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ANTIOXIDANT EFFECTS OF SESAME SEED OIL AND THEIR IMPACT IN IMPROVING MALE FERTILITY OF NORMAL AND DIABETIC RATS

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ABSTRACT

Great efforts have been made to identify an ideal herb with strong and effective anti-metabolic effects on male fertility. The purpose of the present study was to investigate the antioxidant effects of sesame seed oil and their impact on reproductive parameters of diabetic rats. **Materials and Methods:** Rats were divided into four groups. 1st normal group, 2nd normal rats supplemented with oil enriched diet, 3rd diabetic group, 4th diabetic rats supplemented with oil enriched diet for eight weeks. **Results:** Sesame oil increased testosterone, sperm number and motility in both normal and diabetic groups. The normal rats supplemented with oil showing elevation in glutathione peroxidase(GPx) and (GSH) while malondialdehyde (MDA)level was decreased. Superoxide dismutase, GSH and GPx were decreased in diabetic group, but were increased with oil supplementation compared to diabetic group. MDA level was elevated in diabetic group compared with normal group. On the other hand, sesame oil supplementation ameliorated MDA level compared to diabetic group. **Conclusions:** Sesame oil has powerful antioxidant activity, which reflected on improved testosterone level, sperm production and sperm motility in both normal and diabetic groups, but was not effective in reducing plasma glucose level in diabetic group.

KEYWORDS: Sesame seed; Testis; Sperm; Infertility; Diabetes mellitus; Antioxidant.

INTRODUCTION

Male infertility is caused by a broad variety of etiologies; therefore, many of approaches are needed to resolve this problem.[1] Infertility is one of the major health problem in the world, threatening about 10-15% of couples.[2]

Diabetes mellitus is usually accompanied by extensive disturbance in the metabolism of glucose and fatty acids.[3] The extensive impacts of lipid peroxidation in the testis and epididymal sperm of streptozotocin (STZ)-induced diabetic rats have been demonstrated previously.[4] Diabetic patients have been reported with oligospermia and disruption of spermatogenesis.[5] Accordingly, diabetic men usually have abnormal reproductive functions[6,7], manifested by impairment of sexual behavior[8], semen quality[9], ejaculation[10] and decreased sperm motility.[11]

Reproductive complications of diabetes usually undergo through two different mechanisms: endocrine neuropathies[12] and metabolic disturbances leading to oxidative stress.[13] High level of semen reactive oxygen species is considered as an important factor in male infertility.[14,38]

Sesame is one of the richest sources of lignans includingsesamin, episesamin, sesamolin and tocopherol, which are known to have health benefits as anti-tumorigenic, estrogenic and/or anti-estrogenic and antioxidant properties.[15] In addition, lignans have been shown to possess antihypertensive, hypolipidemicand anti-inflammatory properties.[17] Sesamin absorbed from gut and gains access, via portal vein, to liver where it metabolized to catechol that has strong antioxidant activity.[16]

Sesame seed has a high oil content (52%), protein (24%) and ash (5%).[18] Sesame oil enriched diet can improve physiological performance of quails.[19]

*Sesamumradiatum*leaves have found to improvethe testicular structures of normal adult males.[20] These effects of sesame leaves can be mediated through the antioxidative properties of their lignans.[21] Sesame oil is beneficial in improving the blood glucose, glycosylated hemoglobin, lipid peroxidation and antioxidant levels in STZ-induced diabetic rats.[21]

Sesame (*Sesamumindicum*) is one of the oldest cultivated plants in the world and belongs to the Pedaliaceae family.[22] In terms of phytochemistry, this plant has phenolic compounds (Phenols, Sterols, Flavonoids and lignans), non-protein amino acids, cyanogenic glucoside, alkaloids, polyunsaturated oil and lipids with multiple double bonds, glazes, phospholipids and E, B_1 and B_2 vitamins. In addition, minerals or trace elements such as

calcium, iron, magnesium, zinc, copper and phosphorus exist in this plant.[23] The lignans and phytoestrogenswhich exist in sesame were known to human from the beginning of civilization.[24] Phytoestrogens are phenolic compounds which are similar to hormones and nonsteroidal that derived from estrogen of sesame and it was found in sesame seed.[25]

Shittu[26] who evaluated the effect of fluid extract of sesame leaves on epididymal spermatocyte reserves in adult rats, found that it increased the fertility.Also researchers, who evaluated the effects of leaves extract of this plant on the fertility of hypoglysemic rats, found that this extract improved parameters related to the testis and increasing the reproductive potential in mice.[27]

MATERIALS AND METHODES

1. Experimental design

This experimental study was carried out on forty adult male Wister rat weighing 190g. They were obtained from the National Research Centre, Cairo, Egypt. Rats were divided into four groups (10 in each). 1st one is normal control, 2nd is normal supplemented with 5%sesame oil enriched diet, 3rd is diabetic control group (streptozotocin induced diabetes) and finally, 4th group is diabetic supplemented with 5% sesame oil enriched diet. Diet supplementation continued for eight weeks. This period is sufficient to complete spermatogenesispathway in rats.[28]

2. 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. These animals were fed with basic diet with free access to tap water and kept under constant environmental conditions at room temperature (25±2c). 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.

Diabetes was induced by intraperitoneal (IP) injection of STZ, purchased from Sigma-Aldrich Chemie (Deisenhofen, Germany), dissolved in citric acid buffer (PH 4.2) at a dose level 30 mg/kg; body weight for three consecutive days and injected within 10 min of dissolution.[29] One week after induction, the concentration of blood glucose was measured and the rats with a glucose concentration greater than 200 mg/dl were classified as diabetic.

3. Plasma preparation and biochemical analysis

At the end of the experiment, the rats were fasted overnight, the animals were euthanized and blood samples were collected in EDTA-coated glass tubes, centrifuged at 3500 rpm for 15 minutes at –4ºC. Glucose, MDA, GSH, GPx, SOD and hormone assays were determined in separated plasma. Glucose was determined spectrophotometrically as described by Trinder.[30] MDA was determined spectrophotometrically as described by Jain and Janero.[31,32] GSH level in blood was determined according to the method described by Öktem.[33] SOD activity according Liu[34] and GPx activity by Kumar.[35] The plasma testosterone concentrationwas measured using enzyme-linked immunosorbent assay (ELISA; DRG Instruments GmbH, Marburg, Germany).

4. Body weightand blood collection

Rats body weights were measured every week with a digital scale and weights were recorded. After animals were anesthetized and incision made on the chest and abdomen; first, blood sample was taken from the heart and theirtestes were removed.

5. Testicular weight and volume

Both testes were carefully dissected and cleared from all surrounding fats. Testicular weight was measured with a sensitive scale and testicular volume was measured with water displacement in a 10 ml cylinder.

6. 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, 35~37ºC) 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 motility was estimatedby evaluating 4 fields of a sperm droplet under a cover-slip on a warm glass slide (35~37oC) under light microscopy (×40). All of the sperm evaluation procedures were carried out based on the World Health Organization manual for human sperm analysis[36] with some modifications.

RESULTS

1. Body weight and morphologic parameters

The diabetic animals showed a significant reduction in body weight compared to normal control group ($p < 0.001$). Sesame oil supplementation did not affect the body weight in normal ratsbut significantly increased the body weight in diabetic rats (Table 2; $p < 0.001$). Testis weight and volume did not differ significantlyamong the groups (Table 1; $p < 0.001$).

2. Plasma testosterone and glucose concentration

Sesame oil supplementation significantly increased the plasma testosterone concentrations in both normal and diabetic rats ($p < 0.001$). Enrichment of the diet with sesame oil did not affect the glucose concentration in both normal and diabetic rats (Table 2; $p < 0.001$).

3. Sperm evaluation

Sesame oil treatment significantly increased the total sperm count in both normal and diabetic rats compared to their respective control groups ($p < 0.001$). In the same context and similarly, sesame oil supplemented diet significantly counteracted diabetes induced decrease in

sperm motility and improved the sperm motility in normal control group as well (Table 1; p < 0.001).

4. Antioxidant activity

The normal rats supplemented with sesame oil exhibited significant increase inGPx (p<0.01) and GSH (p<0.001) levels, while MDA level was significantly decreased (p<0.01) when compared to the normal group (Table 3). The levels of SOD, GSH and GPx were significantly decreased in diabetic group, while MDA level was significantly increased when compared to the normal group (Table 3; p<0.001). However, sesame oil supplementation for diabetic rats significantly increased SOD, GSH and GPx levels when compared to the diabetic control group but MDA level was significantly decreased (Table 3; p<0.001).

Statisical Analysis

All obtained data were represented as mean ± SE. Differences between the mean value were statistically analyzed by using one way analysis of variance (ANOVA) utilizing computerized statistical program (InStat).

Table -1: Effect of sesame seed oil administration on testis weight and volume; and on sperm number and motility in both normal and diabetic rats.

	Normal	Sesame seed oil	Diabetic (Control)	Diabetic + Sesame seed oil
Testis weight (gm)	**0.151 ± 0.027**	**0.171 ± 0.013**	**0.128 ± 0.021**	**0.184 ± 0.009**
Testis volume (cm^3)	**5.54 ± 0.197**	**5.23 ± 0.205**	**4.80 ± 0.165**	**5.13 ± 0.153**
Sperm number ($x10^6$)	**55.3 ± 1.32**	**69.2 ± 1.59 ***	**46.6 ± 1.28 ***	**60.8 ± 1.42 ****
Sperm motility (%)	**53.9 ± 1.2**	**69.5 ± 1.19 ***	**42.3 ± 1.27 ***	**55.7 ± 2.24 ****

Results are expressed as mean ± S.E.
*Significantly different from normal group (p < 0.001).
**Significantly different from diabetic control group (p < 0.001).

Table -2: Effect of sesame seed oil administration on body weight, plasma testosterone and fasting plasma glucose in both normal and diabetic rats.

	Normal	Sesame seed oil	Diabetic (Control)	Diabetic + Sesame seed oil
Body weight (gm)	**196.7 ± 1.78**	**200.6 ± 1.31**	**169.0 ± 1.84 ***	**184.9 ± 1.70****
Testosterone (ng/ml)	**3.72 ± 0.24**	**6.77 ± 0.19 ***	**2.87 ± 0.23 ***	**3.67 ± 0.18 ****
Glucose (mg/dl)	**98.0 ± 1.29**	**100.3 ± 1.39**	**204.7 ± 1.41 ***	**200.3 ± 1.63**

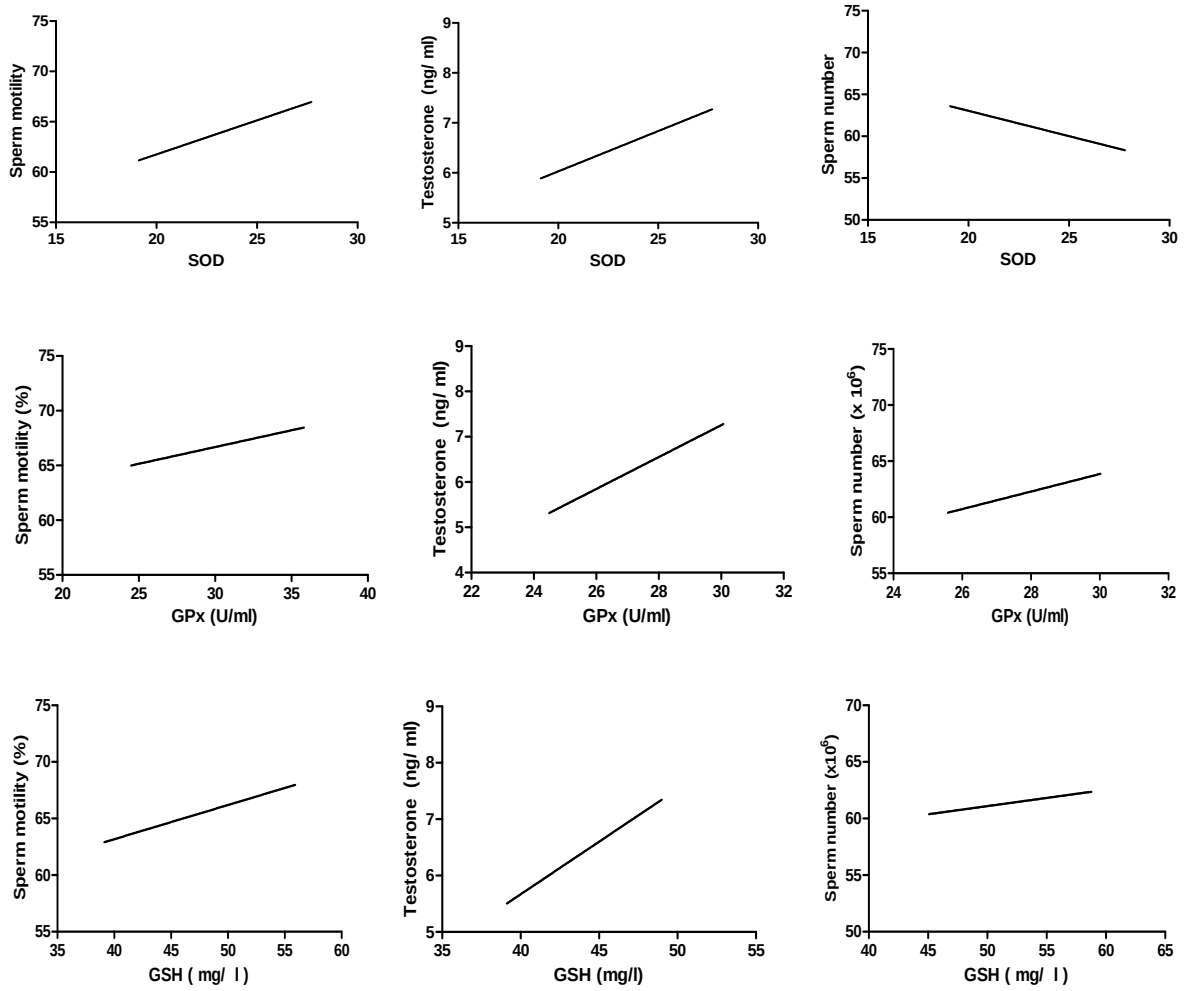
Results are expressed as mean ± S.E.
* Significantly different from normal group (p < 0.001).
**Significantly different from diabetic control group (p < 0.001).

Table -3: Effect of sesame seed oil administration on plasma SOD, GPx, MDA and GSH in both normal and diabetic rats.

	Normal	Sesame seed oil	Diabetic (Control)	Diabetic+Sesame seed oil
SOD (U/ml)	**28.8 ± 1.63**	**30.9 ± 1.47**	**16.9 ± 1.02***	**25.5 ± 0.79****
GPx (U/ml)	**33.9 ± 0.75**	**38.6 ± 0.89[a]**	**17.6 ± 0.88***	**37.1 ± 1.25****
MDA (nmol/l)	**49.6 ± 1.22**	**42.6 ± 1.23[a]**	**117.2 ± 0.78***	**61.6 ± 1.74****
GSH (mg /l)	**49.4 ± 1.39**	**58.5 ± 1.38 ***	**28.6 ± 1.31***	**45.6 ± 1.42****

Results are expressed as mean ± S.E.
a Significantly different from normal group (p < 0.01).
*Significantly different from normal group (p < 0.001).
**Significantly different from diabetic control group (p < 0.001).

In correlation analyses, SOD were positively correlated with sperm motility (r= 0.703, p=0.0001) and testosterone (r= 0.846, p=0.0001) but were negatively correlated with sperm number (r= -0.613, p=0.0001) in fig. (1). GPx were positively correlated with sperm motility, testosterone and sperm number (r= 0.414, r= 0.582, r= 0.442, p=0.0001) respectively, in fig. (2). GSH were positively correlated with sperm motility, testosterone and sperm number (r= 0.707, r= 0.638, r= 0.331, p=0.0001) respectively, in fig. (3).



DISCUSSION

In fact, diabetic men are susceptible to a variety of sexual disorders, including a decreased libido, impotence and infertility.[6,7] Lower pregnancy rates have been noticed among diabetics and raise the issue of the basic fertility potential ofdiabetic men. Analyses of diabetic men semen showed decreased sperm number, motility and abnormal morphology. It is noteworthy that, some diabetic men have normal semen parameters, however there is a higher level of damage to both nuclear and mitochondrial sperm DNA when compared to healthy controls.[6]

Beside altered glucose and lipid metabolism, oxidative stress is strongly implicated in pathogenesis of diabetes mellitus with overproduction of free radicals together with a decline in antioxidant defense mechanisms.[13]

Oxidative stress (OS) is strongly associated with maleinfertility. ROS levels are ranged from 25% to 40% in semen samples of infertile men. Thesesubstantial ROS might eventually trigger histological changes in seminiferous tubules[39], sperm motility and sperm count[40] which ultimately will induce male infertility.It should be noted that spermatozoa are particularly sensitiveto ROS toxicity because their plasma membranes mainly consist of polyunsaturated fatty acids and theircytoplasm contains low concentrations of scavenging enzymes. Oxidative stress induced plasma membrane damage of sperm cells may implicated in sperm dysfunction in patients with infertility.[13]

The present study revealed that diabetic rats exhibited reduced body weight, plasma testosterone and sperm count. This resultin agreement with a previous study, which reported weight loss in diabetics.[5] A deficiency of testosterone is associated with production of immature sperm.[38] In previous studies, an oil supplementation in diabetics improved sperm motility and viability compared to diabetics without supplementation.[7,37]

In the present study, diabetic rats showed a state of oxidative stress as evident by elevated plasma MDA level and reduced plasma SOD, GPx and GSH levels. This state of oxidative stress badly reflected on sperm count and motility.

Sesame is one of the richest dietary sources of lignin and phytoestrogens which were known to human from the beginning of civilization and they are mixed with human food because of having many benefits for health.[24] Phytoestrogens are phenolic compounds which are

structurally similar to hormones and nonsteroidal compounds.[25]

Also, sesame seed oilhasstrong antioxidant properties and lignanssuch as sesamin and sesaminol, which have dietary benefits tohumans. Moreover, due to phytoestrogenic properties of its lignans, the sesame seeds oil isbeneficial for menopausal women through their interaction with sex steroids.[41] The results of this study have clearly shown that the impact of diabetes on several reproductive parameters of male rats was mitigated by sesame seed oil supplementation in term of increased plasma testosterone concentration, sperm count and sperm motility.

However, sesame seed oil supplementation did not decreased the blood glucose levels of diabetic rats. But, it improved the sperm parameters in both normal animals and diabetic animals. An apparent tendency toward a decrease in plasma MDA were also detected in the oil-supplemented animals. These results in parallel with the other study of Zahra and his colleagues[42] who reported that sesame seed oil supplementation did not improve the glucose concentrations of diabetic rats. But, it improved the sperm parameters in normal animals. An apparent tendency toward a decrease in plasma MDA were also detected in the oil-supplemented animals. Lipid peroxidation decreased while the activities of GPX and SOD were increased.[43]

Sesame seed oil supplementation, in the present study, significantly attenuated diabetes induced body weight loss. This effect previously reported in studies concerned with the beneficial effects of some plant extracts on the body weight of diabetics.[44,45] The impact of diabetes on the metabolic profile of STZ-induced diabetes has shown a decrease in the fatty acid metabolism mediators within the liver.[46] On the other hand, in normal animals with normal metabolism, a sesame oil-enriched diet may contribute to providing more useful materials for animal growth, as has been observed in normal animals with this oil enrichment.

Moreover, in the present study the testis weightis slightly reduced in diabetic rats. This finding is in line with-theprevious studies that reported a decline in the testicularweight of diabetics.[47,48] Similarly, enrichment of normal animals' diet with sesame seed oil slightly increasedthe weight of the testis. This finding also in accordance with that of a previous report in which sesame leaf gavages increased the testis weight of normoglycemic rats.[27] *Sesamumradiatum* leaves improved the testicular structures of normo-glycemic adult males.[27] Sesame improved sperm count and motility and can be prescribed as an effective and safe method for male factor infertility.[14]

The inclusion of sesame seed oil in the diet of the normal rats increased the number of sperm cells significantly. This in agreement with previous study which reported that ingestion of sesame seed oil increased the sperm cells number.[42] 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. Sesame improved sperm count and motility and can be prescribed as an effective and safe method for male factor infertility.[14] Consumption of Sesame oil may enhance fertility.[49]

CONCLUSIONS

The results of the present study revealed that sesame seed oil supplemented diet exerted significant antioxidant effect in STZ-induced diabetes in male rats, an effect which positively reflected on the reproductive parameters (increased sperm number and motility) and on endocrine function (elevated plasma testosterone concentration). Also, Sesame seed oil supplementation was effective in improving reproductive parameters in normal rats as well.

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