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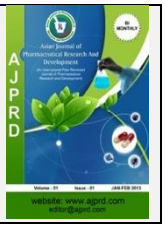

Open Access Research Article

Anti diabetic activity of *Cynodon dactylon* Linn In streptozotocin induced Diabetic Rats and its comparison with some standard flavonoids

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A B S T R A C T

The aim of present investigation is to evaluate Antidiabetic activity of hydroalcohol extract of whole plant of *cynodon dactylon* Linn. In streptozotocin induced diabetic rats. Treatment with *Cynodon dactylon* hydro alcohol extract at two different dose 200 mg/kg and 400 mg/kg and its comparison with standard drug Glibenclamide 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* Linn at dose of 200mg/kg and 400mg/kg shows more significant result than some of standard flavonoids. Thus, whole plant of *Cynodon dactylon* Linn. may have potential Antidiabetic agent.

Key words: *cynodon dactylon*, Streptozotocin, Flavonoids

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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 someof 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 populationworldwide is affected and expected toincrease 5.4% in 2025[4].these facts show that's proposing as immediate strategy for diabetes prevention and treatment is aglobal 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 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 animals8. 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 used9. 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-cells10. Cynodon dactylon Linn.

Belonging to family Gramineae/Poaceae commonly known as doob, durwa or bermuda grass. The grass grows throughout India ascending upto 8000 ft. It is particularly abundant on road sides and paths, and readily takes possession of any uncultivated area. It grows on all kinds of soil, even on alkali soil but prefers heavier types. It flowers nearly throughout the year.[11] *cynodon dactylon* Linn. has been reported for dermatitis[12] hay fever[13]. Analgessic [14]. anticystitis, antihypertensive, antihysteria, antigonorrheal infection, antiviral as well as hypolipidemic, hypoglycaemic agent.[15-18].

It contain flavonoids[19] 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 *cynodon dactylon* Linn. 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 *cynodon dactylon* Linn were collect from local areas of Jaipur. 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 freeaccess to commercial rat pallet diet (Lipton Indian ltd., Mumbai, India) andwater *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 toinduce 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 250 mg/dl were considered diabetic and were included inthe 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 Glibenclamide (5 mg/kg bw, p.o.)

Group IV- Rats were given streptozotocin (50mg/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 *cynodon dactylon* Linn. (200 mg/ kg/ day, bw, p.o.)

Group VIII- Rats were given streptozotocin (50 mg /kg, bw, p.o.) Plus drug *cynodon dactylon* Linn. (400 mg/ kg/ day, bw, p.o.)

For multi dose study blood sample were collected on 0, 5, 10 and 15 days after the administration of the extracts, standard Flavonoids, standard drug (Glibenclamide) and vehicle (water). Glucose level was estimated using glucose-oxidase -perxosidase reactive strips and glucometer.

Serum lipid profiles on day 15 were measured by an autoanalyzer, pancreas histopathological examination was performed after sacrificing the animal under anesthesia on 15th day and body weight measurement were carried out on days 0, 5, 10 and 15 of study. Glucose level was estimated.

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 days.

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

Group	Treatment	Dose (mg/kg)	Blood glucose concentration (mg/dl) (Mean ± S.E.M.)			
			Zero day	5th day	10th day	15th day
I	Control	Vehicle	97.78 ± 0.59	97.18 ± 0.82	96.68 ± 0.80	97.45 ± 0.68
II	Only Streptozotocin	50	265.38 ± 3.86^{+++}	274.21 ± 2.92^{+++}	302.85 ± 4.32^{+++}	301.36 ± 4.82^{+++}
III	Streptozotocin + Glibenclamide	5	263.65 ± 1.79	231.16 ± 3.09***	190.66 ± 2.39***	160.5 ± 1.30*** (39.12%)
IV	Streptozotocin + Quercetin	100	260.63 ± 2.00	231.18 ± 4.78***	199.63 ± 2.67***	164.76 ± 1.93***(36.78%)
V	Streptozotocin + Kaempferol	100	263.25 ± 1.56	235.10 ± 2.14***	198.51 ± 2.28***	168.1 ± 1.65***(36.14%)
VI	Streptozotocin + Epicatchin	100	265.03 ± 3.01	239.4 ± 2.75***	202.56 ± 2.40***	177.36 ± 1.59***(33.07%)
VII	Streptozotocin + CDHAE	200	263.83 ±1.64	242.91 ± 1.36**	203.88 ± 3.09***	184.51 ± 2.20***(30.06%)
VIII	Streptozotocin + CDHAE	400	264.88 ± 2.34	232.13 ± 1.27***	197.0 ± 2.99***	167.46 ± 1.24***(36.77%)

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.

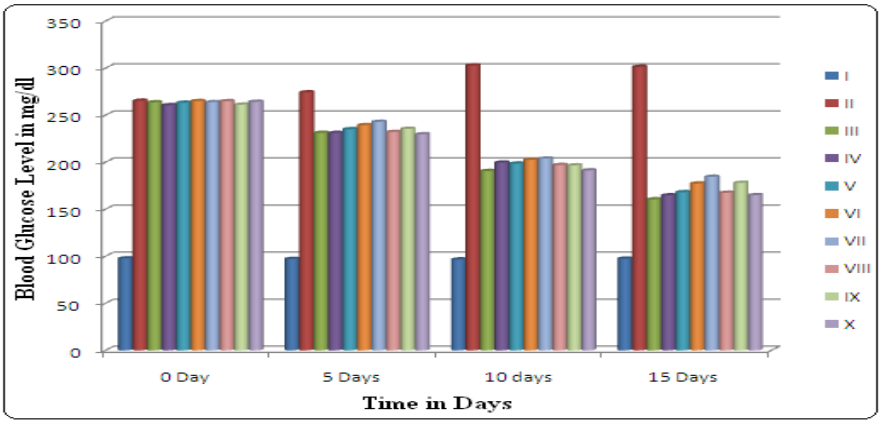


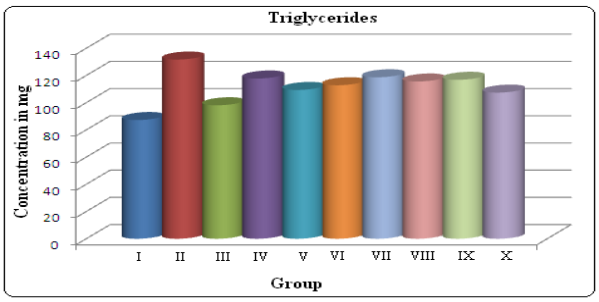
Figure 1: Strepatozotocin Induced Sub-acute (Multi days) Study

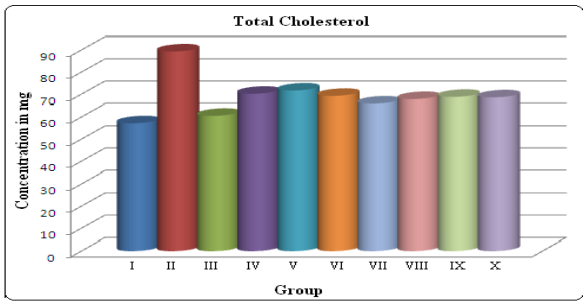
Group	
I	Control
II	Only Streptozotocin
III	Streptozotocin + Glibenclamide (5 mg/kg
IV	Streptozotocin + Quercetin (100 mg/kg)
V	Streptozotocin + Kaempferol (100 mg/kg)
VI	Streptozotocin + Epicatchin (100 mg/kg)
VII	Streptozotocin + *Cynodon dactylon* (200 mg/kg)
VIII	Streptozotocin + *Cynodon dactylon* (400 mg/kg)

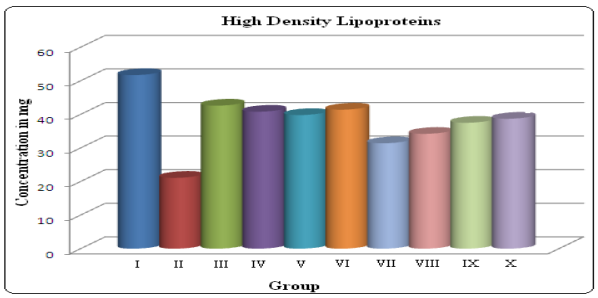
Table 2: Strepatozotocin Induced Sub-acute (Multi Dose) Serum Profile Study

Group	Treatment	Dose (mg/kg)	TG mg/dl	HDL mg/dl	Total Cholesterol mg/dl	Total Protein mg/dl
I	Control	Vehicle	87.28 ± 1.64	51.7 ± 2.37	57.20 ± 1.23	8.7 ± 0.81
II	Only Streptozotocin	50	131.73 ± 2.85^{+++}	21.1 ± 2.42^{+++}	89.38 ± 2.11^{+++}	5.8 ± 0.82^{+++}
III	Streptozotocin+ Glibenclamide	5	98.11 ± 2.63***	42.6 ± 2.13***	60.56 ± 2.73***	7.2 ± 0.63***
IV	Streptozotocin + Quercetin	100	117.80 ± 3.28**	40.8 ± 3.84***	70.21 ± 3.28**	7.6 ± 0.96**
V	Streptozotocin + Kaempferol	100	109.38 ± 3.47***	39.8 ± 2.61**	71.70 ± 4.51**	6.4 ± 0.53***
VI	Streptozotocin + Epicatchin	100	112.84 ± 2.08***	41.4 ± 3.79***	69.26 ± 1.65**	7.2 ± 0.84**
VII	Streptozotocin + CDHAE	200	118.71 ± 1.65*	31.4 ± 2.15^{NS}	65.82 ± 3.20***	6.6 ± 0.73*
VIII	Streptozotocin + CDHAE	400	115.60 ± 2.86**	34.2 ± 2.86^{NS}	67.85 ± 3.48***	6.2 ± 0.62*

All values are represented as Mean ± SEM (n=6)
P Value: +++ <0.001; ++ <0.01; + <0.05 When compared with control animals.
*** <0.001; ** <0.01; * <0.05 When compared with streptozotocin treated model.
NS= Not Significant







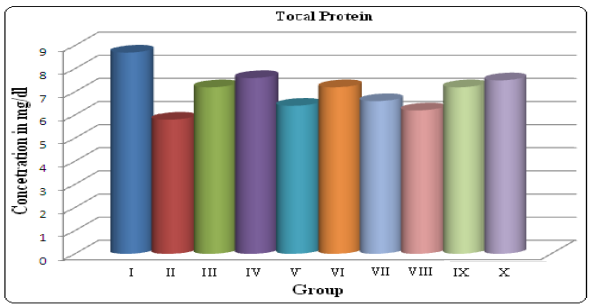


Figure 2: Triglyceride (TG) and High density lipoprotein (HDL) levels in streptozotocin Induced diabetes in rats (Multi days study)

Figure 3: Total cholesterol (TC) and Total protein (TP) levels in streptozotocin Induced diabetes in rats (Multi days study)

Group	
I	Control
II	Only Streptozotocin
III	Streptozotocin + Glibenclamide (5 mg/kg
IV	Streptozotocin + Quercetin (100 mg/kg)
V	Streptozotocin + Kaempferol (100 mg/kg)
VI	Streptozotocin + Epicatchin (100 mg/kg)
VII	Streptozotocin + *Cynodon dactylon* (200 mg/kg)
VIII	Streptozotocin + *Cynodon dactylon* (400 mg/kg)

Group	
I	Control
II	Only Streptozotocin
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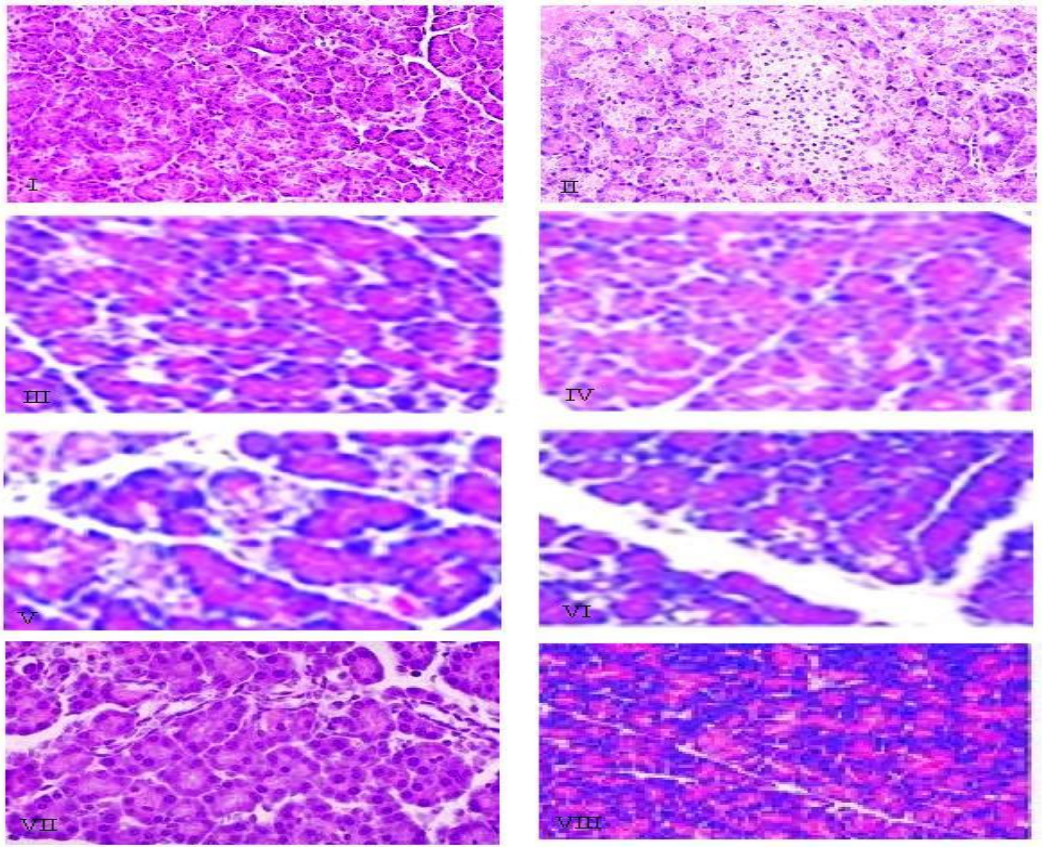

Figure 4: Histopathology of pancreas in streptozotocin induced diabetes in rats (multi days study)

Group	
I	Control
II	Only Streptozotocin
III	Streptozotocin + Glibenclamide (5 mg/kg)
IV	Streptozotocin + Quercetin (100 mg/kg)
V	Streptozotocin + Kaempferol (100 mg/kg)
VI	Streptozotocin + Epicatchin (100 mg/kg)
VII	Streptozotocin + *Cynodon dactylon* (200 mg/kg)
VIII	Streptozotocin + *Cynodon dactylon* (400 mg/kg)

RESULTS AND DISCUSSION

In streptozotocin multi dose 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 ppercent decrease in glucose level was observed in Percentage reductions produce by Glibenclamide, quercetin, kaempferol and epicatchin. The value being 39.12, 36.78, 36.14 and 33.07% respectively for CD-HAE 200 and 400 mg/kg treated group Fig.1

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

Serum lipid profile was studied in streptozotocin induced diabetic grouped on 15th day of treatment. Triglycerides level (TG), HDL level, Total cholesterol (TC) and level of Total protein (TP) was estimated.

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 Glibenclamide, kaempferol, epicatechin, and *cynodon dactylon* -400 showed high significant reduction ($p<0.001$). quercetin and *cynodon dactylon* -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 Glibenclamide, epicatechin and *cynodon dactylon* -400 ($p<0.01$), kaempferol, *cynodon dactylon* -200 and *cynodon dactylon* -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 *cynodon dactylon* 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 Glibenclamide, kaempferol, quercetin and *cynodon dactylon* -400 showed highly significant ($p<0.001$) increase in TP. Whereas epicatechin showed significant level of ($p<0.01$), *cynodon dactylon* -200 showed significant level of ($p<0.05$) when compared with diabetic control group.

Effect of extracts, flavonoids on Histopathological profiles of pancreases on STZ induced diabetic rats:

Figure 4 (I) shows an islet of Langerhans of Wistar rats in the normal control group. The islet shows a high number of beta cells dispersed all through the islet. In the diabetic group, a fall in the number of beta cells was observed as compared to that in the normal control group rats (Figure 4 (II). The degeneration of the beta cells was caused by the streptozotocin used to trigger diabetes. The improvement of necrotic beta cells was remarkably more distinct after treatment with 5 mg/kg Glibenclamide (Figure 4 (III) Histopathology of the Flavanoids -treated groups shows the partial repair of islets of Langerhans, as shown in Figures 4(IV), 4(V), and 4(VI). Treatments with 200 ,400 mg/kg extract have significantly increased the reduction of Langerhans islet diameter. (Figure 4 (VII) , 4(VIII).

CONCLUSION:

In conclusion, our current study has established that the Hydroalcoholic extracts cynodon dactylon Linn . could be considered to be used as antidiabetic drugs. The antihyperglycemic activity is suggested from the significant reduction in blood glucose levels, triglyceride levels and increase HDL level , pancreatic levels Cynodon dactylon Linn. hydro-alcoholic extract is a natural flavanoids with profound biological and pharmacological properties that ameliorate the pancreatic damage induced by the streptozocin.

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