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Original Article

Effect of *Securigera securidaca* Seeds on Blood Glucose Level of Normal and Diabetic Rats

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Abstract

The search for indigenous natural antidiabetic agents is still ongoing. *Securigera securidaca* seeds are reputed in folk medicine for their value as an antidiabetic remedy, so the present study was carried out to investigate the hypoglycemic efficacy in both normal and streptozotocine (STZ)-induced diabetic rats. Hydroalcoholic extract of the seeds were administered orally with doses of 200, 400, and 800 mg/kg and intraperitoneally with a dose of 400 mg/kg to separated groups of male Wistar rats. The control and reference groups received oral vehicle (1 ml/kg) and glibenclamide (10 mg/kg, p.o.), respectively. Blood samples were collected at 0, 1, 2, 3, 4, and 8 h after treatment and blood glucose levels were determined using glucose oxidase method. Results indicated that hydroalcoholic extract of *S. securidaca* was not effective to lower blood glucose level both in normal and diabetic rats. Glibenclamide on the other hand, reduced blood level of glucose in diabetic rats and caused hypoglycemia in normal animals and the effect was time-dependent. It is concluded that seeds of *S. securidaca* were not effective to reduce blood glucose level in this animal model of diabetes.

Keywords: Blood glucose; Diabetic; *Securigera securidaca*; Streptozotocine;
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1. Introduction

Diabetes mellitus is a group of disorders with different etiologies. It is characterized by derangements in carbohydrate, protein and fat metabolism caused by the complete or relative insufficiency of insulin secretion and/or insulin action. It has been estimated that approximately 140 million people worldwide suffer from diabetes mellitus [1]. Life expectancy may fall to half by this disabling disorder, especially in developing countries of the world where its prevalence is increasing steadily, and adequate treatment is often expensive or unavailable [2]. During the last two decades, traditional systems of medicine and medicinal plant research have become topics of global interest and importance. *Securigera securidaca* (Fabaceae) is one of such medicinal plants that have been reported to be useful as an effective remedy against

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epilepsy, hypertension, parasitic infections like malaria, and gastrointestinal ailments [3-6]. Both in Persian and Egyptian folk medicine the seeds of *S. securidaca* have been used as antidiabetic remedy [4, 5]. Pharmacological studies have confirmed such activities like positive chronotropic, diuretic and hypokalemic effects [5]. Antidiabetic activity of the seeds of the plant has been the subject of research in several investigations. Najaragan et al. [7] reported that an aqueous extract of the seeds reduced blood glucose level in anesthetized cats. In another study, carried out by the same investigators, normal blood glucose levels of mice were significantly higher after oral administration of the seeds and the extract was not effective to reduce the blood glucose level in alloxan-induced diabetes [7]. Hosseinzadeh et al. [8] reported that *S. securidaca* seeds extracts (both aqueous and ethanolic) were not effective in reducing blood glucose levels in normoglycemic and glucose-induced hyperglycemic mice; however, oral or intraperitoneal administration of *S. securidaca* seeds extract resulted in blood glucose reduction in alloxan-induced diabetic mice. The controversy was noted above conducted us to further investigate the antidiabetic or hypoglycemic properties of the plant seeds in rats as another animal species to help the health professionals to decide better about its antidiabetic activity.

2. Materials and methods

2.1. Plant material

S. securidaca was prepared from the market and cultivated in the laboratory of Goldaru Pharmaceutical Co. (Isfahan, Iran). The plant was collected during spring and identified by Mr. Iraj Mehregan, Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran. The voucher sample was deposited for reference in the herbarium at the Department of Pharmacognosy, Faculty of Pharmacy Isfahan University of Medical Sciences, Isfahan, Iran. The plant seeds were dried in shade and then finely powdered.

2.2. Preparation of extract

The powdered seeds (250 g) were macerated in 500 ml of 80% ethanol (ethanol/water ratio 4/1) for 48 h. Then the extract was filtered and concentrated in a rotary evaporator under reduced pressure at 40 ± 1 °C [9]. The resulted extract after drying gave 21.32 g (*i.e.* 8.52% yield) of bright brownish extract. The plant extract was dissolved in 0.2% tween 80 in normal saline (vehicle) for pharmacological experiments.

2.3. Animals

Male Wistar rats, weighting 200-250 g, were obtained from Razi Institute, Tehran, Iran. All of the animals were kept under the same and normal laboratory conditions of temperature (20-22 °C), humidity (60-70 %), and light cycle (12 h day/ 12 h night) and had access to water *ad libitum*. Animals were divided randomly into groups of eight. The principles of laboratory animal care and handling were followed throughout the study.

2.4. Experimental procedure

Diabetes was induced by intraperitoneal (i.p.) injection of streptozotocine (STZ, 60 mg/kg in 0.1 M acetate buffer, pH 4.5). Diabetes was identified by polydipsia, polyuria, and measuring fasting plasma glucose level and was allowed to develop in rats over a period of 5-7 days [10]. Before the commencement of each experiment, both the "control" normal and diabetic rats were fasted for 16 h, but still allowed free access to water throughout.

Fasted STZ-treated rats with blood glucose concentrations between 250-400 mg/dl were considered to be diabetic and were used in this study. Blood samples were taken at 0, 1, 2, 3, 4, and 8 h after treatment by heparinized microhematocrit capillaries from orbital sinus plexus and were deposited into NaF

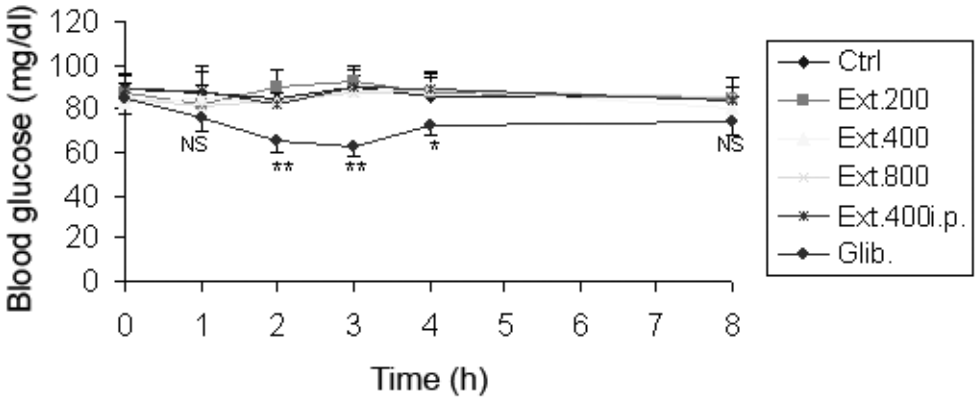

Figure 1. Effect of oral administration of *Securigera securidaca* seed hydroalcoholic extract on fasting blood glucose level of normal rats. Each point represents the mean ± SD, n=8 rats. Scheffe test, NS: not significant, *p<0.05, **p<0.01 *vs* control. Ctrl: control, Ext: extract with doses of 200, 400, 800 mg/kg, p.o. and 400 mg/kg, i.p., Glib.: glibenclamide, 10 mg/kg, p.o.

containing centrifuge tubes for plasma separation. For blood glucose analysis, method of glucose oxidase was used [11]. Glibenclamide (10 mg/kg, p.o.) was used as standard antidiabetic (hypoglycemic) agent for comparison [7]. The test compounds (*i.e.* hydroalcoholic extract of *S. securidaca*, 200, 400, 800 mg/kg, p.o. and 400 mg/kg, i.p.) were administered to four separated groups of normal and diabetic rats.

2.5. Data Analysis

The data are expressed as means ± SD and were analyzed statistically by using ANOVA followed by Post Hoc Scheffe test. Values of p<0.05 were taken to imply significance difference from control.

3. Results

Results indicated that hydroalcoholic extract of *S. securidaca* was not effective to reduce blood glucose level both in normal and STZ-induced diabetic rats (Figures 1, 2). In normoglycemic rats, oral administration of the extract with different increasing doses caused a negligible increase (~10 %) in blood glucose concentrations; however, the activity was not significant compared to the control levels (p>0.05). Glibenclamide, on the other hand, lowered blood glucose level in diabetic rats and caused hypoglycemia in normal rats (p<0.05) and the effect was maximal at 2 and 3 hours after treatment (p<0.01) (Figures 1, 2).

4. Discussion

The present study clearly demonstrated that *S. securidaca* seeds extract had no effect on blood glucose level in STZ-induced diabetic rats, so it has no insulin-like activity or a pharmacological effect similar to biguanids [7, 12]. In addition, the hydroalcoholic extract of plant has no effect on normoglycemia indicating no activity similar to sulfonylureas [13]. Our findings are in contrary with the results obtained by Hosseinzadeh *et al*. [8] and Porchezhian *et al*. [14]. The differences in animal species were used, source of plant which itself determines the content and identity of active constituents, methodological differences in diabetes induction (*i.e*. STZ *vs* alloxan or the dose of STZ) and blood glucose analysis may explain some of these discrepancies. On the other hands, our findings in rats with normoglycemia are somewhat similar to those obtained by Nagarajan *et al*. [7]. In the latter study, blood glucose levels of normal mice

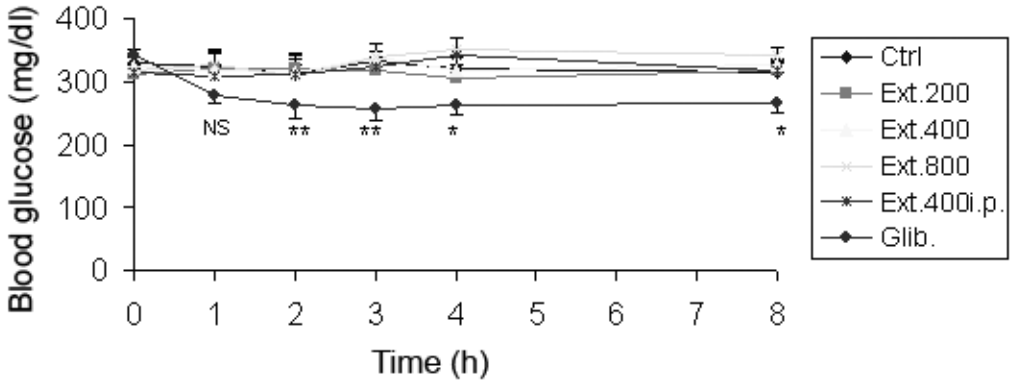

Figure 2. Effect of oral administration of *Securigera securidaca* seed hydroalcoholic extract on fasting blood glucose level of STZ-induced (60 mg/kg) diabetic rats. Each point represents the mean ± SD, n=8 rats. Scheffe test, NS: not significant, *p<0.05, **p<0.01 *vs* control. Ctrl: control, Ext.: extract with doses of 200, 400, 800 mg/kg, p.o. and 400 mg/kg, i.p., Glib.: glibenclamide, 10 mg/kg, p.o.

were significantly higher after oral administration of the plant seeds. In the present study, the seeds extract by oral intake, increased normal blood glucose concentrations in rats however, the activity was negligible and dose-independent. This effect was not detectable in diabetic rats or those received the treatment intraperitoneally. It is assumed that sugar contents of extract or those active materials are apt to breakdown in the gut to form carbohydrates may be responsible for this property. Preliminary phytochemical analysis of the *S. securidaca* both aqueous and ethanolic extract indicated the presence of flavonoids, alkaloids, tannins and saponins. Saponins were detected only in the aqueous extract [8]. Whereas the hypoglycemic effect in some plants are substantially attributed to the flavonoids, but this property dose not necessitate the antidiabetic activity [15, 16].

Our results also indicated that glibenclamide, as a hypoglycemic reference drug, was effective in lowering blood glucose levels in STZ-induced diabetic rats. This is in accordance with the findings reported by Courtois *et al*. [17] and Andrade-Cetto *et al*. [18]. They have reported that oral administration of glibenclamide to STZ-induced diabetic rats decreased the blood glucose level and also could be considered as a standard antidiabetic drug to compare the efficacy of hypoglycemic compounds. The major action of glibenclamide is to increase insulin release from the pancreas. Two other additional mechanisms of action, probably more responsible in our results, are a reduction of serum glucagon levels and an extra-hepatic effect to potentiate the action of insulin on its target tissues [19]. On the basis of current investigation it is strongly recommended that the hypoglycemic effect of *S. securidaca* is controversial and any use of this plant seeds for therapeutic applications needs further confirmations in various animal species and in human.

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