ORIGINAL ARTICLE

The Effect of Teucrium Polium Boiled Extract in Diabetic Rats

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ABSTRACT

OBJECTIVE: In traditional medicaments, Teucrium Polium is used as anti-fungal, antibacterial, anti-inflammatory and antidiabetic. Modern researches have shown that use of T. polium in vitro leads to decrease in fatty acids. To confirm the anti-diabetic evidences of Teucrium polium this survey was done to evaluate the effect of boiled aqueous extract of T. polium on serum lipids, body weight and glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and Creatinine (CRT) in diabetic male rats.

MATERIALS AND METHODS: 20 male rats became diabetic by intraperitoneal injection of streptozotocin (60 mg/kg). The animals were divided randomly into two groups. The aerial parts of Teucrium polium was powdered, drenched and boiled. The experimental diabetic groups received this boiled extract (2% and 4%) freely for two weeks but the control group received tap water. Liver enzymes and biochemical parameters (cholesterol, triglyceride, glucose, alanine transaminase, aspartate transaminase, alkaline phosphatase, urea and Uric Acid) were measured by kinetic (Enzymatic) and colorimetric methods.

RESULTS: Our results showed that 4% dose of T. polium can decrease serum glucose and triglyceride significantly ($P < 0.05$), but cholesterol, urea, U Acid, ALT, AST and CRT were not significant between the test and control groups after using T. polium. 2% concentration of T. polium does not have any effect except on body weight.

CONCLUSION: Although the aqueous extract of Teucrium polium has hypoglycemic properties and can improve body weight in experimental animals, it seems that it does not have any effect on other factors and is not suitable as an alternative treatment.

KEYWORDS: Teucrium Polium, Diabetes, Rat.

INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder resulting from a defect in insulin secretion, insulin action or both (1). Recent estimates indicate that 200 million people are globally suffering from diabetes, making it the most common serious metabolic disorder worldwide (2). Several synthetic oral hypoglycemic agents are used in treatment of diabetic patients, which may produce some undesirable side effects (3). Since medicinal plants are frequently considered to be safer than synthetic drugs, herbal remedies and dietary traditions, play an effective role in attenuating metabolic disorders (4). Phenolic coumarins derived from the plant materials

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(fruits and vegetables) might play a key role as dietary antioxidants (5). The traditional medications demonstrated a clear horizon in treatment of diabetic patients and provided a guideline for investigation in this field (6). Teucrium polium L. is a member of 300 species in the genus Teucrium and mainly is found in the Mediterranean and Western Irano-Turanian sphere (7). Teucrium polium L. has long been recognized in folk medicine in the treatment of many pathophysiological implications, such as gastrointestinal disorders, inflammations, diabetes and rheumatism (8). Several researches have shown that this plan has hypotensive (9), anti-inflammatory (10,11), hypoglycemic (10,12,13), antispasmodic (14,15), antibacterial and antipyretic (16) activities. Various compounds such as iridoids, flavonoids and cirsiliols are characterized in T. polium by phytochemical analyses (11,17). Intra-peritoneal (ip) injection of T. polium extract could decrease blood glucose in rats after 4 and 24 hours (18). Intra-esophageal administration of T. polium aqueous extract, after 24 h, resulted in a significant decrease in the serum glucose level, in streptozocin-induced diabetic rats, which reached those of the normoglycemic animals in 8 days (19). Oral and ip administration of an extract from dried aerial parts and blooms of T. polium led to a reduction in appetite, water and food consumption and consequently body weight in rats (20). Despite of these evidences, Ansari Asl et al., reported that oral administration of T. polium alcoholic extract had no effect on the levels of fasting and postprandial blood sugar in diabetic patients (21). Considering the controversial reports regarding anti-diabetic effects of T. polium, the prime aim of this study was to identify the effect of boiled extract from this herbal medicine on blood glucose, enzymes linked to liver dysfunction and serum lipid in streptozotocin diabetic male rats.

MATERIALS AND METHODS

Animals: In an experimental trial study, 4-8 week-old male Wistar rats weighing 200–250 g were provided from the Pasteur Institute, Tehran, Iran. They were housed under conventional conditions in animal house (School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran). Animals were maintained at 22±2 ◦C with a 12-h light–dark cycle.

Extraction: The aerial parts of Teucrium polium L. were purchased from a popular market in Yazd-Iran. To prepare 2% and 4% extract, we drenched 2 and 4 g of Teucrium polium in 10 ml water and this mixture was boiled for 10 minutes. The solution was cooled and filtered and its volume was adjusted to 100 mL by distilled water. This extract was given to the test groups as their drink ad libitum.

Induction of Experimental Diabetes: Streptozotocin (STZ; Sigma, USA; 60 mg/kg body weight) was dissolved in cold 0.9% saline immediately before use and intraperitoneally injected to the rats. One week after STZ administration, animals with fasting blood glucose levels of 270 mg/dl or more, were considered as the diabetic rats (22).

Experimental Groups: A group of 5 rats was considered as normal group that received normal chow and tap water. 15 diabetic animals were divided randomly and equally into 3 groups: one group considered as sham group (control diabetic animal) and two groups as treatment animals that received different concentrations (2%, and 4%) of boiled extract of Teucrium polium ad libitum for 2 weeks. Blood samples were obtained from orbital sinuses at the start and end of the experimental procedure and body weight was monitored. Biochemical parameters such as blood glucose, cholesterol, triglyceride (TG), alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), urea, uric acid and creatininne (CRT) were measured by kinetic (Enzymatic) and colorimetric methods.

Statistical Analysis: The data were analyzed as Mean ± SEM of variables in different groups using one-way ANOVA fallowed by Tukey's post test. $P \leq 0.05$ was considered as the significant level.

RESULTS

Prior to the onset of this experiment animals were selected in a narrow weight range (200-250 g), so there was no significant difference between the animals weight in different groups. Following the induction of diabetes (1 week after the administration of Streptozotocin), the diabetic rats showed a significant weight loss (175 ± 22 vs. 274 ± 16, $P < 0.05$, Table 1). However, 2 weeks after the initiation of treatments, Teucrium polium-treated rats showed a significant recovery in body weight (230 ± 35.5 and 251 ± 29.7 in 2% and 4% concentrations, respectively vs. 175 ± 20 in untreated diabetic rats $P < 0.05$, Figure 1).

Data from biochemical analysis are summarized in Tables 1 and 2. As shown in Table 1, there are significant changes between the healthy and diabetic rats in all measured biochemical parameters except for the creatininne. According to Table 2, after 2 weeks of experimental procedure, in rats treated with 4% of Teucrium polium, the blood glucose and TG levels were

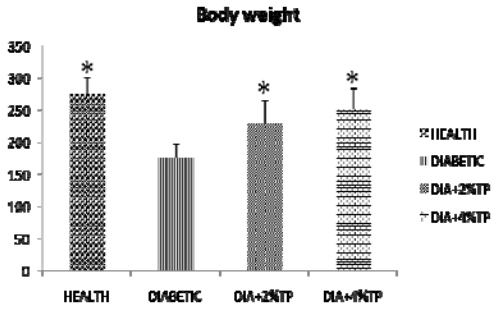

Figure 1: The effect of boiled extract of *T. polium* on the body weight of treated diabetic groups (DIA 2% and DIA 4%), as compared to untreated diabetic rats. There was also a significant weight loss in diabetic rats as compared to healthy control group. Data are presented as mean ± SEM. * indicates a significant difference ($P < 0.05$) as compared to the healthy group, using one way ANOVA fallowed by Tukey's post test .

Table 1- Comparison between the biochemical parameters in diabetic and normal groups.

Group	Biochemical parameters									Body weight	
	ALP	AST	ALT	creatininne	Uric acid	Urea	TG	Cholesterol	glucose	15 days later	Initial
Healthy	182 ± 21	106 ± 32	43 ± 15	1 ± 0.2	0.06±0.01	39 ± 9	74 ± 16	57 ± 24	97 ± 14	274 ± 38	269±25
diabetic	1082*±270	411*±312	148*±127	1.02±019	1.17*±0.7	117*±35	41*±16.9	97*±13.9	557*±149	175*±22	230±18

Data are presented as mean ± SEM. * indicates a significant difference ($P < 0.05$) as compared to the healthy group, using one-way ANOVA fallowed by Tukey's post test .

Table2- Comparison of the biochemical parameters in treated and untreated diabetic groups.

	untreated	2% T.P treated	4% T.P treated
glucose	557 ± 149.8	435.5 ± 55	216* ± 84.7
CHL	67 ± 13.9	85 ± 15.4	66 ± 8.6
TG	41 ± 16.9	44 ± 18.9	18* ± 4.8
UREA	117 ± 35	123 ± 10.2	130 ± 11
UAcid	1.17 ± 0.7	1.75 ± 0.8	1.22 ± 0.4
ALT	148 ± 127	120 ± 67.3	101 ± 17.4
AST	411 ± 312	134 ± 25.3	168 ± 35.4
ALP	1082 ± 270	1437* ± 216.9	1707* ± 142.4
CRT	1.02 ± 019	1.22±0.05	1.1 ± 0.08

Data are presented as mean ± SEM. * indicates a significant difference ($P < 0.05$) as compared to the healthy group, using one-way ANOVA fallowed by Tukey's post test .

significantly lower than the diabetic control group (216 ± 84.7 vs. 557 ± 149.8 and 17.8 ± 4.8 vs. 41.4 ± 16.9, respectively, $P < 0.05$), while the serum ALP was significantly increased in animals that received 2% and 4% T. polium (1437.7 ± 216.9 vs. 1082 ± 270.2 and 1707 ± 142.3 vs. 1082 ± 270.2, respectively, $P < 0.05$). But cholesterol, ALT, AST, Urea, U Acid and CRT were not significantly different after T. polium administration compared to untreated animals.

DISCUSSION

According to this study, boiled extract of T. polium has hypoglycemic activity in diabetic rats. These results confirm several previous studies that T. polium extracts can decrease blood glucose in diabetic animals. Shahraki et al. showed that serum glucose decreased significantly in diabetic rats after receiving 50 mg/kg Teucrium polium for a month (23). Gharaibeh et al. reported a reduction in blood glucose concentrations of streptozotocin-hyperglycemic rats after treatment by a single iv, ip and oral dose of Teucrium polium aqueous decoction (24). Esmaeili and Yazdanparast observed a significant decrease in blood concentration of glucose in streptozotocin induced hyperglycemic rats after six weeks of consecutive oral treatment with aqueous extract of Teucrium polium via a relatively potent insulin tropic action (25). These findings also support the traditional use of this plant as a hypoglycemic agent that has been reported in literature (12,26,27). Phytochemical investigations on Teucrium spp have shown the presence of bioactive compounds such as diterpene derivatives (28), fatty acid esters (29), flavonoids (17) and steroids (30). It has been suggested that hypoglycemic effect of aqueous T. polium extract may be attributed to its constituents such as iridoids, flavonoids and cirsiliol (31,32). Our results also revealed that serum TG value was significantly decreased but cholesterol, ALT, AST, Urea, UAcid and CRT did not show any significant difference in the control and treatment groups. These findings support the previous report by Rasaekh et al. (18) and Karimi F et al. (33), who indicated an antilipidemic effect for T. polium extract, but disagree with Shahraki et al. (23) and Mirzaei et al. (34) who showed that T. polium extract led to an increase in TG and cholesterol. These controversies may be due to the difference in method of T. polium extraction and routes of its administration. Polymeros et al. (35) and Mezokopakis et al. (36) have shown that AST and ALT values are increased after T. polium administration. They attributed a hepatotoxic effect to this plant and suggested that it is not suitable to use in human as an antidiabetic agent. Although in our study boiled T. polium drink did not increase these factors, T. polium consumption, led to a significant increase in ALP. The source of this elevation is not clear to us and needs to be further investigated by using electrophoresis to distinguished bone and liver isoenzymes (37). Our results also showed that in animals treated with 2% and 4% boiled T. polium extract, body weight was significantly decreased after 2 weeks. This finding is in accordance with Ramesh B et al. (38) who showed that T. polium can decrease body weight and weight loss in diabetic rats is due to the decrease in food intake. It is probable that absence of weight loss in treatment group may be attributed to some of components of T. polium extract. In the other study researches have shown that T. polium extract does not have any significant effect on body weight (23). For comprehension of mechanism of T. polium, further studies are needed to elucidate whether T. polium could be useful in the management of human diseases. Previous studies showed that pharmacological and physiological effects of T. polium extract act nonspecifically. Complementary studies will probably show the role of each of these components in reducing serum glucose level and other effects.

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