Effects of Colocynth (Citrullus colocynthis) Pulp on Serum Levels of Testosterone and Changes in Reproductive Organs in Streptozotocin-Induced Diabetic Rats

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Original Article

Abstract

Introduction: Investigating the effects of colocynth pulp on levels of testosterone and changes in the reproductive system organs in streptozotocin-induced diabetic rats.

Methods: In this study, 32 Wistar rats were divided into four groups of normal (N), normal+colocynth pulp (N+C), diabetic control (D), and diabetic+colocynth pulp (D+C). Groups N and D received orally 2 mL normal saline for two weeks, and groups N+C and D+C received orally 10 mg/kg colocynth pulp for two weeks. Diabetes was induced in rats through intraperitoneal injection of 65 mg/kg streptozotocin (STZ).

Results: Group D showed a significant increase in glucose levels compared with Group N (P<0.0001), and testosterone levels, body weight, and reproductive organs weight ratio of group D decreased significantly compared with Group N (P<0.0001). In addition, a significant reduction in glucose level (P<0.01) and a significant increase in testosterone level and reproductive organs weight ratio (P<0.01) were observed in Group D+C in comparison to Group D.

Conclusion: This study showed that consumption of 10 mg/kg colocynth for two weeks relatively improved glucose and testosterone levels as well as reproductive system damage in streptozotocin-induced diabetes in rats.

Key words: Diabetes – Streptozotocin – Testosterone

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Introduction:

Diabetes mellitus is a heterogeneous metabolic disorder which is characterized by altered metabolism of carbohydrates, lipids, and proteins (5). Diabetes leads to hyperglycemia and increased production of free radicals, resulting in oxidative stress in different tissues (15). Oxidative stress induced by advanced glycation end products (AGEs) is one of the complications of diabetes. AGEs are intermediates of reactive species production and can damage different tissues, including reproductive system (26). Diabetes exerts harmful effects on the reproductive system in patients and diabetic animals (3,20,22). Diabetes mellitus is known to cause male infertility,
impotence, retro-ejaculation, hypogonadism, etc. (12). It also induces molecular changes resulting in alterations in the quality and performance of sperms. Impaired reproductive system in diabetics may result from changes in hypothalamic-pituitary-gonadal axis (11). These changes are mostly the result of decreased insulin secretion or resistance to insulin (13). Furthermore, testosterone replacement cannot modify reproductive behavior to normal state, while insulin replacement improves the effects of diabetes on reproductive system (24). The reason for low testosterone in diabetics is not fully understood. Cao and et al. showed that the antioxidant defense system in Leydig cells involves in development of oxidative stress and increased oxidative damage. The researchers also suggest that increased oxidative stress may contribute to age-related defects in testosterone secretion (8). Other researchers have shown that reactive species modulate the function of mature rats Leydig cells at psychological conditions through a variety of functions such as decreasing the activity of steroidogenic enzymes and increasing oxidative stress and apoptosis (10). The use of medicinal plants is increasing given the numerous side effects of synthetic anti-hyperglycemic drugs. As a member of Cucurbitaceae family, colocynth commonly known as bitter apple is one of these herbs. It is a tropical plant and is grown in many Arabic countries and widely in other parts of the world. In traditional medicine, this herb is used to treat constipation, diabetes, edema, fever, leukemia, jaundice, bacterial infections, etc. (18,25).

The present study has evaluated the effects of colocynth pulp on levels of glucose, testosterone, and weight changes in the reproductive system of streptozotocin-induced diabetic rats.

**Methods:**

In this experimental study, dried colocynth was purchased from grocery and its pulp was separated from seeds and skin, the isolated pulp was then ground, and the obtained powder was kept in a cool, dry place.

To induce diabetes in rats, 65 mg/kg streptozotocin (STZ) purchased from Sigma Company was dissolved in cold normal saline and injected intraperitoneally. Those rats with fasting glucose levels of above 300 mg/dL after 72 hours were considered diabetic. In this study, 32 Wistar rats weighing 270-230g were randomly divided into four 8-member groups:

- Group 1 or control group (N) received 2 mL normal saline per day through gavage;
- Group 2 (C+N) received 10 mg/kg/day colocynth pulp powder dissolved in 2 mL normal saline; Group 3 or diabetic control group (D) received 2 mL normal saline per day; and Group 4 or diabetic treatment group (C+D) received 10 mg/kg/day colocynth pulp powder dissolved in 2 mL normal saline.

After two weeks, the rats were anesthetized by CO2 and beheaded by guillotine. Their blood was then collected and centrifuged after 20 minutes at laboratory air, and the serum was separated and kept at -20°C. Testosterone assay was performed using the kit of Darman Kav Company.

The obtained data were analyzed with SPSS and the mean data of different groups with ANOVA (One-way ANOVA) and Tukey test. Final results were reported as mean±SEM, and p-values of less than 0.05 were considered significant.

**Results:**

**Glucose**

The effect of colocynth pulp on serum glucose is depicted in Figure 1. In comparison with Groups N and N+C, Group D had a significant increase (P<0.0001) and Group D+C had a significant decrease (P<0.01). Group D+C showed a significant reduction compared with Group D (P<0.01).

![Figure 1. Effect of Oral Consumption of Colocynth Pulp on Serum Levels of Glucose](http://example.com/figure1.png)
Effect of Colocynth Pulp on Serum Levels of Testosterone

Fereshteh Ostevan, et al

Each column represents the Mean ± ESM, n=8.
*Significant difference compared with Groups N+C and N (P<0.01).
**Significant difference compared with Groups N+C and N (P<0.0001).
§§Significant difference compared with Groups D+C and D (P<0.01).

Testosterone
The effect of colocynth pulp on serum testosterone is depicted in Figure 2. In comparison with Group N, Group D had a significant decrease (P<0.0001) and Groups N+C and D+C had a significant decrease (P<0.05). Group D+C showed a significant increase compared with the diabetic group (P<0.05).

Body weight
The effect of colocynth pulp on body weight is depicted in Figure 3. In comparison with Group N, Groups D and D+C had a significant decrease (P<0.0001). There was also a significant decrease in Groups D and D+C compared with Group N (P<0.05).

Testicular weight ratio
The effect of colocynth pulp on changes in testicular weight to body weight is depicted in Figure 4. Groups D, N+C, and D+C had a significant decrease compared with Group N (P<0.05). There was also a significant decrease compared with Groups D and N+C (P<0.01).

Epididymis weight ratio
The effect of colocynth pulp on changes in epididymis weight to body weight in the studied groups is depicted in Figure 5. Group D had a significant decrease compared with Group N (P<0.0001). There was also a significant increase...
in Group D+C (P<0.01) and Group N+C (P<0.0001) compared with Group D.

Seminal vesicle weight ratio
The effect of colocynth pulp on changes in seminal vesicle weight to body weight in the studied groups is depicted in Figure 7. Group D had a significant decrease (P<0.0001) and Group N+C had a significant increase (P<0.01) compared with Group N. There was also a significant decrease in Group D+C compared with Group N+C (P<0.05).

Prostate weight ratio
The effect of colocynth pulp on changes in prostate weight to body weight in the studied groups is depicted in Figure 8. Group D (P<0.0001) and Group N+C (P<0.05) had a significant decrease compared with Group N. There was also a significant increase in Group N+C compared with Group D (P<0.0001). The weight ratio was higher in Group D+C than Group D, but this increase was insignificant.
The study also found that levels of testosterone and weight of sexual organs was increased compared to the diabetic group. Increase in testosterone levels and the weight of testis, epididymis, and vas deferens was significant, while increase in the weight of gonads was not significant compared to the diabetic group. Therefore, according to the results of this study and previous studies, it is suggested that colocynth exerts hypoglycemic effects with its glycosidic compounds, steroids, saponosids, and terpenoides.
through increasing glucose consumption and secretion of insulin via restoring the damaged beta cells of pancreas.

Increased levels of insulin prevent oxidative stress caused by increased levels of glucose, and hence increase testosterone levels and reduce the developed reproductive damage resulted from increased glucose in diabetics. Since insulin directly affects the hypothalamic-pituitary-gonadal (HPG) axis (2), it is suggested that increase in insulin in the treated diabetic rats and elimination of insulin effect on the HPG result in increased testosterone levels and reduced effects of insulin and testosterone deficiency on sexual organs.

As a general conclusion, it can be stated that administration of colocynth pulp for two weeks has favorable effects on blood glucose and reproductive complications from diabetes, and these effects arise from specific compounds of this plant. It is advised to prolong the period of treatment to achieve better results.

References:


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اثرات پالپ هندوانه ابوجهل (Citrullus colocynthis) بر سطح سرمی تستوسترون و تغییرات ارگانهای تولید سیستم مثلی رتهای دیابتی شده به واسطه استرپتوزوسین

چکیده
مقدمه: بررسی اثرات پالپ هندوانه ابوجهل بر سطح تستوسترون و تغییرات ارگانهای سیستم مثلی رتهای دیابتی شده به واسطه استرپتوزوسین

روش کار: در این مطالعه 90 موش صحرایی نژاد ویستار به تصادف به چهار گروه تقسیم شدند. گروه نرمال (N)، گروه نرمال+ پالپ هندوانه ابوجهل (N+C)، گروه کنترل دیابتی (D)، و گروه دیابتی + پالپ هندوانه ابوجهل (D+C). گروه N و D به مدت دو هفته 2ml نرمال سالین را به صورت دهانی دریافت کرده و گروههای N+C و D+C به مدت دو هفته 10mg/kg.b.w پالپ هندوانه ابوجهل را به صورت دهانی دریافت کرده و به مدت دو هفته 21/2mg/kg.b.w استرپتوزوسین (STZ) به صورت داخلی تزریق شد.

نتایج: سطح گلوکز گروه D افزایش معنی‌داری 2221/2P<0/01 را نسبت به گروه N و میزان تستوسترون، وزن بدن و نسبت وزنی اندامهای تولید مثلی گروه D نسبت به گروه N یافت کرد. گروه D+C نیز کاهش گلوکز و افزایش میزان تستوسترون و اندامهای تولید مثلی نسبت به گروه D نشان داد.

نتیجه‌گیری: این بررسی نشان داد که مصرف 10mg/kg.b.w پالپ هندوانه ابوجهل روبروی دیابت نوزه را بهبودی نسبی در سطح گلوکز و تستوسترون و آسیب سیستم تولید مثلی ناشی از استرپتوزوسین می‌دهد.

کلیدواژه‌ها: دیابت، استرپتوزوسین، تستوسترون