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Hormones and Signaling

Elixir Hor. & Sig. 31 (2011) 1957-1959

ISSN: 2229-712X

Improvement of hyperglycemia in diabetic rats by Ethanolic extract of red date leaves

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ARTICLE INFO

Article history:

Received: 26 January 2011;

Received in revised form:

18 February 2011;

Accepted: 23 February 2011;

Keywords

Ziziphus jujuba,

Glucose,

Glibenclamide,

Diabetes.

ABSTRACT

Diabetes mellitus is the most common endocrine disorder that impairs glucose homeostasis. Hyperglycemia is the defining characteristic of diabetes mellitus. Chronic hyperglycemia is associated with damage to many of the body's systems. Diabetes cases in the world are estimated to increase by 122% between 1995 and 2025. As diabetes prevalence increases so does the need for new and more effective therapies. Studies have indicated some herbal extracts have antidiabetic effects .However, rational prescription of effective medicinal plants for diabetes cure, requires precise information of action mechanism of these plants. *Ziziphus jujuba*, a member of the family Rhamnaceae has been used as a traditional medicinal herb and considered for thousands of years to affect various physiological functions in the body In present study, diabetes induced in rats, and then hypoglycemic effect of Ziziphus jujuba leaves hydroalcoholic extract was evaluated. Then results compared with glibenclamide effect.

Introduction

Ziziphus jujuba, a member of the family Rhamnaceae commonly called jujube, red date, or Chinese date. Its precise natural distribution is in southern Asia, and also southeastern Europe though more likely introduced there. It has been used as a traditional medicinal herb and considered for thousands of years to affect various physiological functions in the body(1). It is used traditionally as Hypnotic-sedative and Anxiolytic(2,3) anticancer(4), Antifungal, Antibacterial(5,6), Anti-inflammatory, Antispastic(7,8), Hypotensive and Antioxidant(9,10), Immunostimulant(7), sweetness inhibitors (11) and Wound healing properties(12).

It possesses allied compounds *viz.* ascorbic acid, thiamine, riboflavin-bioflavonoids and Pectin A and various chemical substances like Ziziphine-A to Q, betulinic acid, alphitolic acid, zizyberenalic acid and saponin, ziziphin, from the dried leaves of *Z. jujube*(13). In present study, diabetes induced in rats, and then hypoglycemic effect of Z.jujuba hydroalcoholic extract was evaluated.

Materian and methods

Plant materials and extraction. Z.jujuba fresh leaves were bought from Tehran Natural Resources Department(1 kg), and authenticated by expert. A specimen voucher (AS-AP-06-01-32) was deposited at the herbarium located at the Department of Biology, University of Esfahan. The leaves was cleaned and dried at room temperature (23–25 °C) for 3 days. The leaves powder was prepared with mill, and were sloped into a beaker and ethanol 96% was added to cover the surface of the powder, beaker was positioned on the shaker for 24 hours. Then, the solution was filtered through filter paper (Whatman qualitative grade 1), and again ethanol 75% was added to the remained waste, and was positioned on the shaker for 12 hours. Finally, the combined filtrate was then concentrated in a rotary evaporator (35–40 °C), to a thick, dark green coloured crude extract up to $^1/_3$ the primitive volume. For proteins isolation and material refining, after the filtered solution decantation 3 times by chloroform, was positioned in incubator at 50 ^{0} C. After a few days, the powder was ready and included net and effective material of the plant. A crude residue (45g) was obtained giving a yield of 4.5%. The powder was dissolved in normal saline for experiments, and dilutions were made fresh on the day of experiment.

Animals. The experiments performed complied with the rulings of the Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council (NRC, 1996) and approved by the Ethical Committee of Esfahan University Iran. Male rats(*Rattus Norvegicus Allivias*) used in the study (200–250 g) were bred and housed in the animal house of the Esfahan Payame Noor University under controlled environment (23–25 °C). Animals were given tap water *ad libitum* and a standard diet. After the adaptation period, each group of rats was weighted and marked, and then treated by the specified dose of materials.

For inducing diabetes in rats, we used alloxan monohydrate (Sigma Chemical Company, Germany) 120mg/kg (i.p.) solved in saline. Glucose and alloxan structural similarity causes alloxan connects and enters beta cells. Alloxan degenerates specially beta cells thus uses as a suitable material to induce diabetes in animals. Meanwhile alloxan causes Reactive Oxygen Species production only in Langerhauns islets(14,15). Alloxan injection causes diabetes induction in rats which it's similar to human type 1 diabetes. In this study, criterion for diabetes induction was blood glucose more than 300mg/dl. 2days after alloxan injection, blood glucose was evaluated by blood glucose test meter(Glutest PRO R; Sanwa-kagaku,Nagoya, Japan), and diabetes verificated. Then, the diabetic rats were separated and used for the study. Animals were assigned to 4 groups having the following characteristics:

1) Normal group: was treated by saline (2 ml/kg, i.p.)

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2) Diabetic control group: was treated by alloxan monohydrate (120mg/kg, i.p.) for 3 days alternately.
3) Extract group: was treated by alloxan monohydrate for 3 days alternately and, after diabetes verification, animals received hydro-alcoholic extract of Z.jujuba (100 mg/kg , i.p.) for 5 days alternately.
4) Group 4 was treated by alloxan monohydrate for 3 days alternately and after 48 hours received also glibenclamide (500mcg/kg/i.p) for 5 days alternately.
72 hours after extract administration, the animals were anesthetized and blood samples were collected from heart of each rat and were analyzed for glucose content by using glucose oxidase peroxidase (GOD-POD) method using a visible spectrophotometer at 505 nm.

Statistical analysis. All the experiments were repeated at least 3 times with appropriate controls. Data are presented as the Mean±SD and $P<0.05$ was considered statistically significant. Statistical analysis was performed using a one-way ANOVA and the relevant figures were drawn with Excel.

Result

According to fig.1, Z.jujuba extract have been reduced significantly glucose level($p<0.001$) from 767.82mg/dl in diabetic rats to 250.94mg/dl in extract group. Glucose reduction by Z.jujuba is similar to glibenclamide effect and there is no significant difference between extract and glibenclamide groups($p>0.05$).

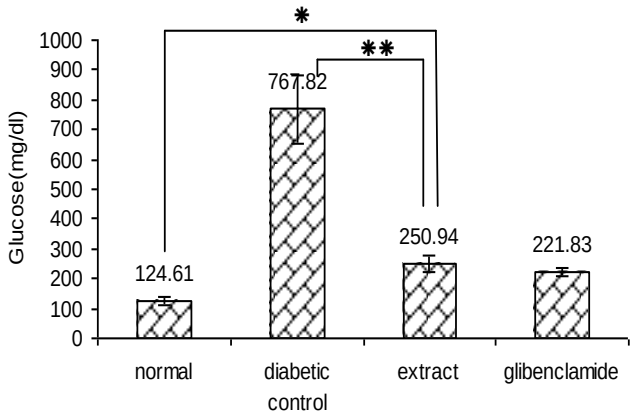

Fig. 1: Glucose level of the extract group compared with other groups

Data are presented as Mean±SD for 10 samples
❋$p<0.01$, ❋❋$p<0.001$

Discussion

In present study hypoglycemic effect of Ziziphus jujuba leaves hydroalcoholic extract was evaluated in diabetes-induced rats and results compared with glibenclamide effect. Glibenclamide is a member of sulfonylureas, and it is very widely used as a hypoglycemic agent in the treatment of diabetes as increases insulin release of beta cells. Glibenclamide decreases glycogenolysis and gluconeogenesis thereupon blood sugar diminish by glibenclamide(16,17).

Alloxan is one of the usual substances used for the induction of diabetes mellitus and has a destructive effect on the beta cells of the pancreas(18,19). Insulin deficiency leads to increased blood glucose and lipids(20,21,22). Alloxan has been shown to induce free radical production and cause tissue injury. The pancreas is especially susceptible to the action of alloxan induced free radical damage(23,24,25,26). Anti-oxidants are compositions which guard cell membranes and different compositions of organism. Mechanism of anti-oxidant action is: free radicals agglomeration, electron transfer to these oxidants and inactivation of them(27,28). Z.jujuba leaf includes anti-oxidants such as alkaloids and flavonoides viz. saponin, ziziphin, isoboldine, asimilobine, iusiphine and iusirine(29,30,31). Recent studies have been shown flavonoides reduce blood sugar(27). The results of the present study demonstrated the significant anti-diabetic activity Z.jujuba leaf extract. Other possible mechanism includes the stimulation of beta-cells and subsequent release of insulin and activation of the insulin receptors. Estimation of insulin level and insulin receptor may give more insight into the mechanism of the anti-diabetic activity exhibited by the extract.

Conclusion:

According to the results, defines Z.jujuba leaf extract has hypoglycemic effect in diabetes mellitus experience model in rat. We suggest more investigations to clear the extract mechanism on blood glucose in both normal and diabetic treatments.

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