Hypoglycemic action of Prangos ferulacea in normal and streptozotocin induced diabetic Wistar rats

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Abstract: Diabetes mellitus is a chronic disease which the body cannot synthesis insulin or use insulin properly. *Prangos ferulacea* is a potential source of natural antioxidants. The aim of the present study was to evaluate the effect of the hydroalcoholic extracts of *Prangos ferulacea* on blood glucose and serum lipids serum in diabetes induced by streptozotocin in Wistar rats. Forty eight rats (150-250g) were divided to six groups randomly. Three groups out of six were administered with intraperitoneal injection of streptozotocin to become diabetic. Group I received distilled water. Group II and III of animals received 300, 500 mg/kg/day *Prangos ferulacea* extract. Group IV received distilled water (diabetic control) and animals of groups V and VI were treated with *Prangos ferulacea* extract 300 and 500 mg/kg body weight respectively. The animals were given the extract orally by an intragastric tube once daily for three weeks. The triglyceride, total cholesterol, LDL and HDL were measured in all groups. The Blood glucose and body weight was recorded weekly for each group. Results were analyzed statistically using an analysis of variance (ANOVA). Treatment with *Prangos ferulacea* extract showed a significant decrease in blood glucose, total cholesterol and LDL and no significant in triglyceride and HDL levels. Also the body weight significantly increased in Group of VI compared to diabetic control group. The findings of this study indicate that the administration of *Prangos ferulacea* improved lipid profile and blood sugar level in diabetic rats.[Jamshid Mohammadi, Tahereh Zare. **Hypoglycemic action of Prangos ferulacea in normal and streptozotocin induced diabetic Wistar rats.** J Am Sci 2013;9(10s):51-54]. (ISSN: 1545-1003). http://www.jofamericanscience.org. 8

Key Words: Diabetes mellitus, Prangos ferulacea, blood glucose, serum lipids, rats

Introduction

Diabetes mellitus is a metabolic disorder characterized with chronic hyperglycemia and disturbances of carbohydrate, lipid, and protein metabolism (Mori *et al.,* 2002). Cardiovascular disease, ocular and renal failure secondary to diabetes related injuries are the main long term debilitating effects of diabetes on the risk of long term complications of diabetes. In the process, diabetes, prolonged periods of hyperglycemia can lead to the production of free radicals and the tissue balance between free radical production and cell defense mechanism is impaired. This disorder leads to destruction, changes in cell function and tissue injury is particularly the pancreas(Halliwell *et al.,* 1989).At present the use of insulin and oral medications, are utilized to treat diabetes mellitus and options for lowering blood sugar, but the chemical drugs have side effects. Study on the plants used in traditional herbal medicine to achieve the synthesis of new compounds is necessary.

Special attention to the various food additives and medicinal plants due to natural and less likely to cause side effects has increased. Some plants are rich sources of natural antioxidants. These plants reduce the effects of oxidation and some of the diseases. Ethnobotanical studies of traditional herbal remedies used for diabetes have identified more than 1200 species of plants with hypoglycemic activity (Geetha *et al.,* 2011). *P. ferulacea* plant belonging to the family *Apiaceae* and growing wild in many parts of Iran including Alborz range, Azerbaijan, Kurdistan and Fars (Coruh *et al.,* 2007, Zargari 1991). *P. ferulacea* were collected from Dena Mountains, west of Iran, in late April and early May 2012. Many species of *P. ferulacea* was observed in India, Anatolia, central Asia and Oceania. *P. ferulacea* leaves have been used to treat digestive disease and shows no toxicity (Wadood *et al.,* 2003). *P. ferulacea* has been used as carminative, emollient, tonic for gastrointestinal disorders, antiflatulent, sedative, anti-inflamatory, anti-viral, antihelminthic, antifuagal and antibacterial (Amiri *et al.,* 2007, Coruh *et al.,* 2007). In addition, the leaf of *P. ferulacea* is consumed for gastrointestinal disorders in traditional medicine (Hiroshi *et al.,* 1989). Recent study has been found that the *P. ferulacea* is a rich sources of antioxidants, including coumarines, flavonoids, alkaloids, umbelliferon, monoterpenes (Coruh *et al.,* 2007). Previous study reported that the *P. ferulacea* have antibacterial activity (Amiri et al., 2007). The present study aimed to examine to investigate the possible

antidiabetic activity of hydroalcoholic extract of *P. ferulacea*.

Materials and Methods

This experimental study was carried out in 48 adult male Wistar rats. The animals weighting 150-250 g were used. Animals had free access to food and water. The animals were placed in a controlled room maintained at temperature (24±2°C) with a 12:12h light/dark cycle. The animals were allowed to acclimatize for 1 week before the start of the experiments. The Institutional Animal Ethics approved the experimental protocols in the present study. The animals were randomly divided into six groups each containing eight animals and the groups were divided as follows: Control received distilled water (I), control received 300 mg/kg/day *P. ferulacea* hydroalcoholic extract (II), control received 500 mg/kg/day *P. ferulacea* hydroalcoholic extract (III), diabetic control received distilled water (IV), diabetic treated with 300 mg/kg/day *P. ferulacea* hydroalcoholic extract (V) and diabetic treated with 500 mg/kg/day *P. ferulacea* hydroalcoholic extract (VI). The animals were injected intraperitoneally, after overnight starvation, with streptozotocin (50 mg/kg body wt. Sigma manufactured in China)) freshly dissolved in a citrate buffer (pH 4.5). Three days after the injection of streptozotocin, the glucose was measured with glucometer in blood obtained from caudal vein to ensure their diabetes. Fresh plants of *P. ferulacea* were collected in highlands of Rustam in Fars province. The authentication of the plant sample was confirmed by a botanist and voucher specimen was 2-11 HMRC. The *P. ferulacea* were cleaned, washed under running tap water, dried outside in the shade for 5 days, and ground to a fine powder using an electric mixer. The powdered plant material (1000 g) was extracted thrice with 70% ethanol at room temperature, with each extraction 24 h. The concentrated solution obtained using a Rotary evaporator under vacuum and dried in an oven at 37 ° C for 4 day. The extract daily was weighted, mixed with distilled water and administrated to the treatment group. After being diabetic, in the groups of III and IV, daily 300 and 500 mg/kg of *P. ferulacea* extract were given by oral gavage for 21 days. At the end of each week and end of experiment, all groups were fasted on the night, but allow free access to water. The blood glucose level was measured by glucometer every week. At the end of the experimental period, the animals were anesthetized with ether. The blood samples were collected in tubes and then centrifuged. The blood glucose and lipid parameters were measured in the routine blood analysis. The data collected are expressed as Mean±SEM. The differences were compared using (ANOVA) followed by Tukey's multiple comparison tests.

Results

There was no significant change in group I and II in blood glucose. The blood glucose concentration in group I and II with group III were significantly compared to diabetic group. The blood glucose levels from this study show after three weeks of treatment in groups of V and VI significantly decreased compared to the diabetic control group (Figure 1) P<0/05.

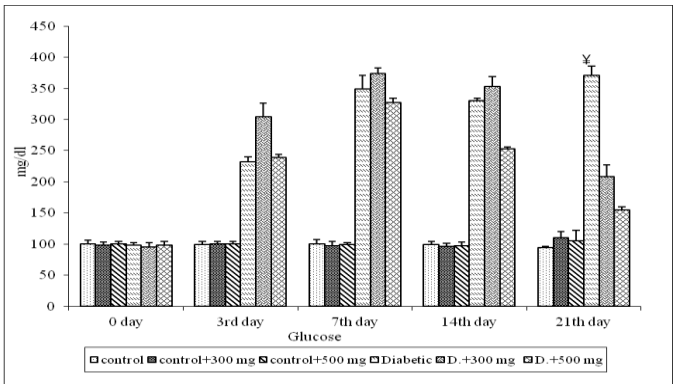

Figure 1: Effects of *P. ferulacea* extract on blood glucose levels. The values are Mean ± SD for 8 rats in each group. The yen symbol (¥) indicates that P < 0.05 when comparing diabetic control group with other group.

The data from this study show, triglyceride concentration in V and VI groups were reduced, but comparison of triglyceride in treatment groups did not show any significant changes (Table 1).

Table 1: The effects of *P. ferulacea* extract on triglyceride, cholesterol, LDL and HDL levels (mg/dl) (Mean ±SD).

Group	Triglyceride	Cholesterol	LDL	HDL
I	80.87±34.9	60.62 ±7.9	22.25±4.1	47.4±7.28
II	77.00±22.4	58.25 ±7.3	22.75±2.6	54.4±9.24
III	89.16±22.4	55.8 ± 4.9	18.16±3.1	44.7±4.84
IV	107±35.4*	67.40±12.1*	25.8±1.9*	40.1±5.8*
V	104±24.7	49.60±4.5¥	17.2±1.8¥	42.6±4.03
VI	92.66±33.2	48.00±4.7¥	18.3±1.6¥	42.7±3.50

The values are mean ±SD for 8 rats in each group. The asterisk symbol (*) indicates that P < 0.05 when comparing Group IV to Group I. The yen symbol (¥) indicates that P < 0.05 when comparing diabetic control group with other group.

In addition, Table 1 shows changes in blood cholesterol levels after 21 days. The results showed that cholesterol in groups V and VI treated with *P. ferulacea* hydroalcoholic extract had a significant decrease compared to the diabetic control group. But given *P. ferulacea* hydroalcoholic extract to the II and III groups, were not significant to the control group. Table 1 also shows changes in LDL and HDL levels after 21 days. In the diabetic control group, LDL levels were elevated after 21 days while

the treatment brought group IV and V levels into near line with the control group level ($P < 0.05$). and II studied ($P < 0.05$). Results showed that diabetes mellitus is decreasing at the rate of HDL and treatment of diabetic rats with the *P. ferulacea* hydroalcoholic extract caused an increase in HDL levels compared to diabetic control group. In our study, in all groups the final body weight showed significant increase from the beginning body weight except in the diabetic control group, in which there was significant decrease in body weight compared to the initial body weight (Table 2).

Table 2: The effects of *P. ferulacea* extract on body weight levels (g)

Group	Initial	Final
I	237.00±2.12	296.00±2.47¥
II	230.50±4.75	272.75±4.31¥
III	221.67±2.61	288.31±2.80¥
IV	225.80±2.09	210.20±4.44
V	206.00±1.08	238.60±5.97¥
VI	205.33±2.75	253.17±3.62¥

The values are mean ±SD for 8 rats in each group. The yen symbol (¥) indicates that $P < 0.05$ when comparing final weight to initial weight.

Discussion

Our finding showed that the blood glucose levels, total cholesterol and LDL in the groups IV and V treated with *P. ferulacea* hydroalcoholic extract has decreased significantly compared to control diabetes group. In the present study, serum glucose increased which was done with destroying β-cells of islets of Langerhans after streptozotocin administration. Streptozotocin induction of diabetes due to irreversible destruction of pancreatic β cells is a direct cause of in insulin secretion is stopped (Konrad *et al.*, 2001). Diabetes mellitus is now one of the most common diseases of the endocrine system is made based on the expected incidence in the human population and has spread to every country in the world (Mohammadi *et al.*, 2012). The search for effective treatments of diabetes mellitus with fewer side effects is needed. Medicinal herbs and their derivatives have been used as a remedy for the treatment of diabetes and its long-term, but their certain effectiveness has not yet been proven by any valid research. Kaleem and colleagues with the extract of *Annona squamosa* in streptozotocin induced diabetic rats have reported the administration of the extract resulted in a significant decrease in blood glucose in the diabetic rats (Kaleem *et al.*, 2008). Soltani band and colleagues reported the *P. ferulacea* hydroalcoholic extract of the root in diabetic rats has antidiabetic effects significantly reduced glucose levels. Additionally the *P. ferulacea* hydroalcoholic extract prevents the histological changes in the pancreas of diabetic rats HDL levels did not change significantly in group I

(Soltani band *et al.*, 2012). Because this could be related to flavonoids, which are antioxidant properties of this plant. According to several studies appears to be due to the antioxidant properties of the *P. ferulacea* hydroalcoholic extract is able to neutralize free radical DPPH and reduce its destroyed effects (Kaleem *et al.*, 2008 and Soltani band *et al.*, 2012). Release of free fatty acids in diabetes and oxygen free radicals, resulting in oxidative stress. Metabolism disorders in cells directly increase insulin resistance and decreased insulin secretion (Paolisso *et al.*, 1996). Other studiy show that the anticxidants in patients with diabetes through effects on protein glycosylatrion and insulin sensitivity have beneficial effects on control of metabolic processes (O'Connel 2001). Tanaka and colleagues demonstrated that the administration of Aloe *vera* extract in normal and diabetic rats decreased blood glucose levels of diabetic rats, which probably antioxidant compounds found in this plant (Tanaka *et al.*, 2006). On the other hand, some flavonoids as antioxidants in medicinal plants and has insulin like properties (Richelle *et al.*, 2004). Furthermore, antioxidants may be able to reduce the symptoms of diabetes mellitus and administration of the extract increases glucose uptake by the cells of the liver, fat and muscle, although the mechanism of insulin is different. Earlier studies have shown that eating fiber can reduce plasma glucose concentration. Fiber is a type of carbohydrate and made by plants, but humans do not have digestive enzymes to process it. With the increased adhesion of viscous polysaccharides, the carbohydrates in the diet play an important role in glucose homeostasis and thus can control the symptoms of diabetes. High levels energy of *P. ferulacea* indicating presence of high concentrations of carbohydrates. Evidence indicates that the carbohydrates in the diet plays an important role in glucose homeostasis and thus can control the symptoms of diabetes. Use sufficient fiber in the diet reduces serum lipid levels in diabetic patients. Results of some studies have shown that eating fiber reduced cholesterol and triglyceride levels, but the amount of HDL did not show significant changes (Daisy *et al.*, 2008, Kamtchouing *et al.*, 2006). Probably to reduce total cholesterol and triglyceride levels, due to increased absorption of bile acids after consumption of fiber is created. Also the fiber, ability to bind the cholesterol and phospholipid and inhibit absorption them. The polysaccharides blocking hepatic circulation of bile acids to caused consumption of free cholesterol (Eilami 2008). *P. ferulacea* plant also contains high levels of fiber and

this could be the reason for the reduction of cholesterol and phospholipids. Daisy and colleagues reported, the weight of diabetic rats treated with the extract of *Costus speciosus* root on diabetic rats, has increased after two months. Kamtchouing and colleagues in a study on methanol extract of the root mark of *Terminalia superb* and *Canariums chweinfurthii* induced diabetic rats have been reported, the metabolic disorders were corrected after two weeks of administration of the plant extract treated diabetic rats and the weight of them increased (Kamtchouing *et al.*, 2006). Dimo and colleagues reported methanol extracts of the root bark of *Sclerocarya birrea* in streptozotocin diabetic rats has been significantly increased in the body weight in treated diabetic rats (Dimo *et al.*, 2007). This loss of body weight in diabetes is due to increased lipolysis and increased muscle wasting and loss of tissue proteins caused by insulin deficiency. The results showed an increase in body weight in diabetic rats treated with the *P. ferulacea* plant extract may cause to improve metabolism in treated rats or effective with absorption of food is to provide energy of the body. According to the finding of the present study it can be concluded that long term administration of *P. ferulacea* extract ability to reduce glucose and lipids parameters in diabetic rats. The exact mechanism for the improvement of diabetes is proposed in each of the compounds in the extract of this plant should be assessed separately in empirical studies.

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