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ANTIDIABETIC EFFECT OF ETHANOLIC EXTRACT OF *MURRAYA KOENIGII* (LINN.) STEM BARK IN ALLOXAN INDUCED DIABETIC RATS

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Keywords:

Murraya koenigii, Stem bark, Ethanolic, Alloxan, Antidiabetic

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ABSTRACT: Introduction: The objective of the present work was to study the antidiabetic effect of ethanolic extract of *Murraya koenigii* stem bark (EEMK) in alloxan-induced diabetic rats. **Materials and Methods:** Male Wistar albino rats weighing between 150-250 g were used for this study. The rats were divided into five groups (n=6). Group, I served as the diabetic control, group II served as diabetic control, groups III, IV served as test groups, and group V served as a standard group. The diabetes was induced by a single dose of alloxan (140 mg/kg, i.p.) in all the groups except normal control group. Then the rats of respective groups were treated with normal saline, EEMK (125 mg/kg and 250 mg/kg) and metformin (50 mg/kg) for 11 days. Blood glucose estimation was performed on 0, 1, and 11 days. At the end of this study period, animals were sacrificed for studying biochemical parameters. **Results:** Alloxan-induced diabetic rats showed marked hyperglycemia at the end of the study period. Body weight and liver glycogen levels were reduced in diabetic rats. The 11-day treatment with EEMK (125 mg/kg and 250 mg/kg) significantly ameliorated the alterations in fasting blood glucose, serum triglycerides, serum cholesterol, liver glycogen, and body weight in diabetic rats. Moreover, the oral glucose tolerance test revealed that the extract was found to increase glucose tolerance. **Conclusion:** Thus, the present study suggested the potential of EEMK in diabetes mellitus.

INTRODUCTION: Diabetes mellitus is a common endocrine disorder caused due to either deficiency in insulin production or due to the ineffectiveness of the insulin produced. Such a deficiency results in impaired metabolism of glucose and other energy-yielding fuels like lipids and proteins [1]. Diabetes mellitus is considered as one of the five leading causes of death in the world as it causes micro and macrovascular complications resulting in significant morbidity and mortality [2, 3].

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As per WHO report, approximately 150 million people have diabetes mellitus worldwide, and this number may well double by the year 2025 [4]. In modern medicine no satisfactory effective therapy is still available to cure diabetes mellitus. Moreover, due to the high cost of allopathic drugs, it is difficult to provide modern medicinal healthcare, especially in developing countries [5].

There is an increasing demand by the patients to use natural products with antidiabetic activity due to side effects associated with the use of insulin and oral hypoglycemic agents available in the market. It is, therefore, necessary to make use of vast reserves of plant origins for medicinal purposes which will help to search effectively as well as safer drug remedy for diabetes mellitus [6-8].

Murraya koenigii Spreng. belonging to family Rutaceae, commonly known as "Curry Patta" is a deciduous aromatic shrub, up to a height of 6 meters. *Murraya koenigii* is native to tropical Asia from Himalaya foothill's of India to Shrilanka eastward through Myanmar, Indonesia, Southern China and Hainan. In India, it occurs in the foothill of Himalaya, Assam, Sikkim, Kerala, Tamil Nadu, Andhra Pradesh and Maharashtra [9, 10].

Various parts of *Murraya koenigii* have been used in traditional or folk medicine for the treatment of rheumatism, traumatic injury [11, 12] snake bite and it has been reported to have antioxidant, antidiabetic, antidysenteric [13, 14], antioxidant, anticancer, anti-inflammatory, antifungal and immunomodulatory activities [15, 16]. EEMK was subjected to preliminary phytochemical investigation, which showed the presence of alkaloids, flavonoids, tannins, and carbohydrates. The phytochemicals are responsible for its potential in the treatment of diabetes mellitus. In light of this, present work was undertaken to study the antidiabetic effect of EEMK in alloxan-induced diabetic rats to focus on the mechanism underlying the activity.

MATERIALS AND METHODS:

Plant Material: The stem bark of *Murraya koenigii* was collected from Moshi, Pune. The plant was authenticated by Dr. Jayanti, Botanical Survey of India, Yerwada, Pune.

Preparation of Extract: The stem bark of *Murraya koenigii* was collected, and shadow dried. It was subjected to pulverization to get a coarse powder. The coarse powder was used for extraction with ethanol in the Soxhlet apparatus. The extract was then evaporated to dryness under vacuum and dried further in a vacuum desiccator.

Animals: For acute toxicity test, Swiss albino mice (25-30 gm) and antidiabetic activity, male Wistar rats (150-250 gm) were used. After randomization into various groups and before initiation of the experiment, the rats were acclimatized for 7 days under standard environmental conditions of temperature, relative humidity, and dark/light cycle. Before and during the experiment, rats were fed with a standard diet (Nutrivet life sciences).

Animals mentioned as fasting were deprived of food and water for 16 h *ad libitum*. The rats were shifted to the laboratory at least 1h before the start of the experiment. The experiments were performed during the day (08:00-16:00 h).

Ethical Clearance: All the studies were carried out as per the guidelines are given by the Indian Council for Medical Research and the Committee for Control and Supervision of Experiments on Animals (CPCSEA), New Delhi (India) and the Institutional Animal Ethical Committee approved the study (Approval No.: 1036/PO/Re/S/CPCSEA/ 16-17/F1).

Acute Oral Toxicity Study: EEMK was tested for its acute and short term toxicity in mice. To determine acute toxicity of the drug, overnight fasted Swiss albino mice were orally fed with extract in increasing dose levels of 100, 500, 2500, and 3000 mg/kg body weight. The mortality and general behavior of these animals were observed periodically for 48 h. The animals were observed continuously for the starting period of 4 h, intermittently for the next 6 h, then again at 24 h and 48 h following after the drug administration. The parameters observed were grooming, hyper-activity, sedation, loss of righting reflex, and convulsions [17].

Determination of Test Dose: During preliminary toxicity study, no adverse effects or mortality was observed in experimental animals with EEMK up to a high dose of 2500 mg/kg body weight observed for 24 h. Hence submaximal doses of 125 mg/kg and 250 mg/kg were selected as a test dose.

Oral Glucose Tolerance Test: The acclimatized animals were fasted for 24 h with water *ad libitum*, fasted animals were divided into three groups of six rats each. Group, I served as control received distilled water. Group II received metformin at an oral dose of 450 mg/kg, p.o. Group III received EEMK at the dose of 500 mg/kg p.o. After initial (0 hrs) withdrawal the of blood samples and after 30 min of extract administration, the rats of all groups were orally treated with 2 gm/kg glucose. Blood samples were collected at the interval of 30, 45, 60, 180 min, after glucose loading from retro-orbital plexus under anesthesia [18].

Experimental Design: The rats were then divided into five groups containing 06 each. Group, I served as a normal control group and received

normal saline solution (1 ml/kg, p.o.). Group II also received a normal saline solution (1 ml/kg, p.o.) and served as BCCAO control group. Groups III and IV served as test groups and received EEMK orally at doses of 125 mg/kg, and 250 mg/kg, respectively and Group V served as a standard group and received metformin (50 mg/kg, p.o.). Rats of all the groups except normal control group were made diabetic by a single intraperitoneal injection of alloxan monohydrate (140 mg/kg) [19]. Alloxan was weighed individually for each animal according to respective body weight and then solubilized using saline (154 mM NaCl) just before injection. Animals were fed with 5% glucose solution to prevent hypoglycemic shock for 24 h. After three days of alloxan injection, rats having plasma glucose levels of >140 mg/dl were included in the study. 72 h after alloxan injection, treatment with respective drugs was started and continued for 11 consecutive days.

Collection of Blood Sample and Blood Glucose Estimation: Blood samples of all the rats were drawn from retro-orbital plexus on 0, 1 and 11 day and fasting blood glucose estimation was done by using glucose oxidase-peroxidase reactive strips (Accu-chek, Roche Diagnostics, USA). Body weights were recorded on days 0, 3, and 11 during the study.

Estimation of Biochemical Parameters: On 11th day, 1 h after respective drug treatments, blood of all the rats was collected from retro-orbital plexus, and the serum was separated for the determination of parameters like total cholesterol, triglycerides, HDL, LDL, creatinine, urea and total protein content using commercially available kits (Span diagnostics). Liver glycogen was estimated by the method of Carroll [20].

Collection of Pancreas, Liver, Kidney, and Heart: The rats were sacrificed after blood collection on day 11 by cervical dislocation and organs were excised immediately, thoroughly washed with ice-cold physiological saline and were fixed in 10% formalin solutions. Organs were immediately processed by the paraffin technique. Sections which are having a thickness of 5µ were cut and stained by using hematoxylin and eosin for histological examination.

Statistical Analysis: All results are expressed in the form of mean ± SEM. The results were analyzed for their statistical significance by applying one way ANOVA followed by Dunnett's test for comparison for oral glucose tolerance test and one way ANOVA followed by Tukey's Kramer multiple comparison test for antidiabetic activity. Values obtained as $P<0.05$ were considered significant.

RESULTS:

Effect on Oral Glucose Tolerance Test: The effects of EEMK (500 mg/kg) on glucose tolerance test are shown in **Table 1**. The supplementation of *Murraya koenigii* improved glucose tolerance in the fasted normal rats. Blood glucose level was lowered significantly at 45 ($P<0.01$) and 180 ($P<0.05$) minutes. The extract showed significant hypoglycaemic effect after 45 min of treatment.

TABLE 1: EFFECT OF ALCOHOLIC EXTRACT OF *MURRAYA KOENIGII* STEM BARK ON ORAL GLUCOSE TOLERANCE TEST IN GLUCOSE LOADED NORMAL RATS

Groups	Fasting Blood glucose (mg/dl)				
	O min	30 min	45 min	60 min	180 min
Normal Control	65 ± 3.6	117 ± 2.2	123 ± 5.6	115 ± 3.6	96 ± 1.9
EEMK 500	76 ± 4.3	103 ± 2.7	97 ± 3.2**	104 ± 4.5*	92 ± 5.5
MET 50	73 ± 3.5	104 ± 4.5	106 ± 5.1**	100 ± 5.2*	91 ± 7.6

All results are expressed as the mean ± SEM. The results were analyzed for statistical significance by one way ANOVA followed by Dunnet's test for comparison. Values of $P<0.05$ were considered significant. *$P<0.05$, **$P<0.01$. EEMK: Ethanolic extract of *Murraya koenigii* stem bark; MET: Metformin

Effect on Blood Glucose Levels: The anti-diabetic effects of the extracts on the fasting blood sugar levels of diabetic one shown in **Table 2**. Administration of alloxan (140 mg/kg, i.p) led to the 1.5-fold elevation of fasting blood glucose levels, which was maintained for a period of 11 days. 11 days of daily treatment of alcoholic extracts of *Murraya koenigii* stem bark (125 and 250 mg/kg) led to a significant ($P<0.001$) fall in blood sugar levels by 36.10% and 15.52% respectively.

TABLE 2: EFFECT OF ALCOHOLIC EXTRACT OF STEM BARK OF *MURRAYA KOENIGII* ON BLOOD GLUCOSE LEVEL IN ALLOXAN INDUCED DIABETIC RATS

Groups	Fasting Blood glucose (mg/dl)		
	0^{th} day	1^{st} day	11^{th} day
Normal control	82 ± 21	90 ± 0.5	92 ± 0.3
Diabetic control	276 ± 20***	247 ± 5.9***	190 ± 5.3***
EEMK 125	215 ± 87***	190 ± 6.0##	136 ± 4.8###
EEMK 250	177 ± 4.9##	165 ± 3.4##	112 ± 19###
MET 50	154 ± 3.5##	142 ± 2.9##	100 ± 5.1###

All results are expressed as the mean ± SEM. The results were analyzed for statistical significance by one way ANOVA followed by Tukey's Kramer multiple comparison test for comparison. Values of P<0.05 were considered significant. *#P<0.05, **, ##P<0.01,***, ###P<0.001. *-Diabetic control group rats compared against normal control rats, #-EEMK, and MET pretreated diabetic group rats compared diabetic control group rats. EEMK: Ethanolic extract of *Murraya koenigii* stem bark; MET: Metformin.

Effect on Biochemical Estimations: Serum urea, creatinine, cholesterol, triglycerides, LDL were decreased while HDL and total protein levels were increased significantly by metformin (p<0.001) and alcoholic extract (125 and 250 mg/kg) (p<0.001) after 11 days of treatment compared with diabetic control. Alcoholic extract (250 mg/kg) and metformin (450 mg/kg) decreased serum urea level significantly (p<0.001) by 44.70% and 22.35% respectively as compared to diabetic control. Alcoholic extract (125 mg/kg) showed significant (p<0.01) decrease in serum creatinine by 33.33% as compared to diabetic control. HDL level was increased by alcoholic extract of *Murraya koenigii* stem bark (125 and 250 mg/kg) (p<0.001) as compared with diabetic control.

TABLE 3: EFFECT OF ALCOHOLIC EXTRACT OF STEM BARK OF *MURRAYA KOENIGII* ON SERUM PROFILE IN ALLOXAN INDUCED DIABETIC ALBINO RATS AFTER 11 DAYS OF TREATMENT

Groups	Urea	CREAT	T-CH	TG	LDL	HDL	PROT
Normal control	74.67 ± 0.2	0.79 ± 0.04	68.70 ± 0.01	147.47 ± 5.2	10.56 ± 1.2	32.68 ± 0.4	13 ± 0.62
Diabetic control	135.8 ± 4.2***	0.148 ± 0.04***	114.15 ± 5.7***	225.09 ± 4.4***	20.31 ± 1.6***	25.33 ± 2.6***	8.2 ± 0.81***
EEMK 125	105.3 ± 3.5	0.85 ± 0.02##	84.45 ± 6.8##	195.54 ± 5.8###	13.89 ± 2.4###	28.03 ± 1.5##	9.5 ± 0.54##
EEMK 250	85.55 ± 4.2###	0.76 ± 0.14###	70.11 ± 5.6###	163.38 ± 4. 3##	11.90 ± 0.23###	30.34 ± 2.3###	10.85 ± 0.44###
MET 50	77.18 ± 2.1###	0.75 ± 0.06###	69.54 ± 0.15###	155.22 ± 3.3###	11.23 ± 0.33###	33.15 ± 1.3###	11.54 ± 0.81###

All results are expressed as the mean ± SEM. The results were analyzed for statistical significance by one way ANOVA followed by Tukey's Kramer multiple comparison test for comparison. Values of P<0.05 were considered significant. *, #P<0.05, **, ##P<0.01, ***, ###P<0.001. *-Diabetic control group rats compared against normal control rats, #-EEMK, and MET pretreated diabetic group rats compared diabetic control group rats. EEMK: Ethanolic extract of *Murraya koenigii* stem bark; MET: Metformin

TABLE 4: EFFECT OF ALCOHOLIC EXTRACT OF STEM BARK OF *MURRAYA KOENIGII* ON LIVER GLYCOGEN LEVEL IN ALLOXAN INDUCED DIABETIC RATS

Groups	Liver glycogen (mg/g)
Normal control	3.9 ± 0.06
Diabetic control	0.92 ± 0.0050***
EEMK 125	2.52 ± 0.0050##
EEMK 250	2.90 ± 0.0050###
MET 50	3.1 ± 0.050###

All results are expressed as the mean ± SEM. The results were analyzed for statistical significance by one way ANOVA followed by Tukey's Kramer multiple comparison test for comparison. Values of P < 0.05 were considered significant. *, #P<0.05, **, ##P<0.01, ***, ###P<0.001. *-Diabetic control group rats compared against normal control rats, #-EEMK, and MET pretreated diabetic group rats compared diabetic control group rats. EEMK: Ethanolic extract of *Murraya koenigii* stem bark; MET: Metformin.

Effect on Liver Glycogen Levels: As shown in **Table 4**, there was a significant decrease in liver glycogen levels in the diabetic control group as compared to normal rats. Oral administration of the alcoholic extract (125 and 250 mg/kg) and metformin (450 mg/kg) significantly (p<0.001) restored the decreased liver glycogen level as compared to diabetic control.

TABLE 5: EFFECT OF ALCOHOLIC EXTRACT OF STEM BARK OF *MURRAYA KOENIGII* OF BODY WEIGHT IN ALLOXAN INDUCED DIABETIC RATS

Groups	Body Weight (gm)	
	Initial	Final
Normal control	195.46 ± 4.5	205 ± 0.7
Diabetic control	198.34 ± 5.0	173.67 ± 0.54***
EEMK 125	179.46 ± 4.7	185.33 ± 0.62##
EEMK 250	196.35 ± 5.8	203.78 ± 5.6###
MET 50	241.78 ± 6.2	235.46 ± 6.1###

All results are expressed as the mean ± SEM. The results were analyzed for statistical significance by one way ANOVA followed by Tukey's Kramer multiple comparison test for comparison. Values of P<0.05 were considered significant. *, #P<0.05, **, ##P<0.01, ***, ###P<0.001. *-Diabetic control group rats compared against normal control rats, #-EEMK, and MET pretreated diabetic group rats compared diabetic control group rats. EEMK: Ethanolic extract of *Murraya koenigii* stem bark; MET: Metformin.

Effect on Body Weight: As shown in **Table 5**, diabetic rats showed significant (p<0.001) reduction in body weight from 198 g to 173 g as compared to the normal group. Oral administration of alcoholic extract of stem bark of *M. koenigii* (125 and 250 mg/kg) significantly (p<0.001) and periodically improved the body weight after 11 days as compared to diabetic control.

Histopathological Studies:

Effect on Histopathology of Pancreas: Histo-pathological studies of Group I show the normal cellular arrangement of pancreatic islets of Langerhans. Group II shows that in diabetic control, there is decline number of β and acinar cells. Normal cellular population in pancreatic islets of Langerhans shows dearrangement.

In Group III, IV, V shows an increase in the number of β cells and restoration of normal islet cells observed. It also shows the maintenance of β cells vacuolization and survival of β cells by less necrosis.

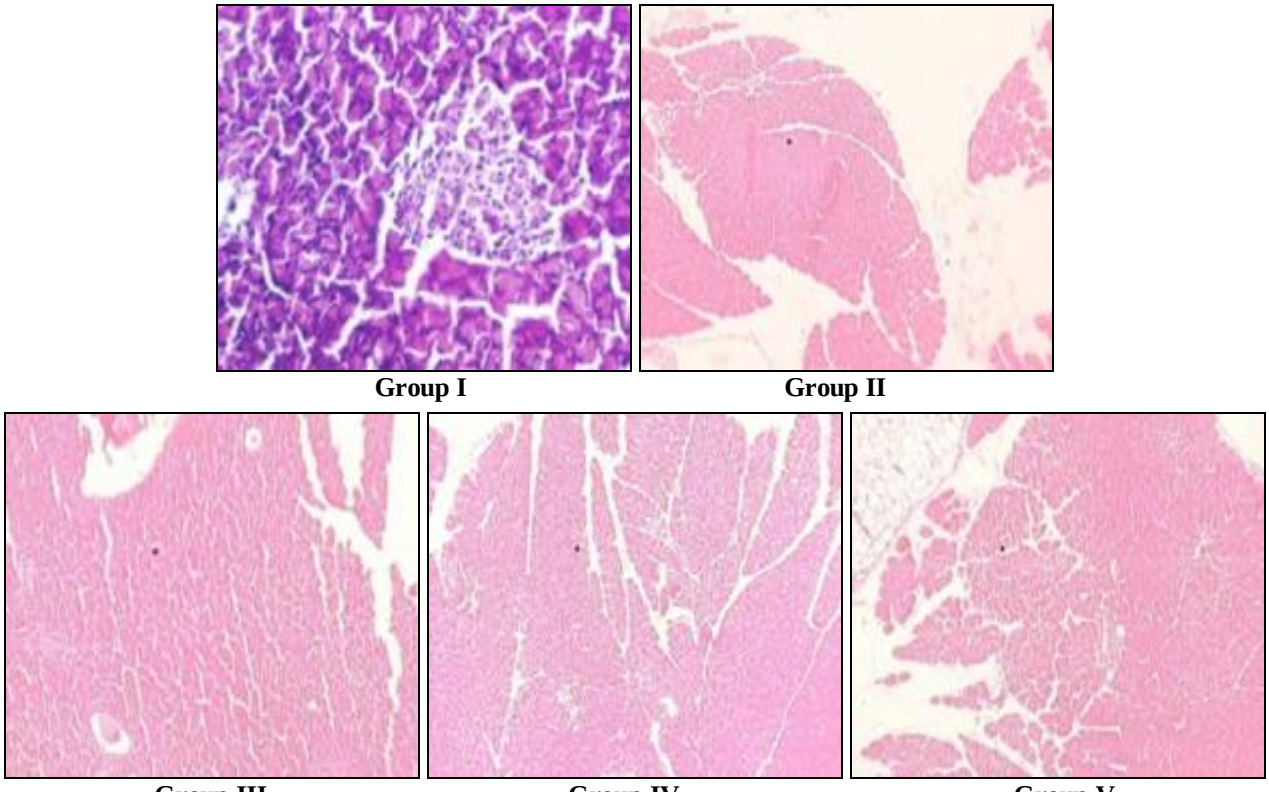

FIG. 1: REPRESENTATIVE PHOTOMICROGRAPHS (H & E STAIN) OF SECTIONS OF PANCREAS OF NORMAL CONTROL GROUP RATS (GROUP I), DIABETIC CONTROL GROUP RATS (GROUP II), EEMK 125 AND 250 mg/kg PRETREATED DIABETIC GROUP RATS (GROUP III & IV), MET 50 PRETREATED DIABETIC GROUP RATS OBSERVED UNDER 40X MAGNIFICATION

Effect on Histopathology of Liver: Histopathological studies of the liver of Group I showed normal histopathological structures of hepatic cords, hepatic artery, central hepatic veins, and hepatic sinusoids. Group II shows hepatic degeneration and intracellular accumulation and severe congestion of the central vein. Vacuolization in necrotic area of hepatocytes and inflammatory cells with fibrosis seen. Group III, IV, V shows regeneration, restoration of hepatocytes.

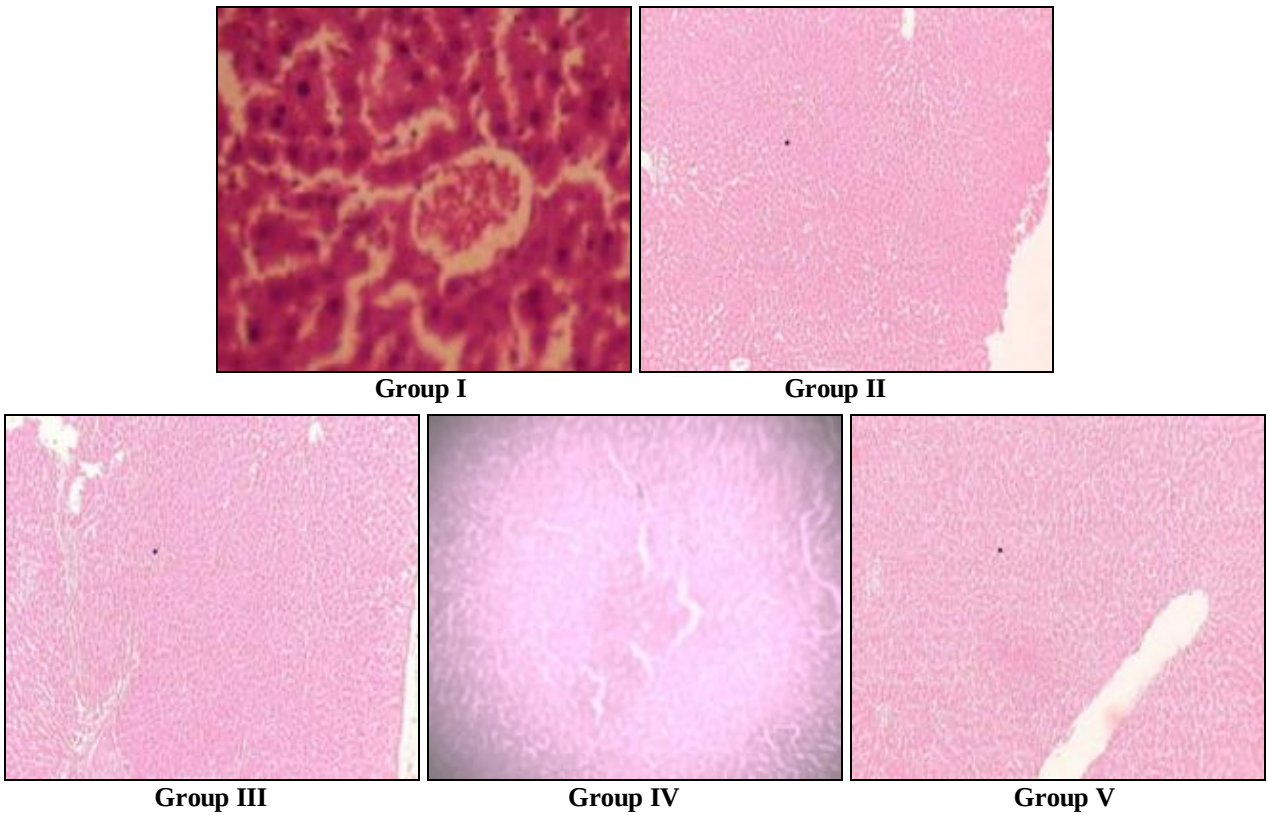

FIG. 2: REPRESENTATIVE PHOTOMICROGRAPHS (H & E STAIN) OF SECTIONS OF PANCREAS OF NORMAL CONTROL GROUP RATS (GROUP I), DIABETIC CONTROL GROUP RATS (GROUP II), EEMK 125 AND 250 mg/kg PRETREATED DIABETIC GROUP RATS (GROUP III & IV), MET 50 PRETREATED DIABETIC GROUP RATS OBSERVED UNDER 40X MAGNIFICATION

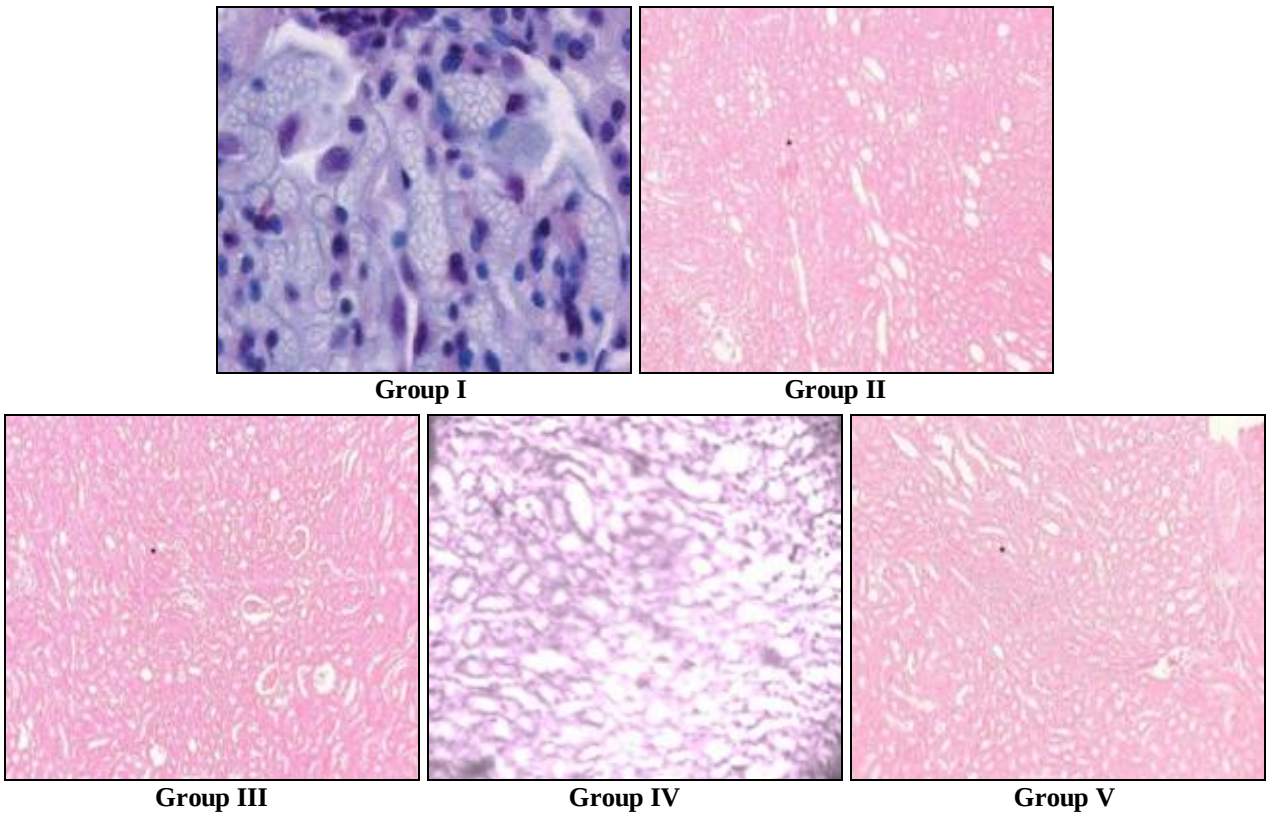

FIG. 3: REPRESENTATIVE PHOTOMICROGRAPHS (H & E STAIN) OF SECTIONS OF KIDNEYS OF NORMAL CONTROL GROUP RATS (GROUP I), DIABETIC CONTROL GROUP RATS (GROUP II), EEMK 125 AND 250 mg/kg PRETREATED DIABETIC GROUP RATS (GROUP III & IV), MET 50 PRETREATED DIABETIC GROUP RATS OBSERVED UNDER 40X MAGNIFICATION

Effect on Histopathology of Heart: Histo-pathological studies of Group I show wavy fibers and scattered neutrophils. Group II show an increase in distance between myofibrils. But the architecture of heart in Group III, IV, and V appear to be normal.

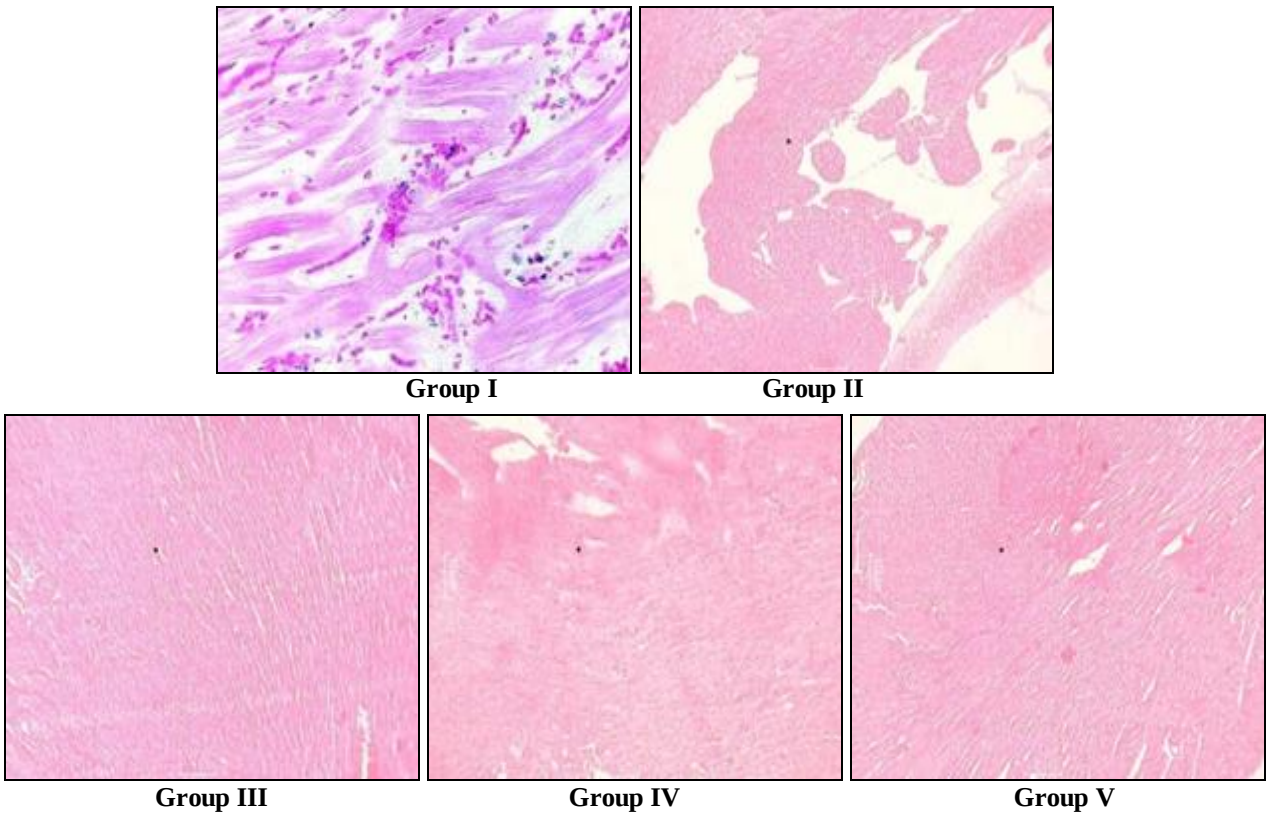

FIG. 4: REPRESENTATIVE PHOTOMICROGRAPHS (H & E STAIN) OF SECTIONS OF HEARTS OF NORMAL CONTROL GROUP RATS (GROUP I), DIABETIC CONTROL GROUP RATS (GROUP II), EEMK 125 AND 250 mg/kg PRETREATED DIABETIC GROUP RATS (GROUP III & IV), MET 50 PRETREATED DIABETIC GROUP RATS OBSERVED UNDER 40X MAGNIFICATION

DISCUSSION: At present, the treatment of diabetes mainly involves a sustained reduction in hyperglycemia by the use of oral hypoglycemic agents and insulin. However, due to untoward side effects, the efficacy of these compounds is debatable, and there is a demand for new compounds for the treatment of diabetes [21]. Hence, plants have been suggested as a rich and important but as yet unexplored source of potentially useful antidiabetic drugs.

The aim of the present study was to evaluate the antidiabetic effect of alcoholic extract of *Murraya koenigii* stem bark against alloxan-induced diabetic rats.

The oral glucose tolerance test results show that the plants extract shows antidiabetic effects on the blood glucose level in the fasting normal rats. Alcoholic extract (500 mg/kg) showed a significant reduction in blood glucose level within 3 h. This may be due to synergistic effects of the chemical constituents of stem bark of *Murraya koenigii* and shows a great promise as an oral antidiabetic agent.

In the present study, alloxan-induced diabetic rats exhibited a significant increase in blood glucose level. Treatment with alcoholic extract of *Murraya koenigii* stem bark (125 mg/kg) reduced blood glucose level significantly throughout the experimental period.

It has been reported that 75% of early deaths in diabetes mellitus are associated with coronary artery disease caused by abnormal lipid metabolism altering the lipid profile in the diabetic state. Metabolic disturbances of carbohydrates, lipids, and proteins during diabetes mellitus causes insulin deficiency stimulating lipolysis in adipose tissues. Diabetes mellitus, therefore, leads to fatty liver, hypercholesterolemia, and hypertriglyceridemia [22].

Furthermore increased triglycerides result in an increase in free fatty acid level and its oxidation, which disturbs glucose metabolism as well as utilization and also impairs insulin action leading to the development of hyperglycemia [23]. The present study showed a decrease in serum urea, triglycerides, cholesterol, creatinine, protein, and LDL with an increase in HDL. Potential of the extract to decrease cholesterol and triglyceride levels could help improve lipid metabolism in diabetics, which in turn will help to prevent diabetic complications [24]. LDL- cholesterol is as involved in the transport of cholesterol from the liver to peripheral tissues considered as the key factor in atherogenesis. Potential activity of the extract to decrease LDL-cholesterol thereby indicates its possible involvement in the prevention of diabetes mellitus induced cardiovascular complications.

The decrease in glycogen content observed may be a result of the disturbances in glycogen synthetase system. Improvement in liver glycogen of diabetic rats after chronic treatment with alcoholic extract of *Murraya koenigii* stem bark indicates that possible way of antidiabetic action of the extract may be by the improvement of the glycogenesis and suppressing the glycogenolysis activity.

In diabetes mellitus, body cells are being unable to utilize glucose as a source for energy due to which proteins are spared as an energy source. This leads to a decrease in protein storage, which in turn reduces body weight [25]. In the present study, alloxan-diabetic rats show a decrease in body weight throughout the experimental period. Oral treatment with alcoholic extract of *Murraya koenigii* stem bark significantly improved the body weight loss in diabetic rats as compared to diabetic control indicating the possible role of the extract in the restoration of protein metabolism. Histo-pathology of pancreas, liver, kidney, and heart shows that treatment of diabetic rats with aqueous extract of *Murraya koenigii* stem bark prevented the alteration in their pathology with the return to their normal texture.

From the above study, it is found that alcoholic extract of *Murraya koenigii* stem bark at a low dose (125 mg/kg) is more effective than the higher dose (250 mg/kg) after 11 days of treatment. Hence the above discussion reveals that alcoholic extract of *Murraya koenigii* stem bark at a low dose (125 mg/kg) is more effective and shows similar curative effects as standard that is, metformin (450 mg/kg). This could be due to the possibility that some β-cells are still surviving to act upon by aqueous extract of *Murraya koenigii* stem bark to exert its insulin-releasing effect. Histopathological studies reinforce the healing of pancreas, liver, kidney, and heart by *Murraya koenigii* stem bark aqueous extract, as a possible mechanism of their antidiabetic activity.

CONCLUSION: From the above discussion it concludes that alcoholic extract of *Murraya koenigii* stem bark at a low dose (125 mg/kg) exhibited significant antihyperglycemic activity than at high dose (250 mg/kg) in alloxan-induced diabetic rats. These extracts also showed improvement in parameters like body weight and lipid profile as well as regeneration of β cells of the pancreas and so might be of value in diabetes treatment. However, further investigation is required to identify the exact phytoconstituents responsible for the antidiabetic activity.

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CONFLICT OF INTEREST: There is no conflict of interest.

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