Hypoglycemic and Hypolipidemic Effects of *Zizyphus jujuba Lam.* In Streptozotocin-Induced Diabetic Rats

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ABSTRACT

Zizyphus jujuba Lam. Is also called as Baer tree, belongs to the family Rhamnaceae. The dried bark was powdered and extracted with various solvents by successive soxhlet hot extraction process with increasing order of polarity. On phytochemical investigation, the methanol extract and aqueous extract has shown steroids, flavonoids and tannins. The present study was designed to evaluate the hypoglycemic and hypolipidemic activity of methanolic extract of zizyphus jujube leaves in normal and streptozotocin inducing diabetic rats. The zizyphus jujube was reported for the many of biological activity, and hypoglycaemic activity of the same has not been reported so far. Streptozotocin is used to induce diabetic in rats and the blood lipid levels were estimated using commercial kits available in the market. The methanolic extract of Zizyphus jujube was administered at the doses 100mg/kg and 200mg/kg doses. Both the doses caused a significant decrease in the levels of total cholesterol, triglycerides and LDL-cholesterol, glucose level. The results indicate that methanolic extract of *Zizyphus jujuba* in the dose dependent manner possess hypoglycaemic and hypolipidemic activity.

Keywords: *Zizyphus jujuba*, Diabetic rats, Streptozotocin, hypoglycemic, hypolipidemic.

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INTRODUCTION

Zizyphus jujuba Lamk is also called as Badar, Baer, Bogari, Barihannu belonging to family Rhamnaceae. The plant is distributed throughout India, Iran, Afghanistan and in china. It is a small sub deciduous tree with dense spreading crown, commonly 0.6m girth and 6m high. Leaves 3-6.3 by 2.5-5 cm oblong or ovate, usually minutely serrulate or apex distinctly toothed, obtuse, base oblique and 3-nerved, nerves depressed on the glabrous shining upper surface, densely clothed beneath with white or buff tomentum [1-2].

A survey of literature on *Zizyphus jujuba* lam. revealed a few pharmacological reports on the plant like antioxidant and antilisterial effect [3], antisteroidogenic activity [4], antiobesity activity [5], sedative and hypnotic [6], anxiolytic [7], anticancer [8].

The plant is reported to contain alkaloid jubanine-E [9]. It contains three flavones-C-glucosides-6"sinapoylspinosin, 6"-feruloylspinisin and 6-"p-coumaroylspinosin. The leaves and stems of ziziyphus jujuba lam contains saponins 3-o-[2-α-L-fucopyrnosyl-3-o-β-D-glucopyranosyl-α-L-arabinopyranosyl]jujubogenin. The fruits of *Zizyphus jujuba* lamk contain zizyphus saponins I, II, III and jujuboside B [10], jujuboside D [11], and jujuboside e [12]. The bark of *zizyphus jujuba* Lamk contains 7% tannin [13].

MATERIALS AND METHODS

The leaves of *Zizyphus jujuba* Lam was collected from Erode district, Tamilnadu, and were identified by Botanical survey of India, Coimbatore, Tamilnadu, India. The voucher specimen was preserved in the laboratory.

Preparation of Extract

The fresh leaves were collected and dried in the drying room, with active ventilation at ambient temperature (25±1ºC) and packed in paper bags. The powdered plant material was extracted with successive solvent extraction ranging from non polar to polar using soxhlet hot extraction process. The solvent was distilled under reduced pressure which gave brownish black color residues. The methanol extract was collected and used for the present study.

Test Animals

Male swiss albino rats (30) weighing between 150-180g each were used. The animals were housed in a temperature (25±1ºC), humidity controlled room and a 12hr light-dark cycle (lights on at 6 hr). Rats were allowed free access to tap water and standard pellet diet.The animal study was carried out in the JKKMMRF College of pharmacy,Institutional ethical committe approval no.1158/ac/07/CPCSEA. Twenty four rats fasted for 18hr, were made hyperglycaemic by intraperitoneal injection to streptozotocin (sigma) dissolved in citrate buffer (pH-4.5), at a dose of 60mg/kg body weight. After 72hr of STZ injection, the rats were fasted for 6hr and their plasma glucose levels estimated. Rats having plasma glucose levels above

250mg/dl[14] were considered diabetic. The remaining 6 rats were injected with equal volume of 10% physiological saline and these were used as healthy control rats (Group I). The 24 diabetic rats were randomly divided into following 5 groups of 6 each [15-20].

Group II: Diabetic rats maintained on unrestricted standard diet and water ad libitum and served as untreated diabetic rats.
Group III: Diabetic rats treated orally with *Zizyphus jujuba* extract (100mg/kg b.w)
Group IV: Diabetic rats treated orally with *Zizyphus jujuba* extract (200mg/kg b.w)
Group V: Diabetic rats received orally glibenclamide (10mg/kg b.w).

Treatments for 21 days in all groups were started 4 days after STZ injection. The bodyweight of the animals was recorded after the termination of the experiment. Blood samples were collected from overnight fasted animals at 0,2,4,6 hr and 21 days after treatment. Whole blood was used for the estimation of haemoglobin and glycosylated haemoglobin (Hg A1C). Hb and glycosylated haemoglobin (Hb A1c) [15] blood glucose, serum triglyceride (TAG) total cholesterol and high density lipoprotein cholesterol (HDL-c) [16] were estimated.

Low density lipoprotein cholesterol (LDL-c) was estimated by the equation of Friedewald et al [17].

$$LDL\text{-}c = TC\text{-}HDL\text{-}c\text{-}TAG/5$$

Statistical analysis:

The data are represented as mean ± SE, and statistical significance between treated and control groups was analysed using students t-test.

Table-1:Anti-diabetic activity of Z. Jujuba extract in Streptozotocin induced hyperglycaemic rats

Treatment and Dose	Serum Glucose level mg/dl time after treatment (hr)			
	0	2	4	6
Group-I Normal control	90±4.8	95±3.5	93±1.8	97±2
Group II Diabetics	500±4	505±3.0	500±4	503±3.5
Group III *Zizyphus jujuba* extract 100mg/kg body wt.	503±3.6	163±3.9*$ (67±6.1)	128±10.7*$ (74±2.2)	125±5.4*$ (74±1.0)
Group IV *Zizyphus jujuba* Extract 200mg/kg body wt.	511±4.2	262±4.5$ (55±6.7)	205±2.8$ (59±5.7)	208±2.3$ (58±4.8)
Group V Glibenclamide 10mg/kg body wt.	510±3.9	388±3.9$ (22.6±0.9)	345±6.0$ (31.2±0.85)	348±6.0$ (31.8±0.8)

*significant difference between *Zizyphus jujuba* extract, $ significantly different from diabetics group

Table: 2 various biochemical parameters of serum and fasting glucose, lipid profile, blood haemoglobin and glycosylated in streptozotocin-induced hyperglycaemic rats before and 3-weeks after treatment with *Zizyphus jujuba* extract

Treatment and Dose	Hb (g/dL)	Hb1Ac Mg/g Hb	Glucose (mg/dl)	TAG (mg/dl)	TC (mg/dl)	HDL-c (mg/dl)	LDL-c (mg/dl)
Group-I Normal control	13.2±0.4	0.35±0.02	90±4.8	97±5.4	65.5±3	27±2.7	24±0.48
Group II Diabetics	7.75±0.4$^@$	0.97±0.04$^@$	505±3.5$^@$	119.5±6.4$^@$	97.1±4.1$^@$	38.7±1.9$^@$	33.7±3.1$^@$
Group III *Zizyphus jujuba* extract 100mg/kg body wt.	14±0.3$^{@\$}$	0.3±0.02$^\$$	72±4.4$^{@\$}$ (84±0.7)	60±3.2$^{@\$*}$ (51±1.4)	47±3$^{@\$*}$ (53±2.8)	17±1.1$^{@\$*}$ (57±3.0)	17±3.3$^{@\$*}$ (67±4.4)
Group IV *Zizyphus jujuba* Extract 200mg/kg body wt.	13.9±0.3$^{@\$}$	0.32±0.03$^\$$	82±4.1$^\$$ (83±0.9)	71±9$^{@\$}$ (36±2.9)	47±3$^{@\$*}$ (53±2.8)	17±1.1$^{@\$*}$ (57±3.0)	17±3.3$^{@\$*}$ (67±4.4)
Group V Glibenclamide 10mg/kg body wt.	12.8±0.5$^\$$	0.35±0.02$^\$$	76±0.3$^{@\$}$ (84±0.1)	86±1.1$^{@\$}$ (26±609)	77±3.2$^{@\$}$ (27±5.4)	38±0.726$^@$ (-)	22±2.5$^\$$ (18±0.9)

Hb=Haemoglobin, HbA1C=glycosylated haemoglobin, TAG=triglycerides, TC=total cholesterol, HDL-c=high density lipoprotein cholesterol LDL-c=low density cholesterol.
@ significantly different from control group
$ Significantly different from diabetics group
*significantly different between *Zizyphus jujuba* extracts.

RESULTS

Body Weight

A significant decrease in body weight was observed in the untreated diabetic group (Group-II:200±6.6g) as compared to the control group. (Group-I: 200±6.1g). The administration of the extracts resulted in a significant decrease in body weight (190±5g) (180±2g) respectively.

DISCUSSION

Blood Glucose Level

The results of blood glucose showed that rats of group II-V, injected with streptozotocin developed severe diabetes with very much higher initial blood glucose level of about 500-511mg/dl when compared to the blood glucose of healthy. (Group-I) control group (90±4.8) feeding diabetic rats with 100mg/kg, 200mg/kg body wt of methanolic extracts of *Zizyphus jujuba* produced significant decreased in blood glucose level after 2,4 and 6 hour of treatment as compared to untreated diabetic rats. Glibenclamide also showed similar results (84% reduction).

Hb and HbA1c level-there was a significant decrease in Hb level in untreated diabetic rats(Group I) as compared to control rats (Group I). After treatment with both the extracts

(Group III and IV) and Glibenclamide (Group V), the levels of HbA1c returned to the normal values (Table 2).

Serum lipid profile- the results of the serum lipid profile (Table 2) showed that in Streptozotocin induced diabetic rats (Group II) there was not only hyperglycemia but also hyperlipidemia in which serum triglycerides, total cholesterol, HDL-c, and LDL-c cholesterols increases significantly when compared to control group (Group I). The treatment of diabetic rats with (Group III) extracts for 3 weeks resulted in significant decrease of serum triglycerides, total cholesterol and LDL-c cholesterols as compared to untreated diabetic rats (Group II) and the values came down significantly below those in the normal healthy control group (Group I).

CONCLUSION

In conclusion MEZJ was shown to have dose dependent glucose lowering and antihyperlipidemic effects. As per the above parameters observed MEZJ showed significant antidiabetic and anti hyperlipidemic effects of STZ induced diabetes. Further studies deals with the isolation of active constituents from MEZJ and their mechanism for the antidiabetic and antihyperlipidemic activity.

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