 shows the micrographs of the testis sections of different groups. The mean spermatogonia number (per tubule) was significantly decreased by either diabetes or sesame oil supplementation (Table 2; p < 0.05). The oil supplementation had no beneficial effect on the spermatogonia number in diabetics (p > 0.05). The value of spermatocyte numbers per tubule was significantly decreased in the diabetics (p < 0.05) and sesame oil increased the cell counts to the level of the normal rats (p > 0.05). Inclusion of 5% sesame oil within the diet did not influence the number of spermatocytes per tubule compared to the non-treated normal animals (p > 0.05). The mean Sertoli cell count was not influenced by either diabetes or oil supplementation (p > 0.05). The mean Leydig cell count was significantly reduced in the diabetic rats and oil supplementation increased it in both the diabetic and non-diabetic rat testes (p < 0.05). The germ cell to Sertoli cell ratio was lower in the diabetic animals compared to the other groups (p < 0.03). Inclusion of 5% and 10% of sesame oil improved the ratio in the diabetic rats compared with the normal animals (p < 0.05).

4. Plasma estradiol, testosterone and glucose

The plasma estradiol concentration was not influenced by diabetes (p > 0.05). However, a tendency toward a non-significant decrease was observed in the plasma concentrations of the oil supplemented animals in both diabetic and non-diabetic rats (p = 0.07). The mean plasma testosterone concentration was not affected in the diabetic rats compared to the normal animals (p > 0.05). A high lev-
el of oil supplementation (10%) significantly increased the plasma testosterone concentrations in diabetic rats (Table 1; \( p < 0.05 \)). Enrichment of the diet with sesame oil, at any value, did not reduce the glucose concentration in diabetic rats (Table 1; \( p < 0.05 \)).

**DISCUSSION**

The dietary benefits of sesame oil and seeds have recently been reviewed by Namiki,23 who addressed the strong antioxidant properties of sesame oil and lignans such as sesamin and sesaminol, which are beneficial to
Table 2. The effects of sesame oil on the cellular composition of the testis in the male diabetic Wistar rats

|                      | Intact (n=10) | Diabetics (n=9) | Diabetics 5% oil (n=9) | Diabetics 10% oil (n=9) | Intact 5% oil (n=5) |
|----------------------|---------------|-----------------|------------------------|------------------------|-------------------|
| Spermatogonia†       | 64.1 ± 7.87   | 48.4 ± 3.20     | 47.2 ± 3.53            | 42.4 ± 4.49            | 42.2 ± 1.78       |
| Spermatocytes‡       | 78.2 ± 10.22  | 48.6 ± 6.04     | 59.1 ± 6.44            | 61.1 ± 4.02            | 70 ± 7.71        |
| Sertoli cells        | 11.2 ± 2.06   | 9.8 ± 0.42      | 7.8 ± 0.56             | 8.00 ± 0.68            | 10.7 ± 1.33      |
| Leydig cells         | 18.3 ± 3.75   | 9.1 ± 1.01      | 16.1 ± 3.36            | 31.8 ± 3.70            | 25.2 ± 0.87      |
| Germ cell/Sertoli cell ratio§ | 14.3 ± 1.2 | 10.5 ± 1.2 | 14.2 ± 1.22 | 14.0 ± 1.22 | 12.9 ± 1.22 |

*Values are presented as least square mean ± standard mean. † Include all different types of spermatogonia (A, intermediate and B) within tubule. ‡ Include all types of spermatocytes (primary and secondary) within tubule. § Calculated as (Spermatogonia + Spermatocyte)/Sertoli cell. †† Values with a common mark within rows are not significantly different (p > 0.05).
not influenced in the diabetic animals, another study reported the impact of the diabetes on the epididymal sperm. The difference may be due to different procedures for epididymal sperm collection. In the present study, 56 days after inducing diabetes, the sperm were retrieved from one side of the epididymides. We found that inclusion of 5% sesame oil in the diet of the normal rats increased the number of sperm cells significantly.

The impact of diabetes on sperm motility, viability, and abnormalities, in the present study, is in agreement with previous studies. Low-level oil supplementation (5%) in diabetics improved sperm motility and viability compared to diabetics without supplementation, which were significantly lower than in normal animals. Incorporation of 10% sesame oil within the diet of diabetics has no beneficial effect on sperm motility and viability. The concentration-dependent effect of sesame oil on the sperm parameters may be based on the nature of sesame oil. Sesame oil, despite its potent antioxidative properties, is rich in polyunsaturated fatty acids. It can be assumed that in chronic metabolic diseases such as diabetes, the extensive disturbances in lipid and glucose metabolism may reduce the efficacy of oil-based antioxidative agents, which was manifested in the present study by the lack of a decline in plasma glucose concentrations.

A significant decrease in the total number of spermatogonia and spermatocytes was observed in the diabetic animals and enrichment of the diet with sesame not only did not improve the spermatogonia numbers in the diabetics, but also significantly reduced their counts in normal animals. However, sesame oil increased depleted numbers of spermatocytes in the seminiferous tubules of the diabetic animals. In the present study, the Sertoli cell number/tubule was not affected. Diabetes decreased the Leydig cell count, and incorporation of sesame oil significantly increased their count, especially with 10% supplementation. The germ cell to Sertoli cell ratio was significantly lower in the diabetics, but was improved by both levels of oil enrichment.

A non-significant decreasing trend in the plasma estradiol was observed in the present study, where oil was incorporated within the diet. Sesame oil, because of its phytoestrogenic components, may exert negative feedback on the hypothalamus-hypophysis-testis axis and contribute to a decreasing trend in endogenous estradiol levels. However, this finding coincided with a non-significant decreasing trend in the Sertoli cell numbers by including oil within the diet of normal and diabetic animals. The marked increase in the serum testosterone in the rats with oil-enriched diets in this study may correlate with the proliferation of the Leydig cell count. The depletion of Leydig cells may lead to lower testosterone concentrations in diabetics. Testosterone deficiency produces immature sperm by early sloughing of spermatids from the Sertoli cells. However, in the present study, the most notable abnormality of the epididymal sperm was detached heads rather than round spermatids (data not shown). Improving the ratio of germ cells to Sertoli cells, in the present study, coincided with an increased plasma concentration of testosterone and the percentage of sesame oil in the diet may confirm the regulatory effect of testosterone on the Sertoli germ cell adhesion mechanism.

CONCLUSIONS

In general, the results of the present study showed that incorporation of sesame oil into the diet may improve the reproductive parameters at the level of the testicular microstructures (germ cell to Sertoli cell ratio) and endocrine function (plasma testosterone concentration) without any beneficial effect on the epididymal sperm parameters in STZ-induced diabetic rats. Sesame oil supplementation was effective in improving reproductive parameters in normal rats as well.

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