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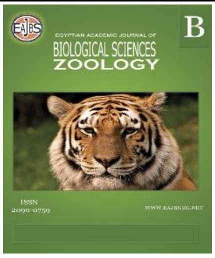

Effects of Celery Leaf Aqueous Extract on Fertility and Liver Enzyme in Diabetic Male Rats

Abdulrahim Aljamal[1], Mahmoud Al Shawabkeh[2], Mariam Abualbasal[3], Taha Alqadi[4], Fatima-Azzahra Delmani[5], and Alia Khwaldeh[6]

[1]Department of Biological Sciences, Al al-Bayt University, Jordan.
[2]Department of Basic Dental Sciences, Faculty of Dentistry, Applied Science Private University, Amman 19328, Jordan.
[3]Department of Medical Analysis, Al al-Bayt University, Jordan.
[4]Department of Biology, Adham University College, Umm-AL-Qura University, Saudi Arabia.
[5]Department of science. Faculty of Science. Jarash University. Amman-irbit Highway.
[6]Faculty of Allied Medical Sciences, Department of Medical Laboratory Sciences, Jadara University, Irbid.

*** E-mail** : aljamalzpu@yahoo.com

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ABSTRACT

The presented study examined the potential effects of celery leaf extract on spermatogenesis in diabetic male rats. **Methodology**: Twenty-four male rats total were used in the study; they were split into three groups of eight rats each: Control group: Every day, one milliliter of distilled water was given to normal rats. Group with diabetes: Every day, 1 ml of distilled water was also given to diabetic rats. Group receiving celery extract: For thirty days in a row, diabetic rats received a daily dose of 200 mg/kg of celery extract. **Results:** Sperm count and seminiferous tubule diameter were significantly higher in the group receiving 200 mg/kg of celery extract compared to the control group. Testicular Volume and Organ Weights: Additionally, the treated group showed a significant increase in the vas deferens, epididymis, and testis testicular volumes and weights. Lipid profile and glucose: Celery extract had a notable impact on glucose and triglyceride levels in diabetic rats. Liver enzymes: The extract markedly raised the levels of the liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT). **Conclusion**: These findings imply that celery juice extract may be advantageous for a number of diabetic male rat parameters, including spermatogenesis, liver enzymes, lipid profiles, glucose concentrations, and reproductive parameters. This suggests that celery may help to improve male fertility and prevent complications from diabetes. Nevertheless, additional investigation is required to clarify the fundamental processes accountable for these impacts and validate the findings.

INTRODUCTION

One of the annual or perennial plants that grow throughout Europe and the tropical and subtropical parts of Africa and Asia is celery (Apium graveolens L), a member of the Apiaceae family. (Gauri *et al.,* 2015). A major global health concern is diabetes mellitus, a chronic metabolic disease marked by increased blood sugar levels.. The incidence of diabetes continues to increase, reaching epidemic proportions and affecting millions of lives worldwide1. Its debilitating complications, including fertility, cardiovascular disease, neuropathy, kidney disease, and liver disease, highlight the urgent need for effective diabetes treatment and management strategies (Wu H *et al.,* 2016). As pharmaceutical interventions play a central role in diabetes care, increasing attention is being paid to exploring complementary and alternative approaches, especially those involving compounds that naturally have potential antidiabetic properties.

Among the natural remedies studied, celery (Apium graveolens) emerged as a topic of interest. Celery, a commonly consumed vegetable, is rich in various bioactive compounds, such as flavonoids, polyphenols and phthalides, which have shown great promise in regulating glucose metabolism and improving blood glucose levels. insulin sensitivity. The antidiabetic effect of celery juice extract was tested on diabetic rats. This is because intraperitoneal administration of the extract causes changes in lipid composition (Roghani *et al.,* 2007).

Because of these qualities, people are more interested in the possible therapeutic benefits of celery, especially with regard to infertility. (Mansouri *et al.,* 2014).

One such natural source of interest is celery leaves, which are high in phytochemicals and may provide health benefits. The anti-inflammatory, antioxidant and anti-diabetic effects of celery leaves are widely known. They contain many bioactive substances, such as flavonoids, polyphenols and essential oils, which can influence many aspects of metabolic and hormonal control (Kooti *et al.,* 2014).

Therefore, scientists began to study how celery leaves affect fertility, especially in male diabetic rats. Serum total cholesterol and low-density lipoprotein concentrations have been shown in studies to be modified by celery extract. (LDL), while increasing triglyceride levels in the liver

According to Mansi *et al.* (2009), this effect is achieved by reducing hepatic triacylglycerol lipase activity in humans. With this study, we hope to add to the knowledge of the potential role of celery in the adjunctive treatment of diabetes. We are specifically testing the effects of celery leaf extract on diabetic male rats, a well-known animal model for diabetes research.Through the analysis of blood sugar, body weight, and biochemical markers, scientists were able to ascertain the effects of celery extract on several physiological processes, including spermatogenesis and alterations in the male rat testicles. (Madkour NK, 2014 and Kooti *et al.,* 2014).

MATERIALS AND METHODS

Plant Material:

Celery (Apium graveolens L.) leaves were obtained from a local market in Mafraq, Jordan.

Preparation of Aqueous Extract:

Celery leaves are cleaned, dried and ground into powder. Mixing 200 g of powder with 1 L of distilled water and boiling the mixture for two hours at 60°C. The aqueous extract was filtered, concentrated and then freeze-dried into powder.

Induction of Diabetes:

Rats were given a single intraperitoneal injection of 60 mg/kg body weight of streptozotocin (STZ) diluted in citrate buffer (pH 4.5) to develop diabetes.

Experimental Design:

For the study, twenty-four adult male Wistar rats weighing between 170 and 220 g at eight weeks of age were employed. The rats were acquired from Applied Sciences Private University's animal breeding facility. For all operations involving animals and their care, the Research Ethics Committee of Al al-Bayt University's ethical norms were adhered to. Rats were kept in normal cages with a light/dark cycle of 12 hours and a temperature of 22 ± 2°C. Throughout the trial, they were given unrestricted access to regular food and drink. The rats were housed in their new homes for a full day before the experiment.

The rats were split into three groups at random, with eight rats apiece, and each group was given its prescribed treatment orally for a 30-day period.

1. Control group: Every day, 1 ml of distilled water was given to normal rats.
2. Diabetes group: Every day, 1 ml of distilled water was also given to the diabetic rats.
3. Group of celery extracts every day, 200 mg/kg of celery extract was administered to diabetic rats.

To make celery extract, the extract's calculated weight was diluted with distilled water to yield a final volume of 1 ml per rat. The day following the final celery extract administration, the rats were put to sleep. The testicles, scrotum, and abdomen are carefully cut vertically. Reproductive structures are accessible through this incision. After that, the connected epididymal ducts are surgically divided. Testicular length, width, and volume were measured precisely in order to assess any possible effects of celery extract.

Turning to epididymal sperm counts, the epididymis, part of the male reproductive system, was meticulously isolated. From this isolated part, spermatozoa (spermatocytes) are separated from the seminiferous tubules and then homogenized to ensure uniform distribution. The resulting sperm suspension was diluted appropriately with physiological saline. Then a technique called sperm counting was performed. This requires placing a sample of diluted sperm solution into a hemocytometer, a specialized chamber. Using an optical microscope, the hemocytometer allows for accurate counting of the number of sperm present in the sample. Sperm count and potential reproductive health can both be determined from this count.

Assessment of Spermatogenesis:

At the conclusion of the treatment period, rats in each group were given ketamine/xylazine anesthesia, and their testes were taken out and weighed. To assess spermatogenesis, the diameters of spermatocytes, spermatids, and spermatids were measured using a light microscope and a calibrated eyepiece. Seminiferous tubule diameter and sperm count were measured..

Assessment of Testis Volume and Organ Weights:

The testicles' volume was computed using the water displacement method. Testicular weight, epididymal tail weight, and vas deferens weight were all noted.

Assessment of Glucose and Lipid Profiles:

At the completion of the trial, rats were given blood samples to test their levels of triglycerides, cholesterol, and glucose. A typical blood glucose meter was used to measure the blood glucose levels during the fast. An enzymatic colorimetric technique was used to measure the concentrations of triglycerides and cholesterol in the serum.

Assessment of Liver Enzymes:

Commercial assay kits were used to measure the concentrations of alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) in serum.

Statistical Analysis:

Version 20.0 of the SPSS software was used to analyze the data. The standard error of the mean (SEM) is represented as the mean ±. One-way analysis of variance (ANOVA) was used to determine statistical significance, and Tukey's post-hoc test was used for multiple comparisons. P values were deemed statistically significant if they were less than 0.05.

RESULTS

A 200 mg/kg dose of celery juice extract was found to have a significant impact on spermatogenesis in male diabetic rats.Table (1), illustrates that there was a statistically significant increase in the diameter of seminiferous tubules, spermatocyte count, and sperm count (epididymal cauda) when compared to the control group (p 0.001). Furthermore, sperm count increased significantly ($p<0.05$) in the 200 mg/kg celery extract group as compared to the control group. Furthermore, there was a statistically significant ($p<0.05$) increase in the mean diameter of seminiferous tubules.

Table 1: Effects of celery aqueous extract on spermatogenesis in diabetic rats.

Groups	Spermatids (mm 2)	Spermatocytes (mm 2)	Spermatogonia (mm 2)	Spermatozoids (10 7)	Seminiferous tubules diameter (µm)
(control)	14.66±0.03	13.51±0.03	12.57±0.02	4.12±0.03	0.34±0.004
Diabetic rats	12.6±0.17	*12.28±0.28	**10.72±0.2	**2±0.17	**0.21±0.001
Diabetic rats fed Celery (200mg/k g)	*15.1±0.02	*14.23±0.05	**13.68±0.22	**4.55±0.17	**0.38±0.006

*p≤0.05, **p <0.001.

Table (2), presents the results of a 30-day treatment with the same celery extract on testicular volume and organ weight. Testicular volume was found to increase significantly ($p<0.001$) in the group treated with 200 mg/kg celery extract as opposed to the control group. In addition, the weight of the vas deferens, epididymis, and testicles all increases. Interestingly, there was a statistically significant increase in epididymal weight ($p<0.05$) in the group treated with 200 mg/kg celery extract when compared to the control group.

Table 2: The impact of celery aqueous extract on the organ weights and testis volume in diabetic rats.

Groups	Testis volume (mm 3 10 -3)	Testis (mg)	Cauda epididymis (mg)	Vas deferens (mg)
(control)	12.86±1.9	1502.4±4.98	459.4±4.64	92±0.29
Diabetic rats	**9.89±1.6	1210±5	298.4±4.64	75.5±55.17
Diabetic Rats fed Celery (200mg/k g)	**13.77±7.5	1610±3.79	*548.2±6.28	96.7±2.9

*p≤0.05, **p <0.001.

Overall, these findings imply that the aqueous extract from celery leaves improves spermatogenesis and reproductive parameters in male diabetic rats. Table (3), shows significant drops in glucose and triglyceride levels at $p<0.001$. Furthermore, Table (4), shows significant drops in liver enzymes, ASL, and ALT at $p<0.001$. These findings suggest that celery may help men with diabetes become more fertile, and they also highlight the need for more investigation and study in this field.

Table 3: Lipid profile levels in diabetic rats following ingestion of celery aqueous extract.

Groups	Glucose (mg/dl)	Cholesterol (mg/dl)	Triglycerides (mg/dl)
(control)	104.7 ±2.92a	62.23 ±2.7	76.56 ±0.62
Diabetic rats	211.13	90.77	166.4
Diabetic rats fed Celery (200mg/k g)	**140.6±0.134	**87.6±2.55	**102.3±0.21

*p≤0.05, **p <0.001.

Table 4: Liver enzyme levels in diabetic rats following ingestion of celery aqueous extract.

Groups	AST (U/L)	ALT (U/L)	ALP. (U/L)
(control)	25.26±0.24	12.5± 0.596	40.38±0.618
Diabetic rats	49.4	25.65	80.49
Diabetic rats fed Celery (200mg/k g)	**33.268±0.219	**15.4±0.416	**45.58±0.163

*p≤0.05, **p <0.001.

DISCUSSION

Our research offers important new information about the possible impacts of celery extract on spermatogenesis and reproductive characteristics in male diabetic rats. Due to their accessibility, lower toxicity, fewer side effects, and affordability, herbal medicines are becoming more and more well-liked as chemical drug substitutes (Miean *et al.*, 2001).

Our study's results, which compared the experimental groups to the control group after celery extract administration, were consistent with this theory. According to our findings, oral administration of 200 mg/kg of celery extract to male diabetic rats for 30 days significantly increased the diameter of the testicular tubules, spermatozoa, spermatocytes, sperm count, and seminiferous tubules.

These findings are in line with conventional wisdom regarding celery extract's potential to enhance men's erotic abilities. Given that sex hormones are known to affect genital weight, the observed increase in testicular weight and size suggests an increase in the number of cells in the testicles, which may be related to the regulation of sex hormone concentrations (Juan *et al.*, 2005; Soliman *et al.*, 2020). Pituitary gland stimulation by celery extract can result in elevated secretion of sex hormones, which can then impact testicular and epididymal function (Tasdighi *et al.*, 2012). Celery extract's possible effects on reproductive function are further supported by elevated epididymal weight at the highest extract dose and increased sperm count in the epididymis.

The inconsistent results reported in the literature about celery extract's impact on male reproductive hormones could be attributed to variations in the solubility profiles of its constituents as well as dose-dependent effects. Depending on the method of administration and the precise concentration of the compound, the complex composition of celery extract may affect the reproductive system in different ways (Modaresi *et al.*, 2012). The potential of celery extract is highlighted by the observed defense of testicular tissue against the toxic effects of sodium valproate, which can be attributed to the antioxidant properties of celery and its apigenin content (Hamza and Amin, 2007).

Moreover, the decrease in elevated liver enzymes (AST, ALT, and ALP) in diabetic rats, as shown in Table (4), demonstrates the hepatoprotective potential of celery extract. These findings are in line with earlier research showing celery can shield the liver from oxidative stress and inflammation (Jun Yan *et al.*, 2022 and Turner *et al.*, 2021).

Consequently, our research offers proof of the possible advantages of celery extract for spermatogenesis and reproductive characteristics in male diabetic rats. More research is necessary to determine the best dosages and deeper mechanistic understandings for prospective therapeutic applications in human fertility and reproductive health. The potential advantages of celery extract for diabetic rats are further demonstrated by **Table 3's** results, which show a decrease in triglyceride and glucose levels two substances that are commonly elevated in diabetes. The extract's less noticeable effect on cholesterol levels is in line with other studies that have shown how celery's antioxidant and anti-inflammatory qualities have antidiabetic and lipid-lowering effects (Zhao *et al.,* 2021and Ingallina *et al.,* 2020).

Finally, our research indicates that celery extract may have a beneficial effect on the reproductive characteristics and metabolic state of diabetic rats. The numerous health benefits of celery are highlighted by these observed effects, which call for more research into the plant's underlying mechanisms and possible uses in therapeutics and human health.

Conflict of Interest:

There are no disclosed conflicts of interest by the writers.

Ethical Approval:

The guidelines of our animal ethics committee, which was established in compliance with the globally recognized standards for the use and care of laboratory animals, were followed in these experiments.

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Data Accessibility:

Upon request, the corresponding author will provide the data supporting the study's conclusions.

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