ORIGINAL ARTICLE

The Effect of Christ's Thorn (Ziziphus Spina Christi) Leaves Extract on Lipid Profile, Lipid Peroxidation and Liver Enzymes of Diabetic Rats

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Received: 10 July 2015

Accepted: 02 September 2015

Published in September 2015

Abstract

Objective: The effect of herbal medicine is more useful than synthetic medicines. The present research paper aims to show the effects of leaves extracts of Zizyphus Spina Christi (ZSC) on lipid profile, lipid peroxidation and activities of aminotransferase enzymes in streptozocin induced diabetic adult male rats.

Materials and Methods: Fifty six male rats weighing 150-200 gm were included in this study. They were divided into 8 groups. The first group, non-diabetic control rats received distilled water. The second, third and fourth groups, non-diabetic rats were given doses 50 mg/kg body weight (BW), 75 mg/kg (BW) and 100mg/kg (BW) ZSC extracts. The fifth group, diabetic control, received distilled water. The sixth, seventh and eighth were given doses, 50mg/kg (BW), 75 mg/kg (BW) and 100mg/kg (BW) ZSC extracts. Weight and fasting blood glucose were measured every week and the period of treatment continued for four weeks. Serum lipid profile, malondialdehyde (MDA) and aminotransferase enzymes (AST, ALT) were measured at the end of experiment.

Results: In diabetic rats ZSC leaves extract significantly reduced serum total cholesterol, triglyceride, LDL-C, AST (aspartate aminotransferase) and ALT (alanine aminotranferase) (P<0.05). The serum malondialdehyde markedly decreased (P<0.001), But HDL – C increased significantly (P<0.05).

Conclusion: The present paper revealed that ZCS leaves extract has beneficial effects on lipid profile, lipid peroxidation and aminotranferase enzymes in diabetic rats.

Keywords: Diabetic rats, Lipid per oxidation, Lipid profile, Ziziphus Spina Christi.

Introduction

Diabetes mellitus is a complex syndrome involving gross abnormalities in glucose and lipid metabolism. Diabetes mellitus is considered an important disease because number of diabetic patients is increasing and diabetes has various side effects (1,2). Use of herbal plants in medicine is increasing because of their abundance and for their curing various diseases. Many herbal plants have been used for the treatment of diabetes (3,4).

Zizyphus Spina Christi (Christ's thorn) is in the family of Rhamnaceae. Christ's thorn leaves extract have hypoglycemic activity.

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Christ's thorn leaves extract contain various beneficial ingredients, triterpenoidal saponin glycosides, betulic acid, ceanothic acid, christinin-A, B, C and D (3). There are some evidence which show Zizyphus Spina Christi leaves decrease the serum glucose level in control and diabetic rats. Hypoglycemic effect of ZSC is mediated by releasing insulin which block KAT P channels in pancreatic beta cell membranes. Zizyphus Spina Christi leaves may potentially be safe for use as an antidiabetic agent (4). Christ's thorn leaves improve glucose utilization in diabetic rats by increasing insulin secretion which may be due to both saponin and polyphenol content (5). Hyperglycemia is controlled by attenuation of glucose absorption which may be due to polyphenol content of ZSC leaves.

Reviewing the current literature, nothing was reported concerning the hypolipidemic effects of Zizphus Spina Christi leaves extract. Therefore, this study aims to investigate beneficial effects of ZSC leaves extract on lipid profile, lipid peroxidation and aminotranferase activity in streptozotocin diabetic rats.

Materials and methods

Extraction of plant leaves: Zizyphus Spina Christi leaves were purchased in Yazd, Iran. Then the leaves were washed, dried and powdered at room temperature .The extraction of powdered material was done with 70% ethanol and then put on shaker at 35 °C for two days. After filtering the extract, dehydrated by adding 50 ml ethanol and dried at 30 °C. The extract powder was mixed with 50 ml benzol and then put in evaporator at 25 °C for five days.

Animals: Male albino rats with weight of 150-200 gm were kept in an air-conditioned animal room (a 12hour light/dark cycle) and fed on a standard diet and tap water.

Study design: Male albino rats were injected streptozocin (65 mg/kg BW) by using one ml solution in 0.1 M citrate buffer with PH 4.5. We measured non fasting blood glucose concentration for detection of diabetes. Three days after injection of streptozotocin (STZ/Zanosar), rats with a blood glucose level over 250 mg/dl were considered as diabetic rats.

Eight groups of rats (each group 7 rat) were seperated as follow:

(1) Non Diabetic rats receiving only distilled water as control of non diabetic groups

(2) Non Diabetic rats receiving 50 mg/kg (BW) ZSC leaves extract

(3) Non-Diabetic rats receiving 75 mg/kg (BW)ZSC leaves extract

(4) Non-Diabetic rats receiving 100 mg/kg (BW) ZSC leaves extract

(5) Diabetic rats receiving only distilled water as control of diabetic groups

(6) Diabetic rats receiving 50 mg/kg (BW) ZSC leaves extract

(7) Diabetic rats receiving 75 mg/kg (BW) ZSC leaves extract

(8) Diabetic rats receiving 100 mg/kg (BW) ZSC leaves extract

The period of treatment for animals in all groups was four weeks. After four weeks, blood samples were collected and serums were kept at -20°C.Serum cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, and activity of AST and ALT were measured by autoanalyzer and enzymatic kit. Serum malondialdehyde was measured by thiobarbituric acid reactive substance (TBARS). Statiscal analysis was done using SPSS15 software. Data were expressed by SPSS as mean±SEM .Statistical differences from control were determined using one way analysis of variance. For this process, we used the method of paired t-test for data analysis between two groups. $P<0.05$ was considered as statistically significant difference.

Results

Table (1) shows the effect of consuming 3 doses of ZSC leaves extract on serum lipid profiles in non diabetic and diabetic rats for 4weeks. As shown, the mean value of blood total cholesterol (TC) and LDL- C of non

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Table 1. Effect of treating 3 doses of Christ's thorn leaf extract on serum lipids and malondialdehyde in non diabetic and diabetic rats

Parameters	Non diabetic groups				Diabetic groups			
	Control	50 mg/kg (BW)	75 mg/kg (BW)	100 mg/kg (BW)	Control	50 mg/kg (BW)	75 mg/kg (BW)	100 mg/kg (BW)
TC (mg/dl)	94.33±6.58	94.13±6.81	88.70±5.61	84.27±4.41[a]	121.87±5.19[a]	107.33±6.33[ab]	94.99±6.83[ab]	88.66±7.33[ab]
TG (mg/dl)	69.27±4.73	67.17±3.27	64.38±4.17	59.60±3.89[a]	78.32±517[a]	71.51±5.46	60.91±4.53[b]	52.33±4.81[ab]
LDL-C(mg/dl)	51.93±5.82	47.31±4.62	43.31±5.55[a]	39.31±6.94[a]	72.31±6.83[a]	66.29±4.16[ab]	62.30±5.71[ab]	58.31±7.26[ab]
HDL-C(mg/dl)	33.53±2.38	34.31±2.62	36.66±2.11	38.61±2.62[a]	30.73±2.59	35.15±2.29[b]	39.83±2.82[ab]	42.51±2.54[ab]
MDA (µM/L)	0.12±0.03	0.09±0.02	0.082±0.04[a]	0.075±0.03 [a]	0.44±0.05[a]	0.35±0.04[ab]	0.33±0.04[ab]	0.30±0.05[ab]

a = significance ≤.05 as compared with nondiabetic control
b = significance≤.05 as compared with diabetic control

diabetic groups treated with 100 mg/kg (BW) of ZSC leaves extract, diabetic control group and diabetic rats treated with the 3 doses of ZSC leaves extract 50, 75 and 100 mg/kg (BW) were significantly (P<0.05) lower than that of the non diabetic control group. Also the mean value of blood total cholesterol and LDL-C of 3 doses of ZSC leaves extract treated groups in diabetic rats were significantly (P<0.05) lower than that of the diabetic control group. The triglyceride (TG) level of non diabetic group treated with 100mg/kg dose of ZSC leaves extract and diabetic control group were significantly (P<0.05) lower than that of the non diabetic control group. The mean value of triglyceride of 2 doses of ZSC leaves extract treated groupies; 75and 100 mg/kg (BW) in diabetic rats were significantly (P<0.05) lower than that of the diabetic control group.

The level of HDL-cholesterol was significantly (P<0.05) increased in non diabetic treated with100 mg/kg (BW) dose of ZSC leaves extract and diabetic treated with 75 and 100 mg/kg (BW) doses of ZSC leaves extract as compared to control group of non diabetic rats. Also the level of HDL-C was increased in the diabetic rats treated with 3 doses of ZSC leaves extract as compared to that of the diabetic control group.

The mean of blood cholesterol, triglyceride and LDL-cholesterol were decreased with increasing doses of ZSC leaves extract while the mean of HDL-cholesterol was increased in the both groups of diabetic and non diabetic rats .The mean value of serum malondialdehyde (MDA) in non diabetic group treated with 2 doses of ZSC leaves extract, 75and 100 mg/kg (BW) and diabetic control group were significantly (P<0.05) lower than that of the non diabetic control group. The MDA level in diabetic groups treated with 3 doses of ZSC leaves extract were significantly lower than control groups of diabetic and non diabetic rats.

Discussion

Diabetes mellitus is a chronic disease characterized by high blood glucose level due to absolute or relative deficiency of circulating insulin level or insulin resistance. Though there are various types of hypoglycemic agent for treatment of diabetes, but diabetic patients used to consume natural products with anti-diabetic activity to overcome side effects and toxicity of chemical drugs. Herbal anti-diabetic drugs are used because they are effective and have low cost and less side effects (7). So the aim of this study was the effect of Zizyphus Spina Christi (ZSC) leaves extract on lipid profile, lipid peroxidation and activities of aminotransferase enzymes in diabetic adult male rats.

The data in the present study showed that, treating diabetic and non diabetic rats with ZSC leaves extract [50 mg/kg (BW), 75 mg/kg (BW), and 100 mg/kg (BW)], for four weeks has significantly reduced the serum lipid profile parameters, especially, serum total cholesterol, serum triglycerides, and low density lipoprotein (LDL-C) and increased the highdensity lipoproteins (HDL-C) as compared to non diabetic control and diabetic control rats.

This result is accordance with that of Bentley et al. (8) and Makni et al. (9). Clinical trials

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Table 2. Effect of treating 3 doses of Christ's thorn leaf powder on serum liver enzymes in non diabetic and diabetic rats for 4 weeks

Parameters	Non diabetic groups				Diabetic groups			
	Control	50 mg/kg (BW)	75 mg/kg (BW)	100 mg/kg (BW)	Control	50 mg/kg (BW)	75 mg/kg (BW)	100 mg/kg (BW)
IU/L(AST)	38.12±1.02	0.88±36.44	34.75±0.75[a]	32.67±0.63[a]	46.66±0.86[a]	42.91±0.78[a,b]	39.61±0.69 [a,b]	36.57±0.65[b]
ALT(IU/L)	36.50±0.55	34.88±0.55	33.27±0.55[a]	31.66±0.63[a]	48.94±0.57[a]	41.23±0.47[a,b]	35.86±0.53[a,b]	32.45±0.52[a,b]

a = significance ≤.05 as compared with nondiabetic control.
b = significance≤.05 as compared with diabetic control

were done on root extracts of Ziziphus Spina Christi. Diabetic rats were treated with 100 mg/kg ZSC root extract. Fasting serum glucose was measured every week and the period of the treatment continued for 2 weeks. At the end of experiment the levels of Serum lipids and lipid peroxidates were measured. Results showed that ZSC root extract significantly reduced lipid profiles and lipid peroxidates. This may be due to functional ingredients, saponins in ZSC which have hypolipidimic effects by decreasing total cholesterol, triglycerides and LDL-C in hyper lipidemic rats (10,11).

The present results showed that, treating diabetic rats with ZSC leaves extract has significantly ameliorated peroxidation of lipids by decreasing the serum MDA. These results were in accordance with the previous studies of Hussein et al (12) .This may be attributed to tannins (13) and carotenes (14) in some Zizyphus species.

Activities of ALT and AST enzymes significantly (P<0.05) reduced by treating diabetic rats With ZSC leaves extract (50 mg/kg, 75 mg/kg and 100 mg/kg body weight) for four weeks. Liver dysfunction in diabetes may results in leaking out of its enzymes from injured tissue and their migration into the blood stream. On the other hand treatment with ZSC leaves extract greatly reduced free radicals and consequently reduced oxidative stress with concomitant hepatic protection. Morever, Zhang et al (10) reported that saponins in herbs have hepatoprotective effects.

The results of this study confirmed that consumption of 100 mg/kg ZSC leaves extract greatly ameliorates the diabetic disorders in rats. In addition, the ZSC leaves extract is effective to reduce hyperlipidemia, lipid peroxidation and activity of liver enzymes. The hypolipidemic effect of ZSC leaves extract could be its phenol constituent which inhibits oxidative stress.

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