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ANTIDIABETIC ACTIVITY OF *PLUMERIA ACUMINATA* LEAVES ON STREPTOZOTOCIN INDUCED DIABETIC RATS

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ABSTRACT

Background: *Plumeria acuminata* belongs to “Apocynaceae” family. Its common name in Tamil is “*Frangipani*” comes from an Italian noble family. The plant material is widely used as a purgative, remedy for diarrhoea and cure for itch. The milky juice is employed for the treatment of inflammation and rheumatism. The bark has been applied as a plaster over inflammation and hard tumors. The leaves are reported to have anti-inflammatory, rubefacient in rheumatism, antidiabetic and have strong purgative effect. **Objective:** The present study was carried out to describe antidiabetic activity of *Plumeria acuminata* leaves on streptozotocin induced diabetic rats. **Materials and methods:** The leaves of *Plumeria acuminata* was extracted with different solvents and phytochemical investigations were done for all extracts. Acute oral toxicity study was carried out to determine the safe dose of methanol extract of *Plumeria acuminata* (MEPA). The anti-diabetic activity of MEPA was evaluated using streptozotocin induced model. **Results:** In this study we estimated the serum glucose levels, SGOT, SGPT, total cholesterol, triglyceride levels. **Conclusion:** Administration of MEPA produced a significant reduction in serum Glucose, Total cholesterol and Triglyceride, SGOT and SGPT in STZ-induced diabetic rats.

KEYWORDS

Plumeriaacuminata, Streptozotocin, Serum glucose, Hematological and Antioxidants.

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INTRODUCTON

Plant derived medicines have been the first line of defence in maintaining health and combating diseases. Many secondary metabolites of plants are commercially important and find use in a number of pharmaceutical compounds. Chemical principles from natural sources have become much simpler and have contributed significantly to the development of new drugs from medicinal plants¹.

Plumeria acuminata belongs to "Apocynaceae" family. Its common name in Tamil is "Frangipani" comes from an Italian noble family. Also known as the *Lei* flower. They are recognized as excellent ornamental plants and often seen in the graveyards². *Plumeria* plants are famous for their attractiveness and fragrant flowers. The Plant possess poisonous, milky sap. Contact with the sap may irritate eyes and skin.

In traditional medicinal system different parts of the plant have been mentioned to be useful in a variety of diseases. The plant material is widely used as a purgative, remedy for diarrhoea and cure for itch. The milky juice is employed for the treatment of inflammation and rheumatism. The bark has been applied as a plaster over inflammation and hard tumors. The leaves are reported to have anti-inflammatory, rubefacient in rheumatism, antidiabetic and have strong purgative effect. Its branches are used like those of '*chitraka*' to produce abortion³. However there is no scientific report or verification of the use of this plant in the treatment of these conditions. Accordingly a pharmacological investigation on the methanol extract of leaves of *Plumeria acuminata* (MEPA) has been done by our team and we have reported its antimicrobial⁴, analgesic and antipyretic⁵, antioxidant and free radical scavenging⁶, anti-inflammatory⁷, anticancer⁸ activities. And now we report the antidiabetic activity results of studies on streptozotocin induced diabetic animals.

MATERIAL AND METHODS

Plant materials

For the present investigation, the leaves of plant *Plumeria acuminata* (Family: Apocyanacea) were collected from different regions of Hanamkonda, Warangal, Telangana. The leaves are botanically authenticated by an expert taxonomist Dr. V. S. Raju, Department of Botany, Kakatiya University, Warangal (KUH 1859). The voucher specimen was stored in our laboratory for future use.

Chemicals

Streptozotocin (Sigmaaldrich, Germany), Glibenclamide (Prudence pharma, Hyd), Glucose kit

(Coral diagnostics, Goa) Total cholesterol and triglyceride kits (Excel diagnostics, Hyderabad).

Extraction

The powdered leaves were defatted with petroleum ether (60-80°C) and the marc thus obtained was extracted with methanol (60-80°C). After completion of soxhlation process the liquid extract was collected and the solvent was removed by distillation. Finally, it was evaporated to dryness at room temperature and kept in a dessicator⁹. The methanolic extract of the leaves of *Plumeria acuminata* (MEPA) in different concentrations was used for the present study.

Animals

Adult male Wister albino rats weighing 180-200g and male Swiss albino mice weighing 20-25g were used for the present investigation. They were housed in colony cages (four per cage) under conditions of standard lighting, temperature (22±3° C) and humidity, and were fed with standard pellet diet (Hindustan Lever, Kolkata, India) and water *ad libitum*. The animals were acclimatized to laboratory condition for one week before start of experiment. All these procedures described were reviewed and approved by the Institutional Animal Ethical Committee (IAEC), Vaagdevi College of Pharmacy, Warangal, Telangana, India.

Acute Toxicity

A safety dose of the synthetic compounds can be determined by performing acute toxicity studies. In present study the procedure was followed by using OECD guidelines (Organisation of Economic Cooperation and Development) 423 (Acute toxic class method)¹⁰. The acute toxic class method is a step wise procedure with three animals of a single sex per step. For the present test procedure, healthy adult male Wistar Albino rats of 10 to 14 weeks old having average weight of 180 ± 20 gm are used. 3 animals were used for each dose. All the test animals were fasted overnight prior to dosing. After the period of fasting, the animals were weighed and the test substance was administered at the dose of 2000 mg/kg body weight in a single dose by oral gavage and they were observed continuously for 1 hour and at intermittently for 24 hours for any signs and symptoms of toxicities. Body weight of the rats before and after treatment were noted and no changes

in skin and fur, eyes and mucous membranes and also autonomic, central nervous systems, somatomotor activity and behavior pattern were observed and also signs of tremors, convulsions, salivation, diarrhoea, lethargy sleep and coma were noted. The onset of toxicity and signs of toxicity was also to be noted. The rats were then observed for another 14 days.

Anti-diabetic activity

Male Albino Wistar rats weighing between 180 ± 20 gms were used for the experiment and were allowed to acclimatize for a week. Six rats were formed into one group; five such different groups of rats were formed and used for studying the antidiabetic effects of MEPA. Diabetes was induced to group II, III, IV and V rats following overnight fasting by an i.p injection of single dose of streptozotocin (40 mg/kg), while normal rats were given acacia suspension. After 24h, animals showing plasma sugar level more than 250mg/dl were considered diabetic. The diabetic animals were stabilized for five days and the next day (day 0) experiment was started. Group II served as diabetic control, standard drug glibenclamide was given to group III at a dose of 5mg/kg, MEPA was given to groups of IV and V rats at a dose of 100mg/kg and 200mg/kg respectively by oral route for 14 days. Blood glucose was measured on 7th day and 14th day. At 15th day all the animals were sacrificed and evaluated for the biochemical and *in vivo* antioxidant status.

Biochemical assays

Fasting blood glucose level, lipid profiles and biomarkers were evaluated in normal and diabetic rats. While liver antioxidant system also were additionally evaluated. The blood glucose level was estimated by one touch glucometer (Accu check). Serum marker such as serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) and lipid profiles like total cholesterol and triglycerides were also measured^{11,12}.

Statistical analysis

The values were expressed as mean \pm S.E.M. The statistical significance was determined by using the student t-test. Values of $P < 0.001$ were considered as statistically significant.

RESULTS AND DISCUSSION

Acute toxicity

In the acute toxicity assay no deaths were observed during the observation period at the tested dose of 2,000 mg/kg b. wt. At this dose, the animals showed no stereotypical symptoms associated with toxicity, such as convulsion, ataxy, diarrhoea or increased diuresis.

Anti-diabetic activity

The present study was undertaken to evaluate the anti-hyperglycemic activity of MEPA in streptozotocin induced diabetic rats. Among the two doses of extract 200mg/kg dose showed significant anti-hyperglycemic effect. As it is evident from the results that maximum reduction in the blood glucose levels were observed on 14th day of treatment. The results of the present study was presented in Table No.1.

Liver is the vital organ of metabolism, detoxification, storage and excretion of xenobiotics and their metabolites¹³. SGOT and SGPT are reliable markers of liver function¹⁴. Liver was necrotized in STZ-induced diabetic rats, therefore an increase in the activities of SGOT and SGPT in serum might be mainly due to the leakage of these enzymes.

From the liver cytosol into blood stream which gives an indication of the hepatotoxic effect of STZ¹⁵. Treatment of the diabetic rats with Glibenclamide (5mg/kg) and MEPA (100mg/kg and 200mg/kg) caused reduction in the activity of these enzymes in serum compared to the diabetic control group and consequently alleviated liver damage caused by STZ-induced diabetes. The results of the present study was presented in Table No.2.

Lipid profile, which is altered in the serum of STZ-induced diabetic rats, appears to be a vital factor in the development of atherosclerosis which is noted in diabetes. Elevated levels of serum triglycerides and total cholesterol in diabetic condition, has influence on cardiac and body function¹⁶. Diabetes induction significantly raised the levels of total cholesterol and triglycerides. In this study, MEPA significantly recovered the levels of serum lipid profile in treated diabetic rats when compared to diabetic control rats (Table No.3).

From this result, it may be stated that the methanol

extract leads to regeneration of the β -cells of the pancreas and potentiation of insulin secretion from surviving β - cells. The increase in insulin secretion and consequent decrease in blood glucose level may lead to inhibition of SGOT and SGPT.

Table No.1: Effect of MEPA on blood glucose levels of streptozotocin induced diabetic rats

S.No	Groups	Glucose Levels (mg/dl)		
		0 Day	7th Day	14th Day
1	Normal (Acacia suspension)	113.3±6.05	113.3±6.05	118.3±2.58
2	Control	290.2±4.26	290.2±4.26	291.7±4.08
3	Glibenclamide (5mg/kg)	290.8±5.47	214.5±4.08	116.3±3.83
4	MEPA (100mg/kg)	287±5.47	246.5±4.84	178.8±4.87
5	MEPA (200mg/kg)	290.5±3.83	228.5±5.43	136.3±4.27

Table No.2: Effect of MEPA on SGPT and SGOT levels of streptozotocin induced diabetic rats

S.No	Groups	SGPT(u/l)	SGOT(u/l)
1	Normal (Acacia suspension)	75±4.47	147.2±4.70
2	Control	176.2±6.33	232.8±9.17
3	Glibenclamide (5mg/kg)	88±2.44	159.2±3.76
4	MEPA(100mg/kg)	138.5±1.97	196.7±6.83
5	MEPA(200mg/kg)	109±4.98	177.2±3.18

Table No.3: Effect of MEPA on total cholesterol and triglyceride levels of streptozotocin induced diabetic rats

S.No	Groups	Total Cholesterol (mg/dl)	Triglyceride (mg/dl)
1	Normal(Acacia suspension)	42.83±2.48	51±4.73
2	Control	63.83±6.70	176.7±6.83
3	Standard(5mg/kg)	37±2.96	68.3±6.05
4	MEPA(100mg/kg)	53.33±5.68	91.17±3.76
5	MEPA (200mg/kg)	42.32±3.20	82.17±2.48

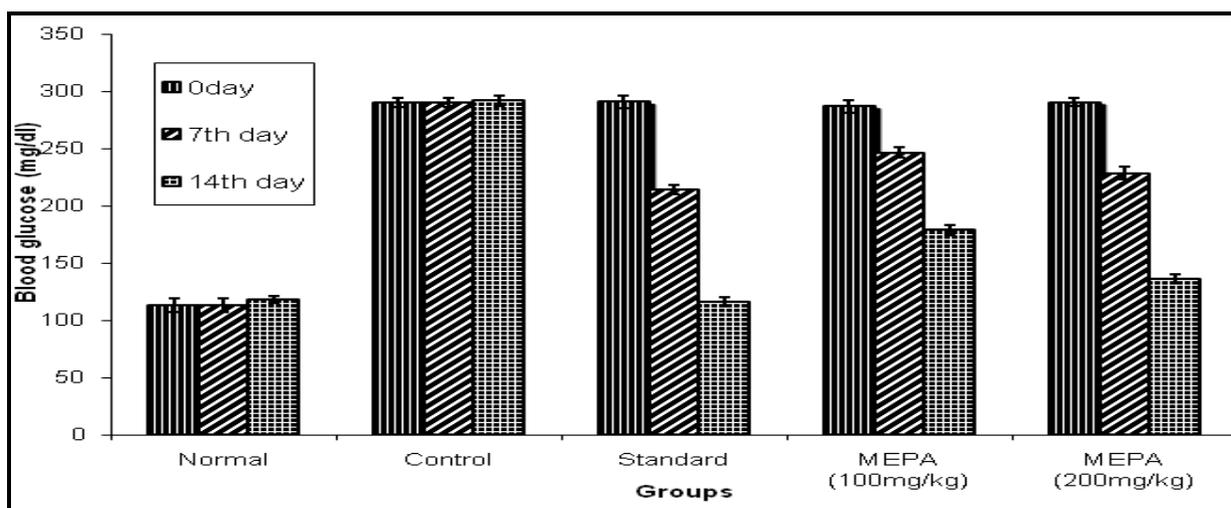


Figure No.1: Effect of MEPA on blood glucose level of streptozotocin induced diabetic rats

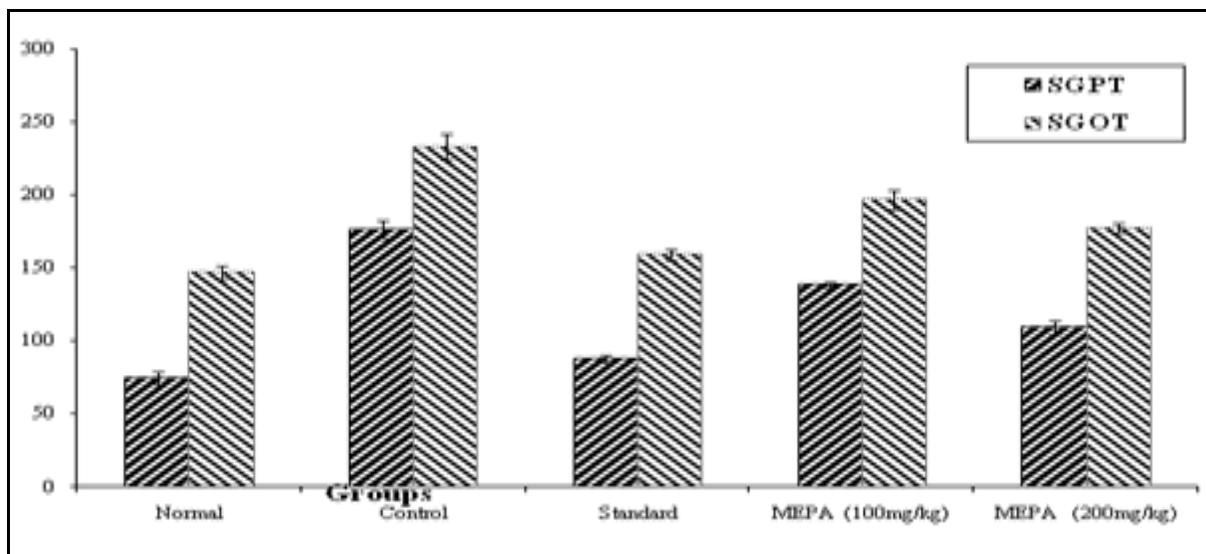


Figure No.2: Effect of MEPA on blood SGPT and SGOT levels of streptozotocin induced diabetic rats

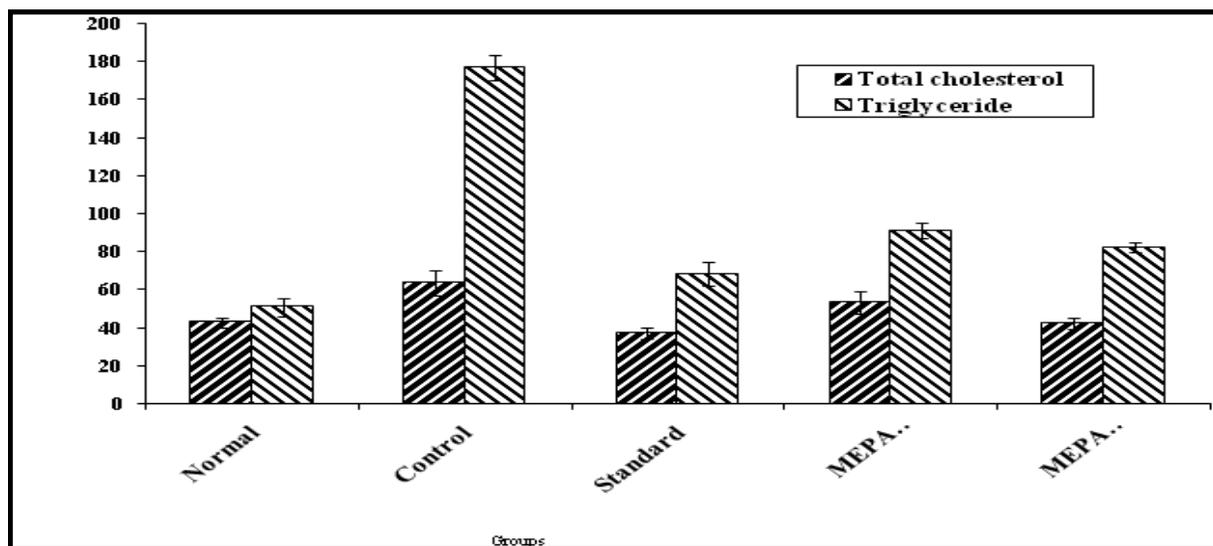


Figure No.3: Effect of MEPA on total cholesterol and triglyceride levels of streptozotocin induced diabetic rats

CONCLUSION

In conclusion, administration of MEPA produced a significant reduction in serum Glucose, Total cholesterol and Triglyceride, SGOT and SGPT in STZ-induced diabetic rats. In hematological parameters estimation MEPA showed good recovery of WBC, RBC, Hb, Platelets and differential leukocyte count also increased. However, comprehensive phytochemical and pharmacological researches are required to find out the exact mechanism of this extract for its anti-diabetic effect

and to identify the active constituent(s) responsible for this effect.

However, it seems promising that if these data will be validated in the future clinical trials, *Plumeria acuminata* extract may offer an alternative treatment for type II diabetes, and further studies are needed to establish its hypoglycemic mechanism for extracts.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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