





# The Protective Effects of *Aloe Vera* Gel Extract on the Sexual Complications Caused by Diabetes in Male Rats

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#### Abstract

**Introduction:** Diabetics usually suffer from chronic complications, including microvascular and macrovascular disorders. The capillaries supplying the sexual organs affect normal sexual functions. The erectile process has been shown to be impaired in diabetics. Vascular damage in diabetics may be associated with decreased testosterone production, sperm count, testicular weight, and seminiferous tubule diameter. In this study, we investigated the effects of Aloe vera gel extract (from Sistan and Baluchistan, Iran) on the male genital system in streptozocin-induced diabetic rats.

**Methods:** A total of 24 male Wistar rats were included in the study. Diabetes was induced in 12 rats by intraperitoneal injection of a single dose of streptozotocin (STZ). The rats were divided into four groups. The first and third groups received saline (NaCl) by gavage daily. The second and fourth groups received Aloe vera gel extract daily by gavage. Treatments were continued for 30 days. At the end of the treatment period, blood samples were taken and serum glucose and testosterone levels were measured by photometric methods. Histological examinations were performed on the prostate and testes.

**Results:** Mean weight index, serum levels of glucose and testosterone, mean sperm count, germinal epithelium (GE) thickness, and seminiferous tubule diameter improved significantly in the diabetes + Aloe vera group.

**Conclusion:** We concluded that consumption of Aloe vera gel extract improved sexual complications in diabetic rats.

Keywords: Type 1 diabetes, Aloe vera gel, Tissue, Sexual tissue, Sexual dysfunctions

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#### Introduction

Damage to blood vessels caused by high blood sugar in diabetics (especially type 1 diabetes) is the basis for their sexual dysfunction. Failure to continuously control blood sugar levels will eventually lead to this damage.<sup>1</sup> In addition to genetic susceptibility,<sup>2</sup> other factors such as inappropriate lifestyle, stress, and consumption of unhealthy foods appear to be important risk factors contributing to the worsening of symptoms. Treatment of these conditions is a challenge for the health care system due to the side effects of chemical medications.<sup>3</sup> Diabetics generally suffer from chronic complications, including microvascular and macrovascular disorders.<sup>4</sup> The main pathological mechanism leading to macrovascular complications is atherosclerosis, which leads to the narrowing of arterial walls in the body.<sup>5</sup> Structural disturbances in the cardiac arteries and capillaries supplying the sex organs impair normal sexual functions. It has been shown that function of genital smooth muscle cells and the erection process are disturbed in diabetics.<sup>6,7</sup> In these patients, there was a decrease in semen volume, sperm motility, and spermatogenesis, and a remarkable increase in cell death.<sup>8</sup> In males, the coagulating glands are located in the middle lobe of the prostate gland and



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secrete fructose- and protein-rich substances into the cavity of the seminal vesicles. In addition, enzymes such as transglutaminases are involved in semen coagulation, sperm motility, and placental abruption. However, all of these components may be affected in diabetics.<sup>8</sup>

Nitric oxide (NO) production is involved in muscle relaxation and increases blood flow to the male genitalia. NO is derived from the amino acid arginine by the collaboration between arginase (isoform 2) and nitric oxide synthase (NOS). Arginine is also converted to urea and glutamate by arginase (isoform 1). Interestingly, the reduction of insulin levels and increment of blood glucose levels and HbA1c lead to an imbalance in the activities of arginase 1,2 and NOS. It causes a decrease in the activity of NOS in the vascular endothelial cells and consequently a relaxation of the vessels as well as a decrease in the hyperemia and erection of the male genitals.9,10 Vascular damage in diabetics may be associated with decreased testosterone production and sperm count, loss of testicular weight and epididymal tubules, and decreased testicular tubule diameter.<sup>11</sup> Although diabetes is not a curable disease, it can be controlled by appropriate pharmaceutical measures. In addition to the use of fast-acting chemical drugs to lower blood glucose levels, herbal medicines with fewer side effects are increasingly being used. The cactuslike plant Aloe vera with more than 360 species belongs to the Liliaceae family and grows in hot and dry areas. Only four species from this plant family have nutritional value.12 In traditional medicine, a pale gel-like component of the grey-green leaves of Aloe vera is used to treat a wide range of ailments, including migraines, indigestion, and skin burns.<sup>13,14</sup> Oral administration of this gel extract has been shown to lower blood glucose levels in diabetic rats compared to conventional antidiabetic drugs.<sup>15</sup> This gel consists of about 99% water and the remaining 1% solid material consists of polysaccharides, glycoproteins, sterols, terpenes, and minerals.16

Acemannan is the main polysaccharide of Aloe vera extract and contains B-(1,4)-acetylated galactomannan linkages, which exhibit antioxidant, anti-inflammatory, anti-cancer, and macrophage-inducing activities. In fact, many medicinal properties of Aloe vera gel are attributed to the presence of acemannan. The concentration and molecular weight of this compound (biological functions) vary depending on the subspecies and geographical location of the plant.<sup>17</sup> In this study, we prepared the crude gel extract (containing polysaccharides, proteins, and minerals) of Aloe vera growing in Sistan and Baluchistan in Iran (a southeastern province with an arid climate) and investigated its effects on diabetes-related sexual disorders in rats.

# Materials and Methods Preparation of Aloe Vera Gel Extract

Aloe vera (Aloe barbadensis Mill) (identified by http://

www.theplantlist.org) was obtained from the Medicinal Plants Research Center of Zabol College, Iran, and identified by Dr. Jafar Valizadeh, a botanist working in the Medicinal Plants Research Center of Sistan and Baluchestan College, Zahedan, Iran. The leaves were cut into pieces of 70-90 cm long. After washing, the leaves were cut at the top and bottom with 5-cm-long incisions and opened lengthwise. Then, the gel was extracted. Afterwards, 3-4 g of the gel was mixed with a solution of distilled water and alcohol (ratio: 1:1). After 48 hours, the mixture was filtered through Whatman paper. Alcohol and water were removed with an extractor, and condensation was performed at 30-35°C in an incubator. The extract was dried in a freeze dryer (TRY Standard Series Freeze Dryer/Lyophilizer Model: TRY -1R-50, Erp code: 100000080), then weighed and finally stored in dark jars at 4°C. Aloe vera extract powder (380 mg) was mixed with 4.75 mL of distilled water. It was administered by gavage to rats at a dose of 380 mg/kg (under the lethal dose (LD50)).18

# Animal Preparation and Diabetes Induction

Twenty-four male Wistar rats weighing  $190 \pm 20$  g with a mean age of  $68 \pm 2$  days were taken from the animal house of Zabol University of Medical Sciences. The animals were maintained in plastic cages covered with sawdust. All ethical rules regarding animal welfare were followed.

Diabetes was induced in 12 rats by a single intraperitoneal injection (50 mg/kg) of streptozotocin (STZ) (Sigma Aldrich). Twenty-four hours after injection, blood glucose levels were measured with a glucometer (AlphaTRAK 2, 50 strips), and a value of 250 mg/dL or more was considered indicative of successful diabetes induction.

# *Experimental Design and Treatment with Aloe Vera Gel Extract*

Rats were divided into four groups (n=6 per group). The first group (i.e., the healthy control rats) received 380 mg/kg 0.9% saline (NaCl) daily by gavage. In the second group, the healthy rats received 380 mg/kg Aloe vera gel extract daily by gavage. The third group (diabetic animals) received 380 mg/kg 0.9% NaCl daily by gavage. Finally, in the fourth group (diabetes + Aloe gel extract treatment), the diabetic animals received 380 mg/kg Aloe gel extract daily by gavage. The treatments were continued for 30 days.

Sampling, Sperm Analysis, and Histological Assessments At the end of the intervention period, rats were anesthetized with ketamine and xylazine (Ket-A-Xyl<sup>\*</sup> 20 mL). Blood samples were collected. Sera were separated and stored at -20°C until the day of study. Serum glucose and testosterone levels were determined by ELISA methods (ZellBio.co). To assess sperm quality, the tail

of the epididymis was cut and placed in T6 medium (simple balanced salt solution T6+streptomycin). Sperm morphology, count, and motility were analyzed using a light microscope and compared between study groups.7 Sperm counts were calculated according to the method described by Oldereid. First, a sperm suspension was mounted on a Neubauer hemacytometer and the slide was placed in a humid environment for 1 hour. The sperms were counted in an appropriate number of squares of the Neubauer hemocytometer at 100×magnification.<sup>19</sup> Abnormally shaped spermatozoa were those with abnormalities in the head (large, small, or double head), neck (long or short neck), and tail (double tail).<sup>20</sup> Regarding motility, spermatozoa were classified as fast (high motility), slow (low motility), or immobile. The prostate and testes of rats were used to prepare tissue blocks for histological studies. Tissues were cut into 5 µm-thick sections with a microtome and stained with hematoxylin and eosin.<sup>21-23</sup> The slides were evaluated using a light microscope and OLYSIA software.

# **Statistical Analysis**

SPSS version 26.0 was used for statistical analysis. First, the Kolmogorov-Smirnov test was used to check the distribution of the data (normal vs. not normal). Then, parametric tests were used to analyze normally distributed variables, and nonparametric tests were applied for variables with non-normal distribution. In our study, we also used one-way analysis of variance (ANOVA) and Tukey post hoc test when appropriate. A *P* value of < 0.05 was considered statistically significant.

#### Results

# The Effect of Aloe Vera Extract on the Weight Index and Glucose Serum Level

Our findings showed a significant decrease in the mean weight index in diabetic rats compared to healthy rats. After the administration of Aloe vera extract in the diabetes + Aloe vera group, the relative weight index significantly improved  $(217.8 \pm 17.06 \text{ g})$  compared to the diabetes control group  $(195.6 \pm 5.98 \text{ g})$  (Figure 1A).

The serum glucose level in the diabetes + Aloe vera group  $(214.2 \pm 14.37 \text{ mg/dL})$  showed a significant

decrease compared to the diabetes group  $(528.8 \pm 27.41 \text{ mg/dL})$  (*P*<0.05) (Figure 1B).

# The Effect of Aloe Vera Extract on Serum Testosterone Level

Our results showed that the mean serum level of testosterone significantly increased in the diabetes + Aloe vera group  $(3.19\pm0.63 \text{ ng/dL})$  compared to the diabetes control group  $(2.32\pm0.44 \text{ ng/dL})$ . The healthy rats treated with Aloe vera extract showed a significant decrease in the mean serum level of testosterone  $(3.39\pm0.51 \text{ ng/dL})$  compared to the healthy control group  $(3.76\pm0.43 \text{ ng/dL})$  (*P*<0.05, Figure 2).

# The Effect of Aloe Vera Extract on the Counts of Sertoli Cells, Spermatogonia, and Leydig Cells

Our results showed that diabetes induction reduced the total number of Sertoli cells, Spermatogonia, and Leydig cells. On the other hand, the administration of Aloe vera extract significantly increased these cell counts (Figure 3A, 3B, and 3C).

The mean counts of spermatogonia (Figure 3A), Leydig (Figure 3B), and Sertoli (Figure 3C) cells significantly increased in the diabetes + Aloe vera group ( $84.8 \pm 3.51$ ,  $7.8 \pm 0.37$ , and  $1.6 \pm 0.2$  n/mm<sup>2</sup>, respectively) compared to the diabetes control group ( $78.4 \pm 4.2$ ,  $7.2 \pm 0.58$ , and  $1.2 \pm 0.2$  n/mm<sup>2</sup>, respectively) (P < 0.05 for all comparisons).

#### The Effect of Aloe Vera Extract on Sperm Morphology

In all of the study groups, we observed a number of abnormally-shaped sperms. There was no significant

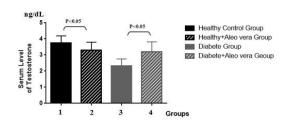
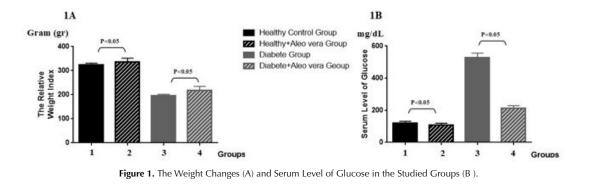


Figure 2. The Changes Serum Level of Testosterone Hormone in the Studied Groups.



difference between the groups (P > 0.05).

# The Effect of Aloe Vera Extract on Sperm Count

The mean sperm counts in the diabetic groups were significantly lower compared to the healthy groups. The administration of Aloe vera extract significantly increased the mean sperm count in the diabetes + Aloe vera group  $(169 \pm 6.1 \text{ n/mm}^2)$  compared to the diabetes control group  $(138.2 \pm 5.21 \text{ n/mm}^2)$  (*P*<0.05, Figure 4).

#### The Effect of Aloe Vera Extract on Sperm Motility

The percentage of immotile sperms in the healthy groups was significantly lower compared to the diabetic groups. The mean percentage of immotile sperms in the diabetes + Aloe vera group ( $68.2 \pm 8.42\%$ ) was significantly lower compared to the diabetes control group ( $82.8 \pm 3.54\%$ ) (P < 0.05, Figure 5A).

Similar results were obtained on the percentage of low-motile sperms, showing a significantly lower value in the diabetic compared to control rats (P < 0.05). The mean percentage of low-motile sperms was significantly lower in the diabetes + Aloe vera group ( $13.6 \pm 2.83\%$ ) compared to the diabetes control group ( $24.4 \pm 6.11\%$ ) (P < 0.05, Figure 5B).

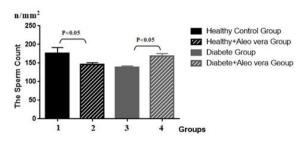
Regarding the percentage of highly-motile sperms, healthy rats revealed a significantly higher value compared to diabetic animals. The mean percentage of highly-motile sperms in the diabetes + Aloe vera group (7.4±2.51%) was significantly higher compared to the diabetes control group (3.6±1.12%) (P<0.05, Figure 5C).

# The Effect of Aloe Vera Extract on Seminiferous Tubule Diameter and Germinal Layer Thickness

The mean diameter of the seminiferous tubule in diabetic rats was lower than that of healthy animals. The mean diameter of the seminiferous tubule in the diabetes + Aloe vera group (255.06±6.22 µm) was significantly higher compared to the diabetes control group (229.45±6.22 µm) (P<0.05, Figure 6A). The germinal layer thickness in diabetic rats decreased compared to healthy animals, but this decline was insignificant. Although insignificantly, the mean thickness of the germinal layer was higher in the diabetes + Aloe vera group (83.71±3.31 µm) compared to the diabetes control group (51.8±2.6 µm) (P>0.05, Figure 6B).

## The Effect of Aloe Vera Extract on the Testicular Tissue

The histological analysis of rat testicular tissue showed that in general, the mean thickness of the germinal epithelium was lower in diabetic rats than in healthy animals. On the other hand, the internal diameter of the germinal tubule increased in diabetic rats while germline cells showed derangement and reduced thickness. The connective tissue surrounding seminiferous tubules was also enlarged (Figure 7B). Our results showed that the thickness of germinal epithelium improved in diabetic rats treated with Aloe vera extract and the inner diameter of germinal tubules decreased compared to the diabetic control group. Moreover, the arrangement and thickness of germline cells improved, and the connective tissue surrounding seminiferous tubules also reduced (Figure 7C).





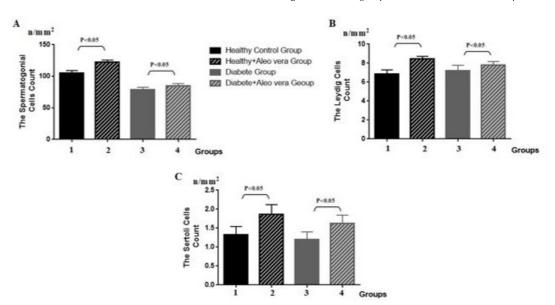


Figure 3. (A, B and C) The Changes Cell Counts of Spermatogonial, Leydig and Sertoli in the Studied Groups.

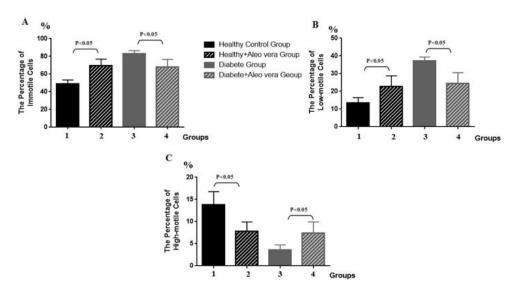


Figure 5. (A) The percentage of immotile sperms. (B) The percentage of low-motile sperms. (C) The percentage of highly-motile sperms.

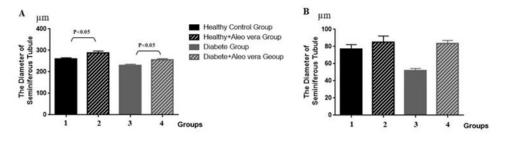


Figure 6. The mean Diameter of the Seminiferous Tubule (A) and the Mean Thickness of the Germline Layer (B) in the Studied Groups.

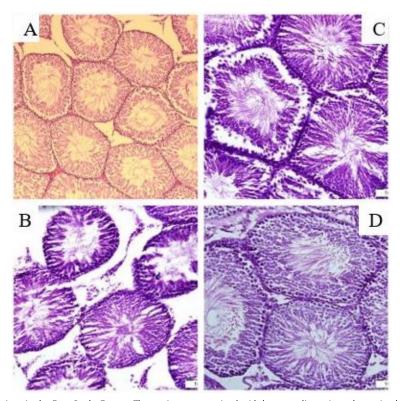


Figure 7. Testicular Tissue Sections in the Four Study Groups. The sections were stained with hematoxylin-eosin and examined at 2x magnification using an Olympus light microscope. Healthy Control Rats (A), Diabetic Rats (B), Diabetic Rats Treated with Aloe Vera Extract (C), and Healthy Rats Treated with Aloe Vera Extract (D)

## The Effect of Aloe Vera Extract on the Prostate Tissue

Our findings showed that in the diabetes+Aloe vera group, the mean epithelial thickness at 50-µm-length of the dorsal lobe of the prostate showed a significant increase compared to the diabetes control group ( $20 \pm 3.17$  vs.  $18 \pm 2.4$  µm, P < 0.05) and an insignificant decrease compared to the healthy control group ( $20 \pm 3.17$  vs.  $21 \pm 3.52$  µm, P > 0.05, Figure 8A).

In the diabetes + Aloe vera group, the mean diameter of alveoli in the dorsal lobe of the prostate showed a significant increase compared to the diabetes group ( $252\pm23.71$  vs.  $247\pm60.22$  µm, P<0.05) but an insignificant decrease compared to the healthy control group ( $252\pm23.71$  vs.  $296\pm59.03$  µm, P<0.05, Figure 8B).

The mean percentage of the scaffold parenchyma in

the dorsal prostate lobe in the diabetes + Aloe vera group ( $59\pm9.5\%$ ) was significantly higher compared to the diabetes ( $55\pm7.61\%$ ) and healthy ( $72\pm2.8\%$ ) control groups (P<0.05, Figure 8C).

At 50-µm-length of the dorsal region of the prostate, there was a significant difference in the mean number of secretory cells comparing the diabetes + Aloe vera group (9±1.64) with the diabetes (8±0.54) and healthy (10±1.3) control groups (P<0.05, Figure 8D).

The mean epithelial thickness in the diabetes + Aloe vera group  $(19\pm1.26 \ \mu\text{m})$  was significantly higher compared to the diabetes control group  $(16\pm1.26 \ \mu\text{m})$  but lower compared to the healthy control group  $(21\pm1.34 \ \mu\text{m})$  (*P*<0.05, Figure 9A). In addition, the mean diameter of alveoli in the diabetes + Aloe vera group  $(252\pm23.71)$ 

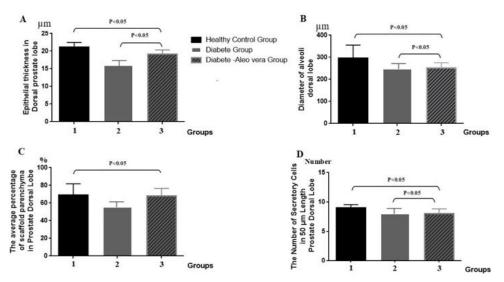
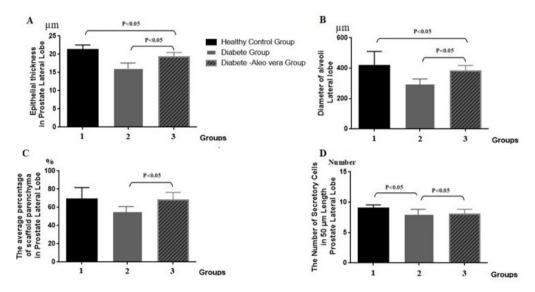


Figure 8. Comparison of the parameters measured in the dorsal prostate lobe [(A) Epithelial thickness, (B) Diameter of alveoli, (C) The percentage of scaffold parenchyma, (D) The number of secretory cells in 50 µm length] between the study group; diabetes +Aloe vera, diabetes control, and healthy.



**Figure 9.** Comparison of the parameters in the lateral prostate lobe [(A) Epithelial thickness, (B) Diameter of alveoli, (C) The percentage of scaffold parenchyma, (D) The number of secretory cells in 50 µm length] between the study group; diabetes +Aloe vera, diabetes control, and healthy.

was significantly higher compared to the diabetes control group ( $247 \pm 60.22 \ \mu$ m, *P*<0.05) but lower compared to the healthy control group ( $296 \pm 59.03 \ \mu$ m, *P*<0.05) (Figure 9B).

The mean percentage of parenchymal scaffold thickness was significantly higher in the diabetes + Aloe vera group than in the diabetes group ( $68 \pm 8.41\%$  vs  $65 \pm 6.68\%$ , P < 0.05) but lower than in the healthy control group ( $68 \pm 8.41\%$  vs  $69 \pm 12.65\%$ , P < 0.05) (Figure 9C).

At 50-µm-length of the dorsal region of the prostate, there was a significant difference in the mean number of secretory cells comparing the diabetes + Aloe vera group ( $8 \pm 0.83$ ) with the diabetes control ( $8 \pm 0.79$ ) and healthy control ( $9 \pm 0.79$ ) groups (P < 0.05 for both comparisons, Figure 9D).

an increase in connective tissue and a decrease in epithelial height in the lateral and dorsal parts of the prostate were observed in the diabetic control group (Figure 10A). In the experimental rats treated with Aloe vera, a decrease in connective tissue (black arrows) and an increase in epithelial height (blue arrows) were observed (Figure 10B).

#### Discussion

Today, the consumption of herbal medicines, due to the harmful impacts of chemical drugs, has increased for treating diabetes and metabolic syndrome and improving patients' quality of life. For example, Aloe vera is believed to reduce the complications of diabetes and improve the indices of metabolic syndrome.<sup>3</sup> In this study, we investigated the effects of treatment with Aloe vera extract on metabolic indices of diabetes and some reproductive parameters in male diabetic rats. The evaluation of weight index showed that there was a significant improvement in the diabetes + Aloe vera group compared to the other groups. In this regard, Choi et al reported in their clinical study that the administration of Aloe vera extract reduced body weight and improved insulin sensitivity in prediabetic subjects.<sup>24</sup>

The gonadosomatic index is a value expressing the ratio of testicular weight to body weight. Oyeyemi and Fayomi reported a decrease in the gonadosomatic index in diabetic rats, and administration of Aloe vera extract increased this index in a dose-dependent manner.<sup>25</sup> Misawa et al reported that the oral administration of the active compounds of Aloe vera in obese diabetic rats caused a significant reduction in abdominal fat.<sup>26</sup> Our study showed that oral administration of Aloe vera extract significantly decreased blood glucose levels in diabetic rats. In agreement with our observation, Misawa et al also showed that oral administration of active ingredients of Aloe vera significantly lowered blood glucose levels.<sup>26</sup>

Ozsoy et al and Choi et al showed that blood glucose levels in diabetic rats decreased significantly after treatment with Aloe vera extract.<sup>24,27</sup>

Our findings showed that the serum level of testosterone was significantly lower in the diabetic groups than in the healthy groups. Administration of Aloe vera extract in diabetic rats improved this condition and increased serum levels of testosterone compared with the control group. Consistent with our results, Estakhr and Javdan in 2011 showed that administration of Aloe vera extract in male rats improved spermatogenesis as well as serum levels of testosterone.<sup>28</sup>

Similarly, Christijanti et al reported that administration of the homogenized extract of Aloe vera skin increased serum levels of testosterone in STZ-induced diabetic rats.<sup>29</sup>

Asgharzade et al investigated the effects of Aloe vera gel extract on serum levels of testosterone in healthy mice and, in contrast to our results, reported that serum testosterone levels decreased compared to the control group. Nevertheless, iNOS enzyme activity and NO production increased in this group, resulting in Leydig cell dysfunction, apoptosis of sperm-producing cells, and infertility.<sup>30</sup> Shahraki et al confirmed, in agreement with our results, that treatment with Aloe vera gel extract significantly reduced serum levels of testosterone in healthy mice.<sup>31</sup>

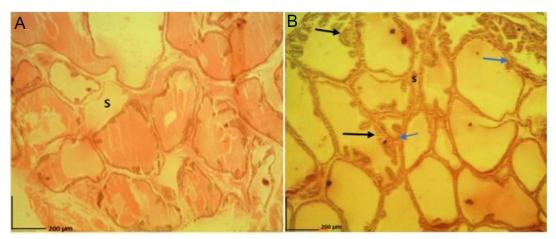


Figure 10. Longitudinal-transverse incision from the lateral dorsal prostate gland of diabetic rats (4× H&E). An increase in scaffolding was visible in the diabetic group compared to other groups.

Our results showed that diabetes caused apoptosis in Sertoli, spermatogonia, and Leydig cells and decreased their numbers and that administration of Aloe vera gel extract significantly reversed these effects. Since the proliferation of Sertoli cells is regulated by the hypothalamic-pituitary axis (GnRH-FSH), it is possible that Aloe vera gel extract may indirectly affect the number of Sertoli cells through this axis, resulting in an increase in the number of spermatogonia and Leydig cells.<sup>32</sup> Leydig cells are the primary source of testosterone,<sup>33</sup> so the increase in testosterone level in the diabetes and Aloe vera treatment group might be related to the pleiotropic effects of Aloe vera extract on Leydig cells. This study did not examine the serum level of NO, but previous studies have shown an increased NO level in diabetic patients, which correlates with a decrease in the number of Leydig cells in these patients.<sup>30</sup> The increase in serum testosterone levels in the diabetes+Aloe vera treatment group compared to the diabetic control group may be related to the antioxidant function of vitamins A, B, C, and E present in aloe vera extract. These vitamins decrease NO synthesis and prevent apoptosis in Sertoli, Leydig, and spermatogonia cells.

We observed an increase in high-motility spermatozoa and a decrease in immotile and low-motility spermatozoa in diabetic rats treated with Aloe vera gel extract compared to the other groups. This could be related to the antioxidant effect of the Aloe vera gel extract. It has been reported that an increase in the peroxidation of the unsaturated lipids of the cell membrane of sperm in diabetic patients negatively affects sperm motility.<sup>34,35</sup> Therefore, the antioxidant properties of Aloe vera may inhibit unsaturated lipid peroxidation and improve sperm motility. Shahraki et al, in agreement with our results, reported that the administration of Aloe vera extract in healthy rats increased sperm count and sperm motility and improved fertility compared to control groups. <sup>31,36</sup>

Behmanesh et al also reported that treatment with Aloe vera extract increased the number of spermatocytes, spermatogonia, and spermatids in the seminiferous tubule of rats, which correlated with the antioxidant properties of the extract.<sup>37</sup>

In addition, Christijanti et al confirmed that oral administration of Aloe vera skin extract in rats with STZ-induced type 1 diabetes increased sperm count and sperm motility.<sup>29</sup>

In contrast to our results, Oyewopo et al reported that administration of Aloe vera extract at doses of 70 and 100 mg/kg (but not 30 mg/kg) for 57 days significantly reduced sperm count, sperm motility, and testicular weight in rats.<sup>38</sup>

It has been reported that the diameter of the seminiferous tubules is reduced in diabetics.<sup>35</sup> In our study, the diameter of the seminiferous tubules significantly decreased in diabetic rats, but the administration of Aloe

vera gel extract compensated for this phenomenon. The increase in the diameter of the seminiferous tubules is probably related to the anti-apoptosis effect of the Aloe vera gel extract.<sup>31</sup>

In our study, a non-significant decrease in the thickness of the germinal layer in the seminiferous tubule was observed in the diabetic control group compared to the healthy control group. On the other hand, the thickness of the germinal layer increased insignificantly in the diabetic group treated with Aloe vera compared to the diabetic control group. There is controversy about the positive or negative effects of Aloe vera extract on sperm-producing cells and sperm motility.<sup>28,39</sup> We did not find any study that investigated the effects of the plant extract on GE thickness in the seminiferous tubule. Therefore, the increase in GE thickness observed in diabetic rats treated with Aloe vera extract requires further investigation. In 2016, Jalili et al studied the protective effect of genistein on fertility parameters in male mice and reported an increase in GE thickness in the seminiferous tubule, which correlated with an increase in reproductive activity and cell growth. Exposure to oxidants and drugs releases mitochondrial cytochrome C into the cytoplasm of spermatozoa, which induces apoptosis in germinal cells and reduces thickness of germinal epithelium. It has been shown that ingestion of genistein reverses these events.<sup>34</sup> Therefore, the extract of Aloe vera gel could act in a similar way as genistein. In addition, the epithelial cell thickness, alveolar diameter, percentage of parenchymal scaffold, and number of secretory cells at 50-µm length of the dorsal lobe of the prostate were examined in the present study. Epithelial thickness decreased insignificantly in the diabetic group compared with the diabetes + Aloe vera group and the healthy control group. The alveolar diameter in the dorsal lobe of the prostate in diabetes and Aloe vera groups decreased significantly compared with the healthy control group and the diabetic control group. The parenchymal scaffold of the dorsal lobe also showed a significant increase in the diabetic rats treated with either Aloe vera extract or saline (i.e., control) compared with the healthy control rats. In addition, the number of secretory cells at 50-µm length of the dorsal lobe increased significantly in the diabetes + Aloe vera group compared with the diabetic control group but decreased significantly compared with the healthy control group. There are few studies on the effects of plant extracts on the histological structure of the prostate in diabetic patients. Testosterone is a vital growth factor for the epithelial layer of the dorsal lobe, and insufficient testosterone levels can cause damage to this cell layer.<sup>40</sup> In this study, the thickness of this epithelial layer increased in diabetic rats treated with Aloe vera extract, reflecting the beneficial effects of this plant on male reproductive function.

# Conclusion

In this study, we showed that consumption of Aloe vera gel extract ameliorated sexual complications in diabetic rats. Testes size, serum level of testosterone, sperm motility, sperm count, and spermatogonia, Leydig, and Sertoli cell counts improved in the diabetic + Aloe vera group compared to the diabetic group. Aloe vera extract negatively affects sperm motility but not cell longevity. Analysis of tissue sections of the testes and prostate indicated a beneficial effect of Aloe vera gel extract in diabetic rats. Based on these findings, it can be concluded that Aloe vera gel extract can compensate for impotence in male diabetics.

# **Authors' Contribution**

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#### **Competing Interests**

The authors have no conflict of interests to declare.

#### **Ethical Approval**

This study was approved by the Research Council of Zabol University of Medical Sciences and the Research Ethics Committee with the code of IR.ZBMU.REC.1397.034.

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