ORIGINAL ARTICLE

The Effect of Ziziphus Jujuba Fruit Extract in Diabetic and Non-Diabetic Rat

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Abstract

Objective: Herbal medicine and medical plants such as Ziziphus Jujuba are widely used in the treatment of diseases such as diabetes mellitus. We investigated the effects of ethanol extracts of Ziziphus Jujuba fruit on serum glucose, triglycerides, LDL-cholesterol, HDL-cholesterol, cholesterol and activities of aminotransferase enzymes in streptozocin-induced diabetic adult male rats.

Materials and Methods: Adult Wistar rats were rendered hyperglycemic. Animals were divided into four equal groups (7 per group). Animals in all groups were treated for 14 days. Blood samples were collected from the heart of the animals.

Results: Continuous supplementation of ethanol extract in drinkable water of diabetic rats resulted to a significant decrease of fasting blood glucose, cholesterol and increase in high density lipoprotein levels after 14 days ($P<0.05$), but the levels of triglycerides, LDL-cholestrol, activities of alanine aminotransferase and aspartate aminotransferase did not changed significantly in treatment group compared to control group($P>0.05$).

Conclusion: This paper discussed the antidiabetic effect of an alcoholic extract of Ziziphus Jujuba on streptozocin-induced diabetes in rats. Researchers showed that Streptozocin injection led to diabetes mellitus, which may be due to destruction of β cells of the islets of Langerhans.

Keywords: Ziziphus Jujuba, Diabetes, Rat, Fasting blood sugar, Antihyperlipidemic.

Introduction

Diabetes mellitus is one of the most common endocrine metabolic disorders. Dual endocrine deficits of impaired insulin action (insulin resistance) and inadequate insulin secretion create an environment of chronic hyperglycemia and general metabolic disorder (1).

Development of novel medicine prototypes with systematic and intensive investigations of plants for new agents to treat diabetes mellitus can be very useful (2).

Increasing interest in herbal medicine, more individuals are exploring the possibility of using natural medicines to complement conventional therapy, as is already the case in certain minority cultures (3). The use of

medicinal plants is increasing because of their curative effects on various diseases.

Recent studies have indicated that some herbal extracts have anti-diabetic effects and can be prescribed in diabetic patients in order to reduce blood glucose; for example, a hypoglycemic effect of alcoholic extract of Dandelion has been recorded by some researchers (4,5).

The Ziziphus (Rhamnaceae) species used in folk medicine for treatment of some diseases such as digestive disorders, weakness, liver complaints, obesity, urinary disorders, diabetes, skin infections, fever, diarrhea and insomnia (6-8).

Ziziphus vulgaris Mill Rhamnaceae, a deciduous tree up to 12 m in height, is indigenous throughout Iran. Ziziphi spinosi semen, the seeds of Ziziphus Jujubaamark var. spinosus Bunge (Rhamnaceae, 'Sanjom' in Korean), is known as the most important herbal medicine for the treatment of insomnia and as a sedative in Chinese medicine. Also it used to treat diabetes in Iranian traditional medicine (9,10).

A survey of the literature revealed that a number of cyclopeptide and isoquinoline alkaloids flavonoids, terpenoids and their glycosides have been found to occur in various amounts in most Ziziphus species.

A survey of the literature revealed that various amounts of cyclopeptide and isoquinoline alkaloids flavonoids, terpenoids and their glycosides have been found in most Ziziphus species.

The leaves of these plants contain betulic and ceanothic acids, various flavonoids, saponins,erols, and triterpenes (11,12).

Furthermore, the butanol extract of Ziziphus spinachristi fruit or its main saponin glycoside, christinin-A, improved glucose utilization in diabetic rats but had no effect on normal rats after 1 and 4 weeks of treatment.

A significant increase in Serum insulin level of diabetic rats was observed after treatment with butanol extract in 4 weeks period. The antidiabetic effect of butanol extract was more pronounced than christinin-A (12, 13).

Also, other reports showed the benefit of using fruit extracts infusion or other parts of the plants to treat patients (13).

Since Ziziphus vulgaris is a wild tree found in Iran and its fruit used to treat of diabetes mellitus, therefore, the aim of this study is to evaluate the anti-diabetic effect of Ziziphus species, Jujuba species on diabetic rats.

Materials and methods

Plant material

Ziziphus Jujuba fruit was prepared in Yazd, Iran. Then this fruit was authenticated by the faculty of Biology, herbarium of Tehran University. The fruits were separated and dried at room temperature. Separated fruits were grinded and then changed to powder.

Extraction of plant material

Powdered plant material was extracted with 70% ethanol (20g +100 ml 70% ethanol). After 3 days, the macerate was filtered and ethanol-water was evaporated on a rotator evaporator at a temperature of 50°C.

Animals

Male adult Albino rats (Wistarrain) with weight of 250-300 g were fed on a pellet diet and tap water for full acclimatization. The animals were kept in an air-conditioned animal room (22 ± 2°C) under a 12-h light/dark cycle.

Study design

Adult Wistar rats were rendered hyperglycemic by a single I.P. injection of streptozocin (65 mg/kg BW) using 1 ml solution in 0.1 M citrate buffer, pH 4.5. Diabetes was identified by polydipsia, polyuria and measuring the non-fasting serum glucose concentration. Three days after injection of streptozotocin (STZ/Zanosar), rats with a blood glucose level over 250 mg/dl were considered as diabetic rats and were used in the experiment. Animals were divided into four equal groups (7 per group) as follows:

(1) Non-Diabetic rats treated with distilled water (controls)

(2) Diabetic rats receiving distilled water.

(3) Non-Diabetic rats receiving the ethanolic extract.

(4) Diabetic rats receiving the ethanolic extract.

Animals in all groups were treated for 14 days. On the 15th day of the experiment, the animals were killed under light ether anesthesia. Blood samples were collected from the heart of the animals. Blood glucose, triglycerides, HDL-cholesterol, LDL-cholesterol, VLDL, cholesterol and activity of AST and ALT were measured by an enzymatic kit.

Statistical analysis

Because of normality of distribution and homogeneity of variance, ANOVA with Dunnett post hoc tests were performed to comparison between variables. SPSS software was performed for analyzing and drawing graphs.

Results

The mean blood glucose levels of control and diabetic rats after oral administration of Ziziphus Jujuba extract are shown in Fig.1**,** which induces a significant reduction in serum glucose level in Ziziphus and Ziziphus+Diabetic treatments animals (P<0.05).

The mean blood cholesterol levels of control and diabetic rats after oral administration of Ziziphus Jujuba extract are shown in Fig.2, which induces a significant reduction in serum cholesterol level (P<0.05).

The mean blood HDL levels of control and diabetic rats after oral administration of of Ziziphus Jujuba extract are shown in Fig.3**.** Treatment with extract has significant effect in high density lipoprotein (HDL) level in intact and diabetic animals (P<0.05).

Discussion

This paper discussed the anti-diabetic effect of an alcoholic extract of Ziziphus Jujuba on streptozocin-induced diabetes in rats. Researchers showed that Streptozocin injection led to diabetes mellitus, which may be due to destruction of β cells of the islets of Langerhans (14).

Blood glucose level in rats indicated that an alcoholic extract of Ziziphus fruit caused significant hypoglycemic in diabetic rats. The continuous treatment with Ziziphus Jujuba fruit extract (4%) for a period of 14 days produced a significant decrease in the blood glucose. The hypoglycemic effect of Ziziphus Jujuba alcoholic extract on streptozocin-induced diabetic rats with destruction of the β cells of the islets of Langerhans demonstrated, this extract may act on glucose homeostasis in an extra-pancreatic way. Previous studies have shown that some medical plants such as Fenugreek inhibit glucose absorption in small intestine of rats. This can be considered as one of the mechanisms by which this extract can regulate glucose homeostasis (15,16). Improvement of liver function, subsequent increases the uptake of blood glucose and its utilization might be other mechanisms of action of Ziziphus vulgaris (15,17).

Another possible interpretation depends on the glucagon-lowering effect of saponin glycoside. Steroid saponin glycosides extracted from Fenugreek seeds have been reported to significantly decrease the level of plasma glucose, glucagon and cholesterol in diabetic dogs (18-19). This glucagon-lowering effect may enhance glucose utilization as indicated by the increased hepatic glycogen, increased plasma pyruvate and decreased plasma glucose, hepatic phosphorylase, and G-6-phosphatase activities.

Glycogen degradation can be rapidly stimulated by the direct hepatic action of different hormones (12).

Our data showed continuous treatment with Ziziphus Jujuba fruit in diabetic rats produced a significant decrease in the blood glucose, cholesterol and increase in HDL-cholesterol level.

Hyperlipidemia and abnormalities in lipid metabolism lead to progression of atherosclerotic disease in the patients. In addition use of medicinal plants as a pharmacologic modality in preventing alteration in lipid metabolism has received wide attention by several studies (20). Insulin

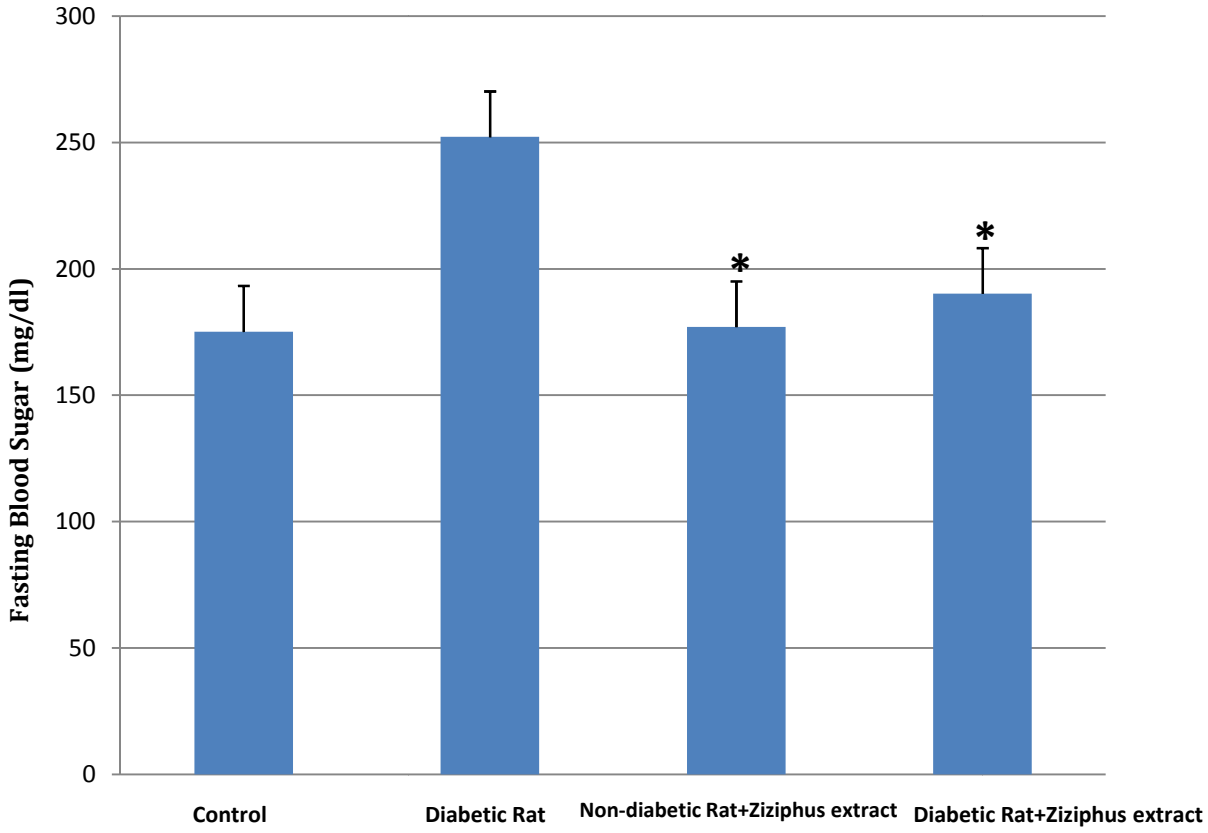

Figure 1. The mean blood glucose levels of four study groups

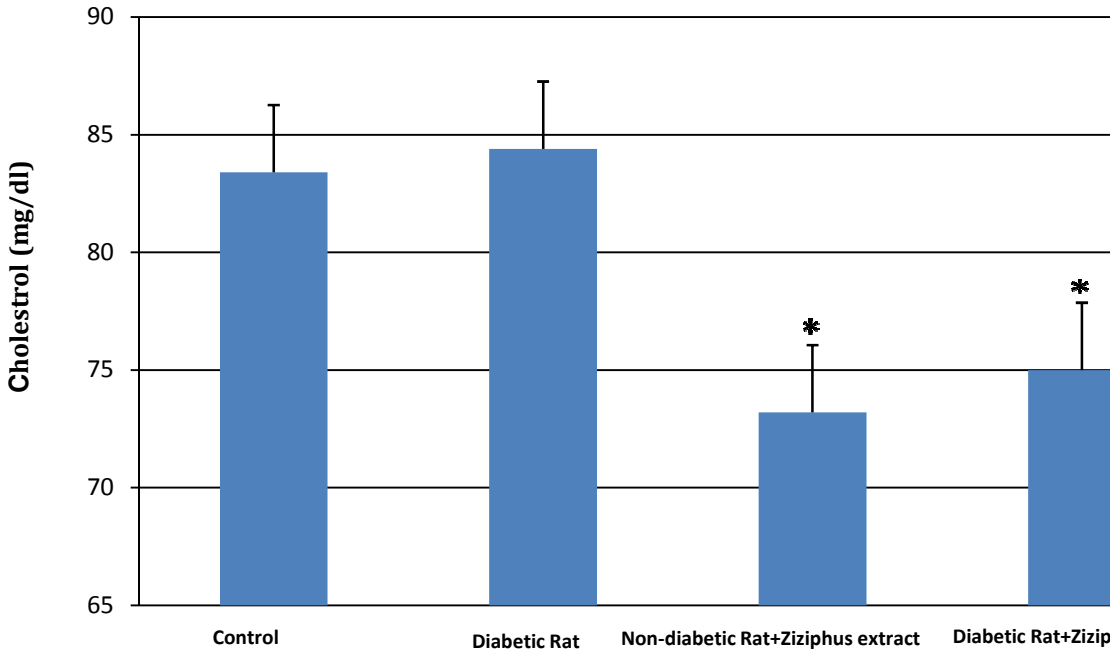

Figure2. The mean blood cholesterol levels of four study groups

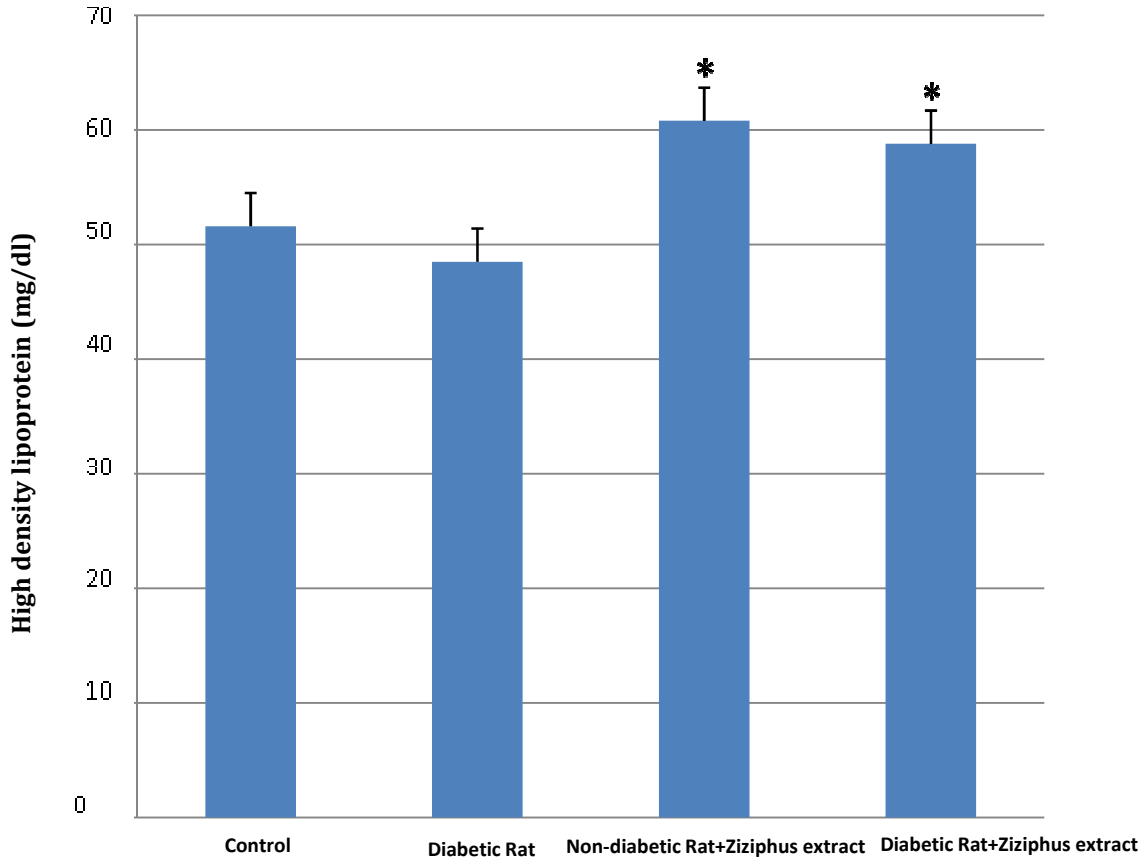

Figure 3. The mean blood High Density Lipoprotein (HDL) levels of four study groups

is a polymer of fructose with glycosidic linkages presented in the Ziziphus species (21). Since it is water-soluble and can't be hydrolyzed by human digestive enzymes, it behaves like a soluble fiber and possesses a hypolipidemic effect (22). Soluble fibers are non-digestible carbohydrates, which are fermented in the colon by resident anaerobic bacteria. The mechanisms by which soluble fibers have hypolipidemic effects are still not clear, though many hypotheses have been proposed by researchers (23,24). For example, soluble fibers may increase the viscosity of the stomach content, which can slow down the rate of gastric discharging from water, nutrients and lipids, or it can cause alterations in hormone secretions, which affect lipid metabolism. In addition, significant reductions of serum cholesterol and triglycerides have been reported in rats fed with insulin (25) or soluble fibers (24,26).

This study showed that rat treatment with alcoholic extract of Ziziphus Jujuba for 14 days decreased level of glucose that may be because of secreting of insulin or increasing insulin receptor sensitivity.

Also, animals treated with the extract of Ziziphus showed significant reduction of cholesterol level which can be related to its effect on cholesterol synthesis. Increased HDL level during treatment with Ziziphus extraction may be related to the effect of extracts on enzymes which interfere with cholesterol biosynthesis resulted to increased HDL level.

Transaminases are an important class of enzymes which link carbohydrates and amino acid metabolism, and these enzymes have a relationship with the intermediates of the tricarboxylic acid (TCA) cycle (29).

During extract treatment, there was no significant change in the activation of these enzymes and the extracts had no toxicity for mammalian systems.

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