Original Article

Antidiabetics activity of water extract of Capparis spinosa on STZ-induced diabetics Rat

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ABSTRACT

Background: Diabetes is the sixth leading cause of death in the world and most patients with the disease have non insulin diabetes mellitus. *Capparis spinosa L.*, a profusely branched hedge plant, is used in Iranian traditional medicine as a folk treatment. The purpose of this research was to experimentally validate the effect of antidiabetic of *C. spinosa* in an animal model of hyperglycemia. Material and Methods: Aerial organs of *Capparis spinosa* were extracted with water and concentrated to dryness. Fifty four wistar male rats were divided into nine groups, which is included six males with weighing 200-250 g. The aqueous extract was investigated for possible blood glucose decreasing effect produced by single oral administration at various dose levels 10, 20, 40, 60 and 80 mg/kg in the Streptozotocin induced diabetic rats and compared against normal saline control and the standard Glibenclamide. Blood glucose was measured from the tail vein of the rats daily before drug administration. The blood glucose concentration was determined by glucometer and the results were recorded for analysis. The LD_{50} (the median lethal dose) value was determined as 160 mg/kg body weight by acute toxicity study. Results: A maximum lowering of blood plasma glucose level was shown after 2 days of treatment when administered with aqueous extract of *Capparis spinosa* at 60 and 80 mg/kg oral administrations and 2 ml Sub Coetaneous administration mg/kg compared to control group ($p<0.001$). Conclusions: The data of this study suggest that the *Capparis spinosa* aerial organs may be prescribed as an adjunct to traditional formulation and drug treatment for controlling and monitoring type 2 diabetes mellitus.

Keywords: *Capparis spinosa L.,* streptozotocin (STZ), antidiabetic activity and Capparidaceae

Introduction

Diabetes mellitus is a type of metabolic diseases in which a person has high blood glucose, either because the pancreas does not produce enough insulin, or cells do not respond to the insulin that is produced [1]. It is classified as: insulin-dependent diabetes mellitus and non-insulin-dependent diabetes mellitus. About 90% of patients are NIDDM with insulin resistance playing a key role in the development of the disease [2, 3]. Many complications can cause in untreated diabetes patients; include diabetic ketoacidosis and non-ketosis hyperosmolar coma as an acute complications and cardiovascular disease, chronic renal failure and diabetic retinopathy as serious long-term complications. Adequate treatment of diabetes is thus important, as well as blood pressure control and lifestyle factors such as stopping smoking and maintaining a healthy body weight [4, 5]. Globally, as of 2010, an estimated 285 million people had diabetes, with type NIDDM making up about 90% of the cases [6]. Incidence diabetes is increasing rapidly; this number is estimated to almost twice till 2030. The greatest increase in prevalence is, however, expected to occur in Asia and Africa, where most patients will probably be found by 2030 [7]. The increase in propagation in developing countries follows the trend of lifestyle changes and urbanization, as well as most importantly a diet. Suggesting

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that an environmental factors, but there is little conception of the mechanism(s) till now, though there is much speculation, some of it most compellingly presented [7]. Since, type 2 diabetes typically progresses over time, causing the body to produce less insulin and resist the action of insulin. Diabetes is a multifactorial disease leading to several side effect and therefore application a multiple therapeutic approach. Diabetes patients either their cells do not respond to insulin or do not make enough insulin. In case of total lack of insulin, insulin injections are given. Whereas in case of those where cells do not respond to insulin many different drugs are developed taking into regards possible disturbances in carbohydrate metabolism. For example, to manage post-prandial hyper-glycaemia at digestive level, glucosidase inhibitors such as voglibose, miglitol and acarbose are used. These inhibit degradation of carbohydrates thereby the glucose absorption decreased by the cell. To enhance glucose uptake by peripheral cells, "biguanidine" such as metphormine is used. Sulphonylureas like glibenclamide is insulin tropic and works as secretaogogue for pancreatic cells. Although several therapies are in use for treatment, there are certain limitations due to high cost and side effects such as development of hypoglycemia, weight gain, gastrointestinal disturbances and liver toxicity [8, 9]. Based on recent advances and involvement of oxidative stress in complicating diabetes mellitus, efforts are on to find suitable anti-diabetic and antioxidant therapy. Prior to the discovery of insulin and other hypoglycemic chemical drugs, herbal medicine has been long used for the treatment of diabetic patients and they are currently accepted as an alternative therapy for diabetic treatment and control. Recent scientific investigations and clinical studies have confirmed the efficacy of many medicinal plants and herbal preparations in the improvement of normal glucose homeostasis [10]. *Capparis spinosa* L (Capparidaceae) is a profusely branched hedge plant with slender prickly shrubs, zigzag stems and they are growing in a broad range of climatic conditions, such as dry deserts to cooler terrains of mountain either as shrubs, trees or creepers. Traditionally the whole plant or parts are used for curing asthma, rheumatism, diabetes, paralysis, toothache, as anti-helmintic, anti-allergic, snakebite antidote [11-14]. Therefore, the present study was undertaken to evaluate the anti-diabetic activity of the raw aqueous extract of the aerial parts of *Capparis spinosa L*. The aim of this study was to validate the use of C. spinosa in the diabetes folk treatment in an animal model of hyperglycemia which is consisted of experimentally induced hyperglycemia in Male Wister rats by 50 mg/kg STZ.

Materials and Methods

Fresh aerial organs of *C. spinosa* were collected form semnan province during June-July and identified by Botanical Survey of Iran, Semnan. The plant material was dried under shade, powdered and extracted with water using a Soxhlet apparatus. The resulting water extract was evaporated on a water bath to give a dry extract which was then stored in a refrigerator. A weighed quantity of the dried water extract of C. spinosa (WECS) was reconstituted in normal saline and evaluated for pharmacological activities. Wistar Male rats (200-250 g) were used for the investigation and were housed in standard environmental conditions and fed with a standard pellet diet. All the pharmacological study protocols have met with the approval of the Institutional Animal Ethics Committee. The method described by Lorke was employed for the determination of the LD50 and the study was approved by the animal ethics committee [15-17]. Animals were observed for 24 h after drug administration. The general signs and symptoms of toxicity, intake of food, water and mortality were observed and recorded. The LD50 value was calculated from the square root of the product of the lowest lethal dose and highest non-lethal dose, i.e., the geometric mean of the consecutive doses for which 0 and 100% survival rate. Fifty four Wistar male rats were separated into nine groups, each consisting of six males and each weighing 200-250 g. They were fasted overnight and administered with the water extract at the following doses: 10, 20, 40, 60 and 80 mg/kg orally and 2 mg/kg injected subcutaneous (SC).

STZ-induced diabetes in male wistar rats

Fifty four Wistar rats of male sex weighing 200-250 g which were divided into nine group, fasted for 18 h were made hyperglycemic by a single intraperitoneal injection of streptozotocin (STZ) dissolved in 3 mM citrate buffer, pH 4.5 at a dose of 50 mg/kg body weight. After 48 h of STZ injection, rats exhibiting plasma glucose level of more than 250–300 mg/dl were included in the study and divided into nine groups of six animals each [18, 19]. One group served as control, which is not received any treatment, second group received the standard drug Glibenclamide (10 mg/kg) as a positive control and third groups served as negative control, which is diabetics and received normal saline and other six groups received WECS reconstituted in saline (10, 20, 40, 60 and 80 mg/kg, orally and 2 mg/kg, SC. Blood glucose was measured from the tail vein of the rats daily before drug administration. The blood sugar concentration was determined by glucometer and the results were recorded for analysis.

Data Analysis

The results were expressed as mean± S.E.M. Statistical difference was tested by using one-way analysis of variance (ANOVA) followed by Student-Newman-Keuls comparison test. A difference in the mean p value <0.05 was considered as statistically significant.

Results

Antidiabetics' activity of water extract of Capparis spinosa aerial organs

In the acute study, male wistar rats (n = 6) were given a single oral dose 10, 20, 40, 60 and 80 mg/kg orally and 2 mg/kg, SC of WECS; Glibenclamide 10 mg/kg) was used as the positive control. Plasma glucose levels were determined at 24 hr after the dose administration. A single oral dose of the Glibenclamid decreased plasma glucose levels with the maximum effect occurring at 5 days after treatments comparisons with control groups (Figures 1).

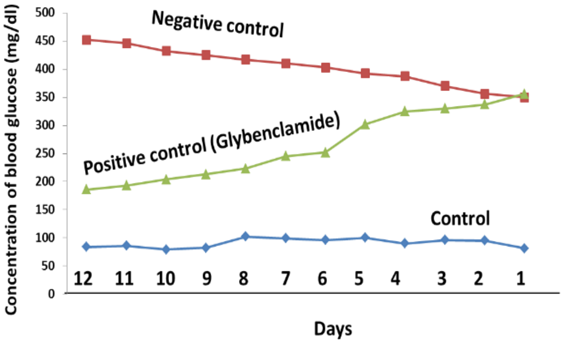

Figure 1. The effect of Glibenclamide on diabetics Rat blood glucose

Figure 2 shows; there is not any effect with 10, 20 and 40 mg/kg administration comparisons with control.

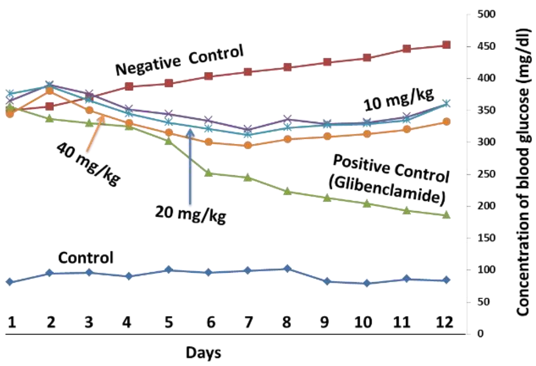

Figure 2. The effect of 10, 20 and 40 mg/kg aqueous extract of Capparis spinosa on decreasing blood glucose in diabetic Rats

A single oral dose 60 and 80 mg/kg decreased plasma glucose levels with the maximum affect occurring at 5 days after the dose significantly (Figure 3) as well as 2 mg/kg SC ($p<0.001$).

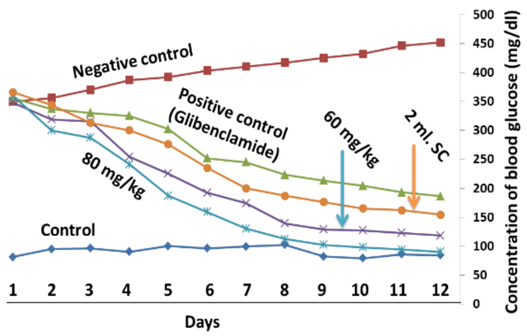

Figure 3. The comparisons effect of 60 and 80 mg/kg orally and 2 ml subcutaneously water extract Capparis Spinosa on decreasing blood glucose in diabetic Rats ($p<0.001$).

Discussion

In this study, daily oral administration of the WECS and Glibenclamide for 12 days to the STZ-induced diabetic's rats resulted in a significant decrease in blood glucose. The effects of treatment with the WECS on blood glucose levels in STZ-induced diabetic rats are shown in figure 2 and 3. Comparison of the average values of blood glucose levels in the treated and untreated (control) groups of STZ-induced diabetic rats suggest some favorable antidiabetic effect of *C. spinosa*. The WECS exhibited significant ($P<0.001$) anti-hyperglycemic effect at 5 days post oral administration, at a dose of 60 and 80 mg/kg and 2 mg/kg SC injection. Phytochemical screening of some plants extract revealed the presence of alkaloids, flavonoids, steroids, glycosides, tannins and saponins. Herbal extracts containing flavonoids and tannins were reported to demonstrate antidiabetic activity [20, 21]. The aqueous leaf extract also decreased total plasma glucose levels; the plant may be useful in the management of secondary complications of diabetes such as dyslipidemia [5, 10]. On the basis of the above evidence, it is possible that the flavonoids and tannins present in C. spinosa may be responsible for the observed antidiabetic activity. Our data showed no significant difference between C. spinosa 10, 20 and 40 mg/kg and placebo in lowering blood glucose levels but 60 and 80 mg/kg was well tolerated. The data obtained from the present study clearly confirm that the WECS tested to possess marked hypoglycemic activity on the STZ-induced diabetic rat model and exhibited dose dependent action in a similar mechanism as Glibenclamide i.e., by stimulation of surviving beta cells to release more insulin [10, 11, 20]. The LD_{50} of WECS was estimated to be 160 mg/kg in rats when administered intraperitoneally. These data suggest that water extract of C. spinosa has a possible highest effect in decreasing plasma glucose levels in animal diabetics' model with type 2 diabetes. However, clinicians are strongly urged to refrain from recommending C. spinosa supplementation in place of the proven standard of care, which includes lifestyle modifications, oral antidiabetic agents, and insulin therapy.

References

1. Gardner D, Shoback D. Greenspan's basic & clinical endocrinology 9th Ed. New York: McGraw-Hill Medical.2011; pp. Chapter 17.
2. Elbessoumy A, Mahmoud E. Biochemical and Clinicopathological Studies on Some Antihyperglycaemic Herbal Preparations in Alloxan induced Diabetic Rats. Sch. J. App. Med. Sci., 2013; 1(2):48-55.
3. EL.Rahman S, Haleem A, Mudhaffar H. Anti-Diabetic effect of Cinammon powder and Cinammon aqueous extract on serum Glucose of rats. J Food, Nutrition and Public Health 2010 ;(3)2:183-185.
4. Sarwar N, Gao P, Kondapally Seshasai SR, Gobin R, Kaptoge S, Angelantonio E Di, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: A collaborative meta-analysis of 102 prospective studies. The Lancet, 2010; 375 (9733): 2215–22.

5. Boussageon R, Bejan-Angoulvant T, Saadatian-Elahi M, Effect of intensive glucose lowering treatment on all-cause mortality, cardiovascular death, and microvascular events in type 2 diabetes: meta-analysis of randomised controlled trials". BMJ 2011; 343: 4169.
6. Williams's textbook of endocrinology, 12th ed.Philadelphia: Elsevier/Saunders. pp. 1371–14350
7. Wild S, Roglic G, Green a, Sicree R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care, 2004; 27 (5): 1047–53.
8. Nathan DM, Buse JB, Davidson MB, and Management of hyperglycemia in type 2 diabetes: A consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2006; 29:1963.
9. Modak M, Dixit P, Londhe J,et al. Indian Herbs and Herbal Drugs Used for the Treatment of Diabetes. J Clin Biochem Nutr. 2007; 40(3): 163–173.
10. Hashemnia M, Oryan A, Hamidi A, Mohammadalipour A. Blood glucose levels and pathology of organs inalloxan-induced diabetic rats treated with hydro-ethanol extracts of Allium sativum and Capparis spinosa. J African Pharmacy, 2012; 6(21):1559-1564.
11. Al-Mustafa AH, Al-Thunibat OY. Antioxidant activity of some Jordanian medicinal plants used traditionally for treatment of diabetes. Pak J Biol Sci. 2008; 11(3):351-8.
12. Mathew KM. The Flora of the Tamil Nadu Carnatic: Ranunculaceae-Labitae (Lamiaceae), Part 1. 1983. p. 43.
13. Anonymous, The Wealth of India (Raw materials) Vol. III. New Delhi: CSIR, PID; 1992; p. 215.
14. Mirheidari H. and Zargari A .Encyclopedia of medicinal plants of Iran. Islamics Culture Press. 2004; 211-4
15. Hebbar SS, Harsha VH, Shripathi V, Hegde GR. Ethnomedicine of Dharwad district in Karnataka, India - Plants used in oral health care. J Ethnopharmacol. 2004; 94:261–6.
16. Mukherjee PK. Quality control of Herbal drugs. New Delhi: Business Horizons Publication; 2002. pp. 246–78.
17. Lorke D. A new approach to practical acute toxicity testing. Arch Toxicol. 1983; 54:275–87.
18. Chattopadhyay RR. Hypoglycemic effect of Ocimum sanctum leaf extract in normal and streptozotocin diabetic rats. Indian J Exp Biol. 1993; 31:891–3.
19. Tomlinson KC, Gardiner SM, Hebden RA, Bennett T. Functional consequences of streptozotocin-induced diabetes mellitus, with particular reference to the cardiovascular system. Pharmacol Rev. 1992; 44:103–50.
20. Selvamani P, Latha S, Elayaraja K, Suresh Babu J,Gupta K. and Pal TK. Antidiabetic Activity of the Ethanol Extract of Capparis Sepiara L Leaves. Indian J Pharm Sci. 2008; 70: 378-380.
21. Suba V, Murugesan T, Bhaskara Rao R,. Antidiabetic potential of Barleria lupulina extract in rats. Fitoterapia. 2004;75:1–4