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EVALUATION OF ANTI-DIABETIC ACTIVITY OF METHANOL EXTRACT OF *FLACOURTIA JANGOMAS* (LOUR) IN STREPTOZOTOCIN INDUCED DIABETIC RATS

N. SURJIT SINGH*, M. GEETHA, P. AMUDHA AND AVIJIT CHAKRABORTY

Department of Pharmacology and Toxicology, C.L. Baid Metha College of Pharmacy, Jyothi Nagar, Old Mahabalipuram Road, Thoraipakkam, Chennai-600097, India.

****Corresponding Author*** surjitpharma@gmail.com

ABSTRACT

The present study was undertaken to evaluate the antidiabetic activity of methanol extract of *Flacourtia jangomas* (lour) in streptozotocin induced diabetic rats. In this study, the acute and subacute anti hyperglycaemic effect of the two different doses (200 and 400 mg/kg b.w.p.o) of plant extracts were investigated. Fasting blood glucose level, body weight and serum lipid profiles were evaluated in normal and diabetic rats. The liver and muscle glycogen level were also evaluated. Supplementation of this extract significantly reduces the fasting blood glucose level and increases the -8.1359(y)rmal and diabetic rats. The liver an d muscle glycogen level were also evaluated. Supplementation of this extract significantly reduces the fasting blood glucose level and increases the -8.1359(y)rmal and diabetic rats. The liver an d muscle glycogen level were also evaluated. Supplementation of this extract significantly reduces the fasting blood glucose level and increases the -8.1359(y)rmal and diabetic rats. The liver an d muscle glycogen level were also evaluated. Supplementation of this extract significantly reduc

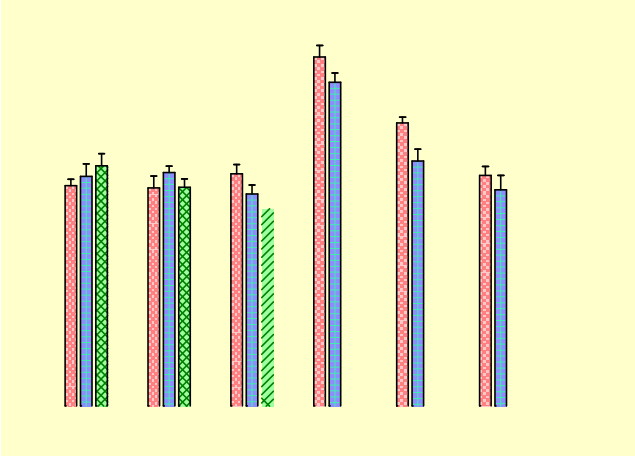

Table 1.

Effect of MEFJ on Total Cholesterol, HDL-Cholesterol, Triglycerides, LDL and VLDL in STZ induced diabetic rats

Group	Treatment	Total Cholesterol (mg/dl)	HDL-Cholesterol (mg/dl)	Triglycerides (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
I	Control (distilled water)	99.78±5.34	34.35±2.34	87.56±2.43	47.8±2.56	17.4±1.56
II	Diabetic control (STZ)	177.60±2.37[a]**	23.34±1.67[a] **	172.5±3.45[a] **	119.4±2.04[a] **	34.4±1.85[a] **
III	MEFJ (200mg/kg)+ STZ	128.6±2. 89[b]**	29.45±2.05[b]*	122.3±2.93[b] **	74.6±2.8[b] **	24.4±1.09[b] **
IV	MEFJ (400mg/kg)+ STZ	112.7±3.57[b]**	34.10±1.43[b]**	102.7±3.76[b]**	57.8±3.2[b] **	20.4±2.30[b] **
V	Glibenclamide +STZ	104.56±4.63[b]**	40.21±2.06[b]**	92.12±1.87[b] **	45.6±2.7[b] **	18.4±1.32[b] **

*n = 6, *p < 0.05, **p < 0.01, ns- non-significant, (one way ANOVA followed by Dunnett's 't' test)*
a- Group II is compared with Group I.
*b- Groups III, IV, V are compared with group II **P<0.01,*P<0.05*

Administration of the MEFJ (200 and 400mg/kg) increased liver and muscle glycogen level significantly (p<0.05) and (p<0.01) in respective group. Glibenclamide (0.5mg/kg) show significant (p<0.01) increase when compared to STZ induced diabetic animals. (Table 2)

Table 2.

Effect of MEFJ on the liver and Muscle glycogen in STZ induced diabetic rats

Group	Treatment	Liver glycogen (mg/g wet tissue)	Muscle glycogen (mg/g wet tissue)
I	Control(distilled water)	50.0±2.13	8.21±0.54
II	Diabetic control (STZ)	17.56±0.72[a] **	2.62±0.30[a] **
III	MEFJ(200mg/kg)+STZ	22.50±0.98[b] *	4.65±0.36[b] *
IV	MEFJ(400mg/kg)+STZ	35.53±0.57[b] **	6.18±0.33[b] **
V	Glibenclamide +STZ	42.62±0.76[b] **	7.15±0.27[b] **

*n = 6, *p < 0.05, **p < 0.01, ns- non-significant, (one way ANOVA followed by Dunnett's 't' test)*
a- Group II is compared with Group I.
*b- Groups III, IV, V are compared with group II **P<0.01,*P<0.05*

Histopathological study of pancreas

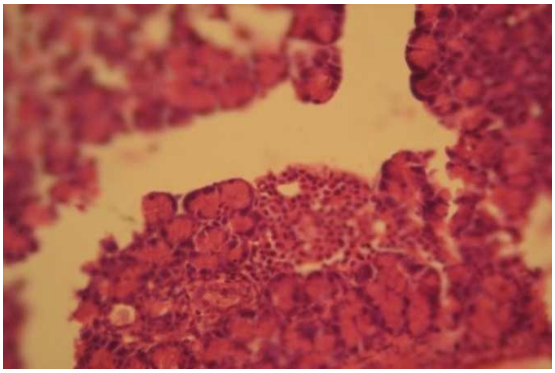

Fig: A

Fig-A: ***The Pancreatic islets of langerhans of normal rat show normal islets and acini.***

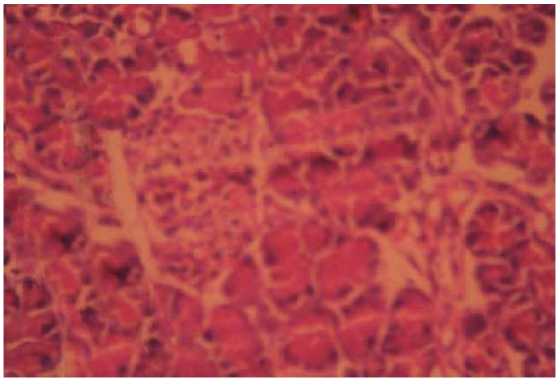

Fig: B

Fig-B: ***Streptozotocin induced diabetic pancreatic islets shows damaged and atrophic islet with acni***

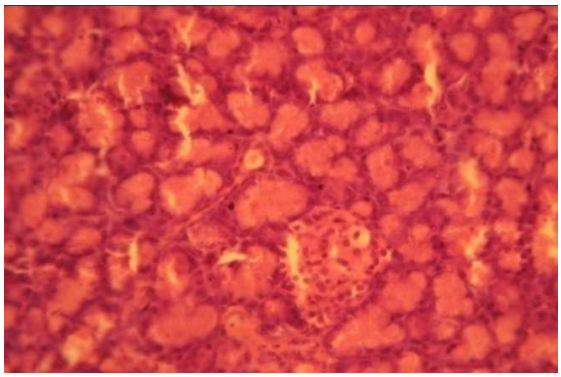

Fig: C

Fig-C: ***MEFJ (200mg/kg) treated pancreatic islets show small pancreatic islet cells.***

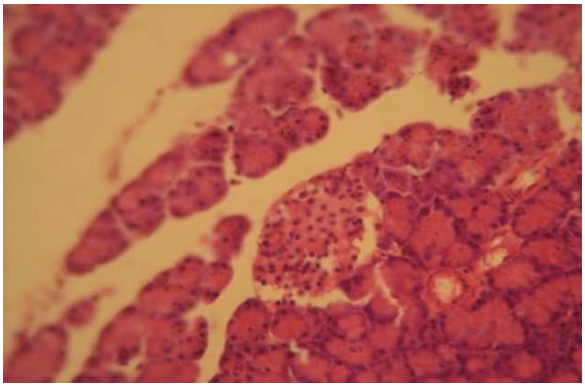

Fig: D

Fig-D: ***MEFJ (400mg/kg) treated pancreatic islets show hyperplastic islet with acni.***

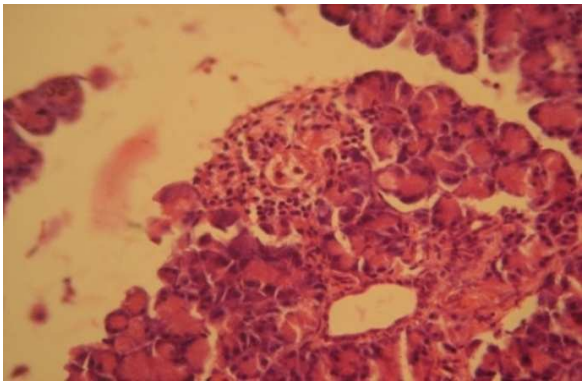

Fig: E

Fig-E: ***Glibenclamide (0.5 mg/kg) treated pancreatic islets shows preserved cells.***

DISCUSSION

The present study was undertaken to investigate the antidiabetic activity of methanol extract of *Flacourtia jangomas* (lour).in STZ induced diabetic rats. The MEFJ at a dose 200mg/kg and 400mg/kg did not significantly suppress blood glucose level in over night fasted normoglycaemic animals but showed significant improvement in glucose tolerance in glucose fed hyperglycaemic normal rats. Such an effect may be accounted for, in part, by a decrease in rate of intestinal glucose absorption, achieved by an extra pancreatic action including stimulation of peripheral glucose utilization or enhancing glycolytic and glycogenic process.[20] However, the effect was significant when compared to standard drug glibenclamide. A single dose administration of MEFJ at a dose 200mg/kg and 400mg/kg significantly reduce blood glucose level at 120 and 240min. In the sub-acute study, glibenclamide treatment reduces blood sugar level from the first week to third week. Treatment with MEFJ at dose 200mg/kg and 400mg/kg significantly decreased the blood glucose level after the second and first week. At the end of the study a marked anti hyperglycemic effect was observed in the MEFJ treatment. Possible mechanism involved with suppressing blood glucose levels by MEFJ are 1) modulation glucose transport, 2) glucose disposal, 3) insulin secretion, which in turn control the hyper glycemic state.[21]

Induction of diabetes with STZ is associated with the characteristic loss of

body weight which is due to increased muscle wasting and due to loss of tissue protein. Diabetic rats treated with MEFJ show an increase in the body weight as compared to the diabetic control which may be due to its protective effect in controlling muscle wasting i.e reversal of gluconeogenesis and may also be due to the improvement in insulin secretion and glycemic control.[22]

Lipid plays an important role in the pathogenesis of complications involved with diabetes mellitus. The elevated level of serum cholesterol and reduced level of serum HDL cholesterol in diabetic condition, poses to be a rises of factor for developing microvascular complication leading to atherosclerosis and further leads to cardiovascular diseases like coronary heart disease. The abnormal high concentration of serum lipid in diabetic mainly due to increased mobilization of free fatty acids from peripheral fat depots, since insulin inhibits the hormone sensitive lipase, insulin deficiency or insulin resistance may be responsible for dislipidimia.[23] Present study showed rat streptozotocin treated diabetic rats has abnormal lipid profile whereas the MEFJ treated group showed significant improvement in the lipid profile comparable to glibenclamide treatment group. This effect not only due to better glycemic control but could also been due to inhibition of the pathway of cholesterol synthesis and increased HDL/LDL ratio may be due to the activation of LDL receptors in hepatocyte, which is responsible for taken up LDL into the liver and reduce the serum LDL level.[24] Hypolipidemic effect could represent a protective mechanism against the development of atherosclerosis. It is well known that hyperlipidemia has an association with atherosclerosis's and the incidence of atherosclerosis is vastly increased in diabetics.[24]

Insulin is the main regulator of glycogenesis in muscle and liver. The decrease of liver glycogen level observed in this study may be due to lack of insulin in diabetic condition or oxidative stress by diabetes may inactivate the glycogen synthetase. The marked reduction in liver and muscle glycogen level is observed (21 days) in streptozotocin induced diabetic animals. Treatment with MEFJ extract remarkably increased the glycogen level in liver and muscle. In the view of glycogen level, there may be three possible ways of antidiabetic action; one possible way may be increased insulin level by preventing the inactivation of the glycogen synthetase and by synthesize the glycogen synthatase.[25]

Histopathological studies, revealed in streptozotocin treated group necrosis of β-cells were confirmed. Glibenclamide treated group show preserved cytology. At 200mg/kg MEFJ treated rats shows small islet cells whereas 400mg/kg MEFJ treated rats shows an hyperplastic i.e, regulation of β-cells confirms the MEFJ at 400mg/kg.

CONCLUSION

From such information it may be stated that the antidiabetic activity of MEFJ may be by sensitize the insulin receptor or stimulation of insulin from β-cell of islets of Langerhans in pancreas of STZ induced diabetic rats.

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