International Journal of Pharmaceutical Science and Research
ISSN: 2455-4685
Impact Factor: RJIF 5.28
www.pharmacyjournal.net
Volume 3; Issue 1; January 2018; Page No. 15-17

Effect of *Premna coriacea* on oral glucose tolerance test in rats

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Abstract

Objective: The aim of the present study is to study the effects of ethanolic extract of *Premna coriacea* on Oral Glucose Tolerance Test (OGTT) in diabetic rats.

Methods: Acute oral toxicity test was performed based on OECD guidelines, with reference to behavioural aspects, in Swiss Albino mice. Oral Glucose Tolerance Test are carried out in diabetic rats, Spargue Dawley male rats weighing 140-280 gm were divided into 7 groups consisting of 5 rats in each group. After 60minutes of drug administration, the rats were orally treated with 2g/kg of glucose. The blood samples were collected through femoral vein at 0,15, 30, 60, 120 minutes. Blood glucose level was estimated at various time intervals.

Results: PCEE did not produce any mortality and sign of lethality throughout the study period of 14 days. Normal control from 155 to 103 mg/dl, disease control from 715 to 496 mg/dl, PCEE 180 to 147 mg/dl, PCEE from 198 to 116 mg/dl and Standard 234 to 127 mg/dl

Conclusion: The toxicity study reveals that the extract is nontoxic and can be used in further bioactivity test. The study reveals the positive effect of extracts in maintaining glucose homeostasis in rats.

Keywords: oral glucose tolerance test; *Premna coriacea*; antidiabetic activity, STZ

Introduction

Diabetes is a disease state when the blood sugar, is too high. Blood glucose is your main source of energy and comes from the food you eat. Insulin, a hormone made by the pancreas, helps the glucose to get into the cells to be used for energy. Sometimes the body doesn't make enough or any insulin or doesn't use insulin well. Glucose then stays in your blood and doesn't reach the cells for energy, so the blood glucose level will increase, this condition is called diabetes. The too much glucose in your blood may cause health problems. The diabetes has no cure, there are steps to manage the diabetes. The most common types of diabetes are type 1, type 2, and gestational diabetes [1].

As of 2015, 30.3 million people in the United States, or 9.4 percent of the population, had diabetes. Diabetes affects 1 in 4 people over the age of 65. About 90-95 percent of cases in adults are type 2 diabetes [2]. American Indians/Alaska Natives had the highest prevalence of diabetes about 6.0% among Alaska Natives and 22.2% among American Indians. American Indians/Alaska Natives (15.1%), non-Hispanic blacks (12.7%), Hispanic ethnicity (12.1%), non-Hispanic whites (7.4%) and Asians (8.0%), Mexicans (13.8%), Puerto Ricans (12.0%), Cubans (9.0%), and Central/South Americans (8.5%). Among Asians, Asian Indians (11.2%), Filipinos (8.9%), and Chinese (4.3%). Other Asian groups (8.5%). Prevalence varied significantly by education level, which is an indicator of socioeconomic status [2].

Premna is widely distributed in the tropical and subtropical regions of Austrilia, Africa and Asia. The genus accommodated earlier in the family Verbenaceae has be recently been transferred to the family Lamiaceae based on the molecular data. The generic is derived from the Greek word "Premnon" the stump of a tree; dwarf type species. The genus comprises of 200 species distributed worldwide and among 31 districts in India. There are 8 species and one variety in Kerala. In that one the variety is *Premna coriacea* var. villosa C.B. Clarke A Rajedran & P. Daniel. Based on the literature review there is no scientific reports on oral glucose tolerance test of Premna coriacea. The present study aimed to made an attempt to study the effect of *Premna coriacea* on oral glucose tolerance test in rats.

Materials and methods

Plant material

The plant Premna coriacea was collected from Kesavanpara, Nellliyampathy, Palakkad District, Kerala, India and It has been identified and authenticated by Dr. Udyan P.S., Assistant Professor, Sreekrishna College, Guruvayur, Thrissur, Kerala, India. The leaves of the *Premna coriacea* were collected during November- December month and washed with water. Then the plant leaves material was shade dried for 10 days. The dried plant materials have been powdered using mechanical grinder to get uniform coarse particles. The powdered plant material was stored in polythene air tight containers at room temperature for further use.

Preparation of plant extract

The shade dried coarse powdered bark of *Premna coriacea* (100 g) was packed in the soxhlet extraction apparatus and extracted with 1 L of 95% ethanol at a temperature of 40-50°C for 72 hr. The extract was filtered and the filtered extract was then concentrated to dryness in a rotary evaporator under reduced pressure at temperature of 40°C. The resultant green color residue was stored in a desiccator for use in subsequent experiments and considered as the crude ethanol extract. The yield of the ethanolic extract was 12% w/w.

Animals

The animals used in the experiment were Spargue Dawley male rats weighing 140-280g were used. They were housed in well ventilated polypropylene cages at controlled temperature of 24± 10C, with a 12 h light / 12 h dark cycle and they had been provided with standard pellet diet and water ad libitum. The rats were assimilated to laboratory conditions for 7 days. Animals were kept under fasting for overnight, but allowed for free access of water before commencement **o**f experiments. The experiments were conducted according to the guidelines and ethical norms, approved by ministry of social justice and empowerment, Government of India and the study was got approved from the Institutional Animal Ethical Committee (IAEC) (Approval No.: IAEC/KMC/23/2017) of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

Acute toxicity studies

Acute toxicity studies were carried out using acute toxic class limit test dose guidelines 423 of Organization for Economic Co-operation and Development (OECD). Acute toxicity of the *Premna coriacea* plant extract was carried out, using six Swiss albino mice, by administering a dose levels of 50,100,500,1000 and 2000 mg/ kg body weight, p.o., The toxicological effects were assessed on the basis of mortality and behavioral changes were observed for 14 days.[3]

Induction of Diabetes in Experimental animal

The rats were feed with high Fat diet (HFD) (Fat 58%, Protein 25%, carbohydrates 17%) ad libitum for two weeks period of time. The composition described in the table 1 [4] and the preparation of HFD as were described elsewhere. After two weeks of dietary manipulation, the animals were injected intra peritoneally (i.p.) with low dose of STZ (35 mg / kg), while the respective control were given vehicle citrate buffer (pH 4.4) in a dose volume of 1ml/kg, i.p, respectively. The feed and water intake of the animals were also measured. The rats were allowed to continue to feed on their respective diets until the end of the study.

Table 1: Composition of HFD

Ingredients	Diet (g/kg)
Powdered NPD	365
Lard	310
Casein	250
Cholesterol	10
Vitamin and mineral mix	60
dl-Methionine	03
Yeast powder	01
Sodium chloride	01

Experimental design

In the present study, Oral Glucose Tolerance Test are carried out in diabetic rats, the grouping were made as following. Spargue Dawley male rats weighing 140-280 gm were divided into 7 groups consisting of 5 rats in each group.

Groups:

- Group I- Normal control received 0.9% saline
- Group II- Disease control received 0.9% saline
- Group III- Ethanol extract of *Premna coriacea* (200mg/kg p.o)
- Group IV- Ethanol extract of *Premna coriacea* (400mg/kg p.o)
- Group V- Standard drug Metformin (500mg/kg p.o)

After 60minutes of drug administration, the rats were orally treated with 2g/kg of glucose. The blood samples were collected through femoral vein at 0, 15, 30, 60, 120 minutes. Blood glucose level was estimated at various time intervals.

Results and discussion

In our previous study phytochemical screening of ethanol extract of *Premna coriacea* leaves revealed the presence of Alkaloids, Carbohydrates, Glycosides, Steroids and Flavonoids [5]. Acute toxicity study revealed that the behavior of the animals are normal and no toxic effects were observed to 10 times of the effective dose of *Premna coriacea* ethanolic extract and it was found to be safe. Therefore the LD50> 2000 mg kg -1 body weight may be assumed. The blood glucose levels were estimated at 0, 15, 30, 60, 120 minutes respectively are shown in Table-2. *Premna coriacea* extracted treated rats suppress its rise in blood glucose level with 200mg/kg and 400 mg/kg as compared with vehicle control, disease control. Metformin (250mg/kg) treated group showed suppress in blood glucose during the 2nd hr (Table-2).

The experiment showed that Glucose Tolerance Test (GTT) measures the body ability to use glucose, the body's main source of energy [6]. This test can be used to diagnose pre-diabetes and diabetes. Glucose lowering effects were found after oral administration of ethanol extract in rats. This may be due to the presence of phytochemicals like hypoglycemic property of the alkaloids flavonoids etc. this is to be confirmed by further investigation.

The extracts could have the properties to stimulate or regenerate the β cell for the secretion of insulin and are most effective for controlling diabetes by various mechanisms which may finally lead to improvement of carbohydrate metabolizing enzymes towards the re-establishment of normal

blood glucose level [7]. This is the first study to show Blood glucose lowering property of ethanol extract of *Premna coriacea* cause rapid induction of hypoglycaemia in orally glucose induced hyperglycemic rats.

Table 2: Oral Glucose Tolerance Test in diabetic rats treated with *Premna coriacea* leaves extract

	Treatment	Blood glucose levels in mg/dl				
		0 Min	15 Min	30 Min	60 Min	120 Min
Group I	Normal control _Normal saline 0.9%	89.8 ± 3.5	155 ± 9.5	148.2 ± 10	117.6 ± 6	103 ± 3
Group II	Diseases control - Normal saline 0.9%	418.6 ± 37	715.4 ± 24	610 ± 32	562 ± 36	496.8 ± 18
Group III	PCEE 200mg/kg	104.9 ± 9	180.3 ± 3.1	165.8 ± 9	159.1 ± 4	147.6 ± 1.2
Group IV	PCEE 400mg/kg	107.3 ± 4	198.2 ± 7.4	178.4 ± 12	153.3 ± 7.2	116.2 ± 6.3
Group V	Metformin 500mg/kg	106.8 ± 11	234.4 ± 16	187.8 ± 10	147 ± 9.3	127.6 ± 7.2

Note: Premna coriacea ethanolic extract (PCEE), all values are expressed in SEM

Conclusion

Bases on the results it could be concluded that the administration of ethanol extract of *Premna coriacea leaves* promotes glucose tolerance. *Premna species* plant is gaining much importance in diabetic control, since the phytochemical tests has shown the presence of phytochemicals like Alkaloids, Carbohydrates, Glycosides, Steroids and Flavonoids. Several authors reported that flavonoids, alkaloids, glycosides could have antidiabetic activity. Flavonoids are known to regenerate the damaged beta cells in the alloxan induced diabetic rats and acts as insulin secretagogues. This evidence suggests that the whole plant of *Premna coriacea* could be beneficial for the treatment of diabetes. Further studies need to be carried out to define the active principles present in the ethanol extract.

Acknowledgments

The Authors are thankful to Dr. Udayan PS, Assistant Professor, P.G, Department of Botany and Research Centre, Sree Krishna College, Ariyannur P.O., Guruvayur, Thrissur District, Kerala, for the identification and Authentication of the plant material.

Conflicts of interest

The authors declares no conflict of interest

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