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Research Paper

Anti diabetic activity of *Zizipus mauritiana* Lam. In streptozotocin induced Diabetic Rats and its comparison with some standard flavonoids

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The aim of present investigation is to evaluate Antidiabetic activity of hydroalcohol extract of whole plant of *Zizipus mauritianan* Lam. In streptozotocin induced diabetic rats. Treatment with *Zizipus mauritiana* hydro alcohol extract at two different dose 200 mg/kg and 400 mg/kg and its comparison with standard drug gilbenclamide at dose of 5 mg/g and some flavonoids i.e. quercertin, kaempferol and epicatichin each at dose of 100mg/kg for 15 days, after induction of diabetes by streptozotocin 50 mg/kg , caused significant decrease in level of tri glycerides, total cholesterol and significantly increase in level of HDL and body weight compared to disease control group. It is furthermore *Cynodon dactylon* at dose of 200mg/kg and 400mg/kg shows more significant result than some of standard flavonoids. Thus, whole plant of *Zizipus mauritiana* Lam. may have potential Antidiabetic agent.

Key words: *Zizipus mauritiana*, Streptozotocin, Flavonoids

INTRODUCTION

There are hundreds of medicinal plants that have a long history of curative properties against various diseases and aliments however, screening of plants for their activity is very essential and needs urgent attention in order to know the value of plant. There are questions about some of diseases and their related treatment[1]. Diabetes mellitus is a metabolic disorder of the endocrine system. The disease occurs worldwide and its incidence is increasing rapidly in most part of the world. People suffering from diabetes are not able to produce or properly use insulin in the body, so they have a high level of blood glucose[2]. Diabetes is becoming the third 'killer' of mankind, after cancer and cardiovascular diseases, because of its high prevalence, morbidity and mortility[3]. Approximately 4% of the population worldwide is affected and expected to increase 5.4% in 2025[4].these facts show that's proposing as immediate strategy for diabetes prevention and treatment is a global subject. For a long time, diabetics have been treated with several medicinal plants or their extract based on their chemical constitutents like flavonoids[5]. Flavonoids are the compounds that are widely found in fruits and vegetables. They have a broad range of biological activities[6]. They function as powerful antioxidants, as phytoestrogens and can alter the activities of important cell

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signallling enzymes, such as tyrosine kinase, phosphodiesterases and phosphoinositide kinase[7]. Some amy also have antidiabetic activity. Studies of the in vivo and in vitro effects of varios flavonoids on glucose metabolism have shown opposite and often controversial results. This is probably because of the different structural characteristics of the molecules and the different experimental designed used[6].

Streptozotocin (STZ) is well known for its selective pancreatic islet cell toxicity and has been extensively used for the induction of diabetes mellitus in animals[8]. Streptozotocin induced diabetes is a well documented model of experimental diabetes. Previous reported literature indicates that the type of diabetes and characteristics differ with the employed dose of STZ and animal and species used[9]. STZ induced diabetes provides a relevant example of endogeneous chronic oxidative stress due to the resulting hyperglycemia. STZ is a pancreatic β-cell toxin that induces rapid and irreversible necrosis of β-cells[10]. *Ziziphus mauritiana* Lam. belongs to Rhamanceae family and is a small evergreen tree of variable size, found both wild and cultivated throughout India. Common in hotter parts of India, cultivated in gardens, village roadsides, found in wild, tropical forests and in outer Himalaya[11]. *Zizipus mauritiana* Lam. has been reported for antisteroidogenic[12], anxiolytic[13], sedative-hypnotic[14]and CNS functions[15]

It contain flavonoids[16] which plays an important role for its medicinal properties. The purpose of this study to investigate and comparison of anti diabetic activity of hydro alcohol extract of whole plant of *Zizipus mauritiana* Lam. and to standard flavonoids like qurecetin, kaempferol and epicatchin for anti diabetic activity, and to know how much do they produce action with standards.

MATERIAL AND METHODS

Plant material

The whole plant of *Zizizpus Mauritiana* Lam. were collect from local areas of Udaipur. Selected medicinal plants were cut into small pieces, cleaned and shade dried at room temperature. Then these selected medicinal plants were subjected to size reduction to get coarse powder, separately, in a mechanical grinder and then passed through sieve no. 40 to get desired particle size and stored in well closed glass jars. And preapared hydro alcohol (70:30) extract with cold maceration process. Obtained extract were used for this study.

Experimental animals

Male Albino rats weighing 150-200g breed in the animal house, were used in this

study. The animals were allowed free access to commercial rat pallet diet (Lipton Indian ltd., Mumbai, India) and water *ad libitum.* Rats were housed in a group of six in clean cages at 25^{o} C and 12 hours photoperiod with relative air humidity of 30 to 60%. The bedding material of the cages was changed everyday. All the experimental procedures were carried out accordance with committee for the purpose of control and supervision of experiments on animal (CPCSEA) guidelines.

Experimental models

Anti-diabetic activity study

The animal were selected and weighed, then marked for individual identification. The rats were injected with streptozotocin dissolve in 0.1 M citrate buffer at a dose of 50 mg/kg body weight, interpertonally to induce diabetes in overnight fasted male wistar albino rats weighing 175-200 g. after one hour of streptozotocin administration the animals were given feed ad libitum. A 5% dextrose solution was given in feeding bottle for a day to overcome the early hypoglycaemic phase. After 72 hours animal with blood glucose levels higher than 250mg/dl were considered diabetic and were included in the study. Rats were divided into eight groups containing six rats each.

Group I- Rats were given only vehicle (only water)

Group II- Rats were given streptozotocin (50 mg /kg, bw, p.o.)

Group III- Animal were given streptozotocin (50 mg /kg, bw, p.o.) single dose plus drug Gilbenclamide (5 mg/kg bw, p.o.)

Group IV- Rats were given streptozotocin (50 mg /kg, bw, p.o.) Plus drug Quercertin (100 mg/ kg/ day, bw, p.o.)

Group V- Rats were given streptozotocin (50 mg /kg, bw, p.o.) Plus drug kampferol (100 mg/ kg/ day, bw, p.o.)

Group VI- Animal were given streptozotocin (50 mg /kg, bw, p.o.) Plus drug Epicatchin (100 mg/ kg/ day, bw, p.o.)

Group VII- Rats were given streptozotocin (50 mg /kg, bw, p.o.) Plus drug *Zizipus mauritiana* Lam. (200 mg/ kg/ day, bw, p.o.)

Group VIII- Rats were given streptozotocin (50 mg /kg, bw, p.o.) Plus drug *Zizipus mauritiana* Lam. (400 mg/ kg/ day, bw, p.o.)

Measurement of Biochemical parameters

The total protein, total carbohydrate, triglycerides and high density lipoprotein (HDL) level were measured in serum of streptozotocin induced sub acute study after 15th day.

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Table-1 : Strepatozotocin Induced Sub-acute (Multi Dose) Study

Group	Treatment	Dose (mg/kg)	Zero day	5th day	10th day	15th day
I	Normal	Vehicle	97.78 ± 0.59	97.18 ± 0.82	96.68 ± 0.80	97.45 ± 0.68
II	Only Strepatozotocin	50	265.38 ± 3.86^{+++}	274.21 ± 2.93^{+++}	302.85 ± 4.32^{+++}	301.36 ± 4.82^{+++}
III	Strepatozotocin + Glibenclamide	5	263.65 ± 1.79	231.16 ± 3.09***	190.66 ± 2.39***	160.5 ± 1.30*** (46.74%)
IV	Strepatozotocin+ Quercetin	100	260.63 ± 2.00	231.18 ± 4.78***	199.63 ± 2.67***	164.76 ± 1.93** (45.32%)
V	Strepatozotocin+ Kaempferol	100	263.25 ± 1.56	235.10 ± 2.14***	198.51 ± 2.28***	168.1 ± 1.65*** (44.21%)
VI	Strepatozotocin+ Epicatchin	100	265.03 ± 3.01	239.4 ± 2.75***	202.56 ± 2.40***	177.36 ± 1.59*** (41.14%)
VII	Strepatozotocin + *Zizipus mauritiana*	200	261.18 ± 0.94	235.51 ± 2.12***	196.63 ± 3.23***	178.01 ± 3.08*** (40.93%)
VIII	Strepatozotocin+ *Zizipus mauritiana*	400	264.18 ± 2.23	229.71 ± 1.94***	191.28 ± 1.38***	164.9 ± 1.88*** (45.28%)

All values are represented as Mean ± SEM (n=6) ; values in parentheses are represents percentage of reduction in glucose level.
P Value : +++ <0.001; ++ <0.01; + <0.05 When compared with control untreated animals.
*** <0.001; ** <0.01; * <0.05 When compared with glucose treated model.

RESULTS AND DISCUSSION

In streptozotocin multidose treatment, there was significant decrease in glucose level from 5th day to 15th day was observed in groups of extracts of plants, flavonoids and standard. The highest percent decrease in glucose level was observed in Glibencliimde treated group (46.74%) followed by quercetin (45.32), *Zizipus mauritiana*-400 (45.28%), kaempferol (44.21%), epicatechin (41.14%), and *Zizipus mauritiana*-200 (40.93.%). The glucose reduction percentage of *Zizipus mauritiana*-400 was higher than the

Table- 2 :Strepatozotocin Induced Sub-acute (Multi Dose) Serum Profile Study

Group	Treatment	Dose (mg/kg)	TG mg/dl	HDL mg/dl	Total Cholesterol mg/dl	Total Protein mg/dl
I	Normal	Vehicle	87.28 ± 1.64	51.7 ± 2.37	57.20 ± 1.23	8.7 ± 0.81
II	Only Strepatozotocin	50	131.73 ± 2.85^{+++}	21.1 ± 2.42^{+++}	89.38 ± 2.11^{+++}	5.8 ± 0.82^{+++}
III	Strepatozotocin + Glibenclamide	5	98.11 ± 2.63***	42.6 ± 2.13***	60.56 ± 2.73***	7.2 ± 0.63***
IV	Strepatozotocin+ Quercetin	100	117.80 ± 3.28**	40.8 ± 3.84***	70.21 ± 3.28**	7.6 ± 0.96**
V	Strepatozotocin+ Kaempferol	100	109.38 ± 3.47***	39.8 ± 2.61**	71.70 ± 4.51**	6.4 ± 0.53***
VI	Strepatozotocin+ Epicatchin	100	112.84 ± 2.08***	41.4 ± 3.79***	69.26 ± 1.65**	7.2 ± 0.84**
VII	Strepatozotocin + *Zizipus mauritiana*	200	116.85 ± 3.98**	37.5 ± 3.12**	68.82 ± 3.87**	7.5 ± 0.71**
VIII	Strepatozotocin+ *Zizipus mauritiana*	400	107.43 ± 2.61***	38.7 ± 2.89**	68.60 ± 2.51**	7.2 ± 3.09**

All values are represented as Mean ± SEM (n=6)
P Value: +++ <0.001; ++ <0.01; + <0.05 When compared with control untreated animals.
*** <0.001; ** <0.01; * <0.05 When compared with glucose treated model

flavonoids epicatechin and kaempferol.

Effect of extracts, flavonoids on serum lipid profile on STZ induced diabetic rats:

Triglyceride(TG):

After treatment with Streptozotocin there was significant increase in TG level was observed in diabetic control group when compared to normal control. The Triglycerides level in glibenclimide, kaempferol, epicatechin, and *Zizipus mauritiana* -400 showed high significant reduction ($p<0.001$). quercetin and *Zizipus mauritiana* -200 showed significant reduction at level of ($p<0.01$) when compared to diabetic control group.

High Density Lipoprotein (HDL):

After treatment with Streptozotocin there was significant decrease in HDL level was observed in diabetic control group when compared with normal control. The treatment with glibenclimide, epicatechin and *Zizipus mauritiana* -400 ($p<0.01$), kaempferol, *Zizipus mauritiana* -200 and *Zizipus mauritiana* -400 ($p<0.01$) significantly restores the decrease HDL level on 15th day. when compared to diabetic control group.

Total Cholesterol (TC):

There was significant increase in TC level was observed after 15th day of STZ administration in diabetic control group when compared to normal control. Whereas, treatment with flavonoids and both doses of *Zizipus mauritiana* showed significant decrease ($p<0.01$) in TC level on 15th day Glibenclamide showed significant level of ($p<0.001$).

Total Protein (TP):

Streptozotocin treatment produces the significant decrease in TP level in diabetic control group when compared to normal control. The TP level in glibenclimide, kaempferol, quercetin and *Zizipus mauritiana* -400 showed highly significant ($p<0.001$) increase in TP. Whereas epicatechin showed significant level of ($p<0.01$), *Zizipus mauritiana* -200 showed significant level of ($p<0.05$) when compared with diabetic control group.

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