Research Article

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Hypolipidemic Effects of *Eryngium Caucasicum* Leaves Extract on Rats with Induced Diabetes Mellitus

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Abstract

This research aimed to assess the hypolipidemic effects of an extract from *Eryngium caucasicum* in a Rat model of Type 2 Diabetes Mellitus produced by Streptozotocin. Forty adult male Wistar rats were divided into five groups, with a total of eight rats in each: (1) healthy control rats, (2) diabetic rats with no diabetes, (3) diabetic rats given insulin, (4) diabetic rats given 200 mg/kg orally for 30 days of *Eryngium caucasicum* extract, and (5) diabetic rats given 300 mg/kg orally for 30 days. Injecting Nicotinamide and Streptozotocin intraperitoneally caused diabetes. Fasting blood sugar, hepatic enzymes, and lipid profiles were determined from blood samples taken after the trial. The levels of HDL were increased significantly in G3, G4, and G5 compared to G2. The insulin group and the group given 300 mg/kg of *Eryngium caucasicum* substantially reduced LDL cholesterol compared to the G2. It should be mentioned that the diabetic control group had higher TC compared to the healthy control group after rat diabetes induction ($P = 0.020$). Compared to the G2, G3 treated with insulin and groups treated with extract at dosages of 200 as well as 300 mg/kg body weight had a substantially lower TC ($P < 0.01$). Serum TG was improved when insulin and *Eryngium caucasicum* extract were administered at 200 and 300 mg/kg dosages, respectively ($P < 0.05$). Serum ALT and AST levels were shown to be elevated after STZ diabetes induction as compared to the G1. Even though diabetic rats' ALT and AST levels were enhanced by insulin and all 2 plant trial dosages, 200 and 300 mg/kg. In summary, our findings suggest that the antidiabetic, hypolipidemic, and hepato-protective properties of *Eryngium caucasicum*, when administered to an animal model of Type 2 diabetes mellitus, may vary with dosage.

Keywords: *Eryngium caucasicum*, STZ, Diabetes, Liver function and Hypolipidemia.

التأثيرات الخافضة للدهون لنبات *Eryngium caucasicum* على الجرذان المصابة بمرض السكري المستحث

يهدف هذا البحث إلى تقييم التأثيرات الخافضة للدهون من مستخلص نبات Eryngium caucasicum في نموذج الفئران المصابة بمرض السكري من النوع 2 المنتج بواسطة الستربتوزوتوسين. تم تقسيم اربعين ذكرًا بالغًا من الجرذان إلى خمس مجموعات، بإجمالي ثمانية فئران في كل مجموعة: (1) فئران سليمة، (2) فئران مصابة بمرض السكري، (3) فئران مصابة بمرض السكري تم إعطاؤها الأنسولين، (4) فئران مصابة بمرض السكري تم إعطاؤها 200 مجم / كجم عن طريق الفم لمدة 30 يومًا من مستخلص نبات Eryngium caucasicum، و(5) فئران مصابة بمرض السكري تم إعطاؤها 300 مجم / كجم عن طريق الفم لمدة 30 يومًا. أدى حقن الستربتوزوتوسين داخل البريتون إلى الإصابة بمرض السكري. تم تحديد نسبة السكر في الدم خلال فترة الصيام، والإنزيمات الكبدية، ومستويات الدهون من عينات الدم المأخوذة بعد التجربة. ارتفعت مستويات HDL بشكل ملحوظ في G3 وG4 وG5 مقارنة بـ G2. أظهرت مجموعة الأنسولين والمجموعة التي أعطيت 300 مجم / كجم من E. caucasicum انخفاضًا كبيرًا في كوليسترول LDL مقارنة بـ G2. ومن الجدير بالذكر أن مجموعة السيطرة في مرض السكري كان لديها TC أعلى مقارنة بمجموعة التحكم الصحية بعد استحداث مرض السكري لدى الجرذان ($P = 0.020$). عند المقارنة بـ G2، كان لدى G3 المعالجة بالأنسولين والمجموعات المعالجة بالمستخلص بجرعات 200 بالإضافة إلى 300 مجم / كجم من وزن الجسم TC أقل بكثير ($P < 0.01$). لوحظ ان هناك تحسن في مستوى ال TG في المصل عند إعطاء الأنسولين ومستخلص E. caucasicum بجرعات 200 و 300 مجم / كجم على التوالي ($P < 0.05$). أظهرت مستويات ALT و AST في المصل ارتفاعًا بعد استحداث مرض السكري STZ مقارنة بـ G1. على الرغم من أن مستويات ALT وAST لدى الجرذان المصابة بمرض السكري قد تعززت بواسطة الأنسولين وجميع جرعات التجارب النباتية، 200 و300 مجم/كجم. نستنتج إلى أن لمستخلص E. caucasicum خصائص مضادة لمرض السكري وخافضة الدهون وحماية الكبد، عند إعطائها لنموذج حيواني لمرض السكري من النوع 2، وقد تختلف النتائج مع اختلاف الجرعة.

Introduction:

Hyperglycemia that does not go away, whether from insulin resistance or decreased secretion, is a hallmark of Diabetes mellitus (DM), a complex chronic disease with several aetiologies (1). One of the most prevalent endocrine disorders, DM has lately reached epidemic proportions on a worldwide scale. According to the World Health Organisation, 333 million people, or 6.3% of the global population, will be living with diabetes by 2030 (2,3). More people have type 2 diabetes (T2DM) (4). With a global healthcare budget ranging from 7 to 13 percent, DM poses a significant challenge to healthcare systems worldwide (5, 6). Patients with diabetes are more likely to die or have serious problems due to the long-term effects of hyperglycemia, which include vascular disorders, retinopathy, neuropathy, and nephropathy (7). The development of atherosclerosis and cardiovascular problems is thought to be significantly facilitated by DM-related aberrant lipid metabolism.(8) There is mounting evidence that inflammation plays a role in the development of type 2 diabetes, insulin resistance, and the vascular problems associated with diabetes (9). Inflammation may be exacerbated by hyperglycemia and elevated free fatty acids (FFA) because they trigger glucose utilization and oxidative phosphorylation alterations (10,11). Adipose tissue, pancreatic islets, and vascular cells are all invaded by macrophages in this environment, which triggers a pro-inflammatory characteristic (12). The release of active interleukin (IL-1β) is increased and oxidative stress is exerted by both glucose and lipotoxicity (10,11). The production of several cytokines in diabetes β-cells, adipose tissues, as well as blood vessels is how IL-1β in situ enhances inflammation (13). Theoretically, reducing inflammation may halt the development of diabetes mellitus (DM) and associated vascular consequences.(14)

Several diabetic medications have been developed, but their negative side effects, such as gastrointestinal distress, peripheral edema, as well as hypoglycemia, have increased the need for safer alternatives (15). Herbal remedies for type 2 diabetes are gaining popularity due to their cheap cost, increased safety, and perceived efficacy (16). An estimated one thousand herbal treatments are now in use to combat DM (17). Plants' biological benefits in treating DM may be due to their chemical makeup. Flavonoids, terpenoids, phenolic compounds, and other components with effects on reducing fasting blood glucose (FBS).(18,19)

Among the Apiaceae (Umbelliferae) family of genera, Eryngium is both the biggest and most taxonomically complicated. In the Americas, Australia, North Africa, and Eurasia, you may find more than 250 species of Eryngium L. (20,21). Countries in the Middle East, such as Iran and Turkey, produce *Eryngium caucasicum*, also known as Eryngo (22). This extract has several traditional uses in northern Iran, including in pickles and other condiments (23). Many medicinal applications for Apiaceae have been documented, including those of stimulant, diuretic, expectorant, stone inhibitor, diuretic, and anthelmintic (24). As a treatment for edema, sinusitis, urinary tract infections, inflammations, and other inflammatory illnesses, it has a long history of use in traditional Turkish medicine (21). In addition to its diuretic, lenitive, and appetizer properties, *Eryngium caucasicum* has a history of usage as a generative power enhancer (25, 26). Reports have shown that the leaves of *Eryngium caucasicum* exhibit antihypoxic, antioxidant, free radical scavenging, as well as reno-protective properties (23, 27, 28). Other varieties of *Eryngium* grown in Turkey have also had their anti-inflammatory effects studied

in living organisms. There was a high concentration of recorded activities in the aerial portions and roots (29). The genus *Eryngium* contains several bioactive chemicals, including terpenoids, triterpenoids, flavonoids, coumarins, and acetylenes (30), the majority of which are phenolic compounds.

This investigation was done to know the Hypolipidemic effects of *Eryngium caucasicum* on rats with induced diabetes mellitus

Materials and Methods:

For this experiment, we used electric grinders to crush and mill fresh leaves that had been dried in the shade. After 72 hours of storage at room temperature, 300 g of powdered *E. caucasicum* leaves were dissolved in 1.2 L of a 70:30 combination of distilled water and ethanol to make the hydroalcoholic extract. Next, the mixture was filtered using Whatman No. 1 filter paper and then centrifuged at 3500 rpm for 20 minutes. We used a rotating evaporator to do the condensation. Finally, the liquid was drained out and allowed to dry at 37 °C. were given orally, the semi-solid bulk was refrigerated.

Diabetes induction:

To initiate the process of producing type 2 diabetes, a single intraperitoneal (IP) injection of a mixture of normal saline, distilled water, and NA (120 mg/kg) was administered. Additionally, a single intraperitoneal injection of 55 mg/kg of STZ, dissolved in citrate buffer, was administered after 15 minutes. The induction was performed after the rats had starved the night before. By testing FBS 72 hours after injecting NA-STZ, the progression of T2DM was assessed. Diabetic status was deemed to exist when FBS levels exceeded 250 mg/dL. Experiment animals were culled if their serum glucose levels were too low.

Design of the study:

The following was done with forty mature male rats: eight rats in each of five groups:

G1, rats in good health were given 0.5 mL/kg of normal saline orally.
G2: diabetic rats that did not receive any medication were given 0.5 mL/kg of normal saline orally.

G3: rats with diabetes who received the gold standard treatment for diabetes, insulin.
G4: rats with diabetes given 200 mg/kg of hydro-alcoholic *E. caucasicum* extract
G5: water-alcoholized *E. caucasicum* extract given orally to diabetic rats at 300 mg/kg.

To estimate biochemical tests, blood samples were drawn via heart puncture to separate the serum. These biochemicals include AST, ALT, TG, TC, HDL, and LDL. These kits were purchased from Biolabo company, these methods were done according to manufacturer instructions.

Statistical analysis was done by using SPSS version 23.

Results and Discussion

As shown in Table 1, the levels of HDL were increased significantly in G3,G4, and G5 as compared with G2. The insulin group and the group given 300 mg/kg of *E. caucasicum* had a substantial reduction in LDL cholesterol compared to the G2. It should be mentioned that the diabetic control group had higher TC compared to the healthy control group after rat diabetes induction ($P = 0.020$). When compared to the G2, G3 treated with insulin and groups treated with extract at dosages of 200 as well as 300 mg/kg had a substantially lower TC ($P < 0.01$). Serum TG was improved when insulin and *E. caucasicum* extract were administered at 200 and 300 mg/kg dosages, respectively ($P < 0.05$). Serum ALT and AST levels were shown

to be elevated after STZ diabetes induction as compared to the G1. Even though diabetic rats' ALT and AST levels were enhanced by insulin and all 2 plant trial dosages, 200 and 300 mg/kg (Table 1).

Table 1. Liver function and lipid profile in studied groups

	G1	G2	G3	G4	G5
LDL (mg/dL)	21.37 ± 1.13c	30.01 ± 4.78a	19.86 ± 2.33c	24.04 ± 3.54b	21.99 ± 3.68c
HDL (mg/dL)	51.48 ± 2.86a	32.96 ± 1.87c	39.04 ± 3.59b	39.99 ± 5.27b	48.98 ± 3.08a
TC (mg/dL)	59.04 ± 5.76c	73.19 ± 7.67a	58.09 ± 5.06c	64.24 ± 6.38b	59.37 ± 2.47c
TG (mg/dL)	37.50 ± 9.43b	46.14 ± 24.16a	38.83 ± 2.71b	39.28 ± 4.63b	37.71 ± 4.28b
ALT (U/L)	46.87 ± 4.60c	78.21 ± 4.54a	53.28 ± 1.86b	45.57 ± 5.62c	46.13 ± 7.42c
AST (U/L)	116.20 ± 3.52d	158.11 ± 6.37a	128.71 ± 6.29c	137.43 ± 8.43b	119.05 ± 9.21d

Among the many organs profoundly impacted by diabetes mellitus is the liver, which is critically important for insulin production (31,32). Damage to the liver cells in type 2 diabetes is characterized by an increase in ALT and AST levels in the blood (33). Serum levels of liver enzymes were likewise much higher in the diabetes group than in the control group in our study. As a protective mechanism against cellular and tissue damage, diabetes conditions are thought to cause ALT and AST activity to reverse towards near normal levels (34,35).

As a result of its hepato-protective actions, the *E. caucasicum* extract significantly reduced AST and ALT levels in the diabetic groups that were treated. All dosages increased ALT, however, only the highest dose improved AST. One explanation for *E. caucasicum* extract's reno-protective properties is its free radical scavenging capabilities (36). There were hepato-protective properties seen in other species of the Eryngium family as well. The presence of significant phenolic components in *E. caucasicum*. extract shows protective effects on tricyclazole-induced hepatotoxicity, according to one research in particular (37). It is proposed that *E. caucasicum* extract has an antioxidant effect. When a person has diabetes, their lipoprotein metabolism becomes imbalanced due to reduced lipoprotein lipase activity (38,39). Conversely, an increase in LDL formation and hepatic triglyceride synthesis are both stimulated by free fatty acid inflow (40). There has been a report of an increase in the expression of fatty acid synthase and sterol regulatory element-binding protein-1 in rats with STZ diabetes (41). The two dosage of *E. caucasicum* reduced blood levels of LDL, TC, and TG. There was increase of HDL in G3, G4 and G5 groups when compared with G1. Both the lowest and highest dosages of TC were effective. In dyslipidemia, the likely pathways involve increasing the activity of cholesterol-7-alpha-hydroxylase, an enzyme that changes cholesterol into bile acids; decreasing the activity of HMG-CoA reductases; and preventing the intestinal absorption of cholesterol as a result of complex formation with substances like glycosides and saponins (42,43). Moreover, insulin-regulated alterations in lipolysis and an uptick in insulin secretion

(44). Saponins have been shown to enhance lipid metabolism, which in turn leads to a decrease and excretion of plasma cholesterol (45, 46). Lipid profiles in diabetic rats may be improved by different species of *Eryngium*, according to previous research (47).

Conclusion:

Our findings suggest that the antidiabetic, hypolipidemic, and hepato-protective properties of *E. caucasicum*, when administered to an animal model of type 2 diabetes mellitus, may vary with dosage.

Conflict of Interest:

The author declares that there was no conflict of interest.

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