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ANTIDIABETIC ACTIVITY OF *LANNEA COROMANDELICA HOUTT.* LEAVES IN ALLOXAN INDUCED DIABETIC RATS

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ABSTRACT

Diabetes mellitus is one of the most challenging diseases facing health care professionals today. This resulted in a growing interest in the therapeutic use of natural products especially those derived from plants for the treatment of diabetes. The present study is designed to evaluate the effect of ethanolic leaf extract of Lannea coromandelica (Houtt) Merril. in alloxan induced hyperglycemic male wistar rats. The leaves of the plant were shade dried, powdered and were subjected to soxhlet extraction. The leaf extract produced significant hypoglycemic activity in alloxan induced hyperglycemic effect in rats at oral doses of 100 and 200 mg/kg body weight ($p<0.001$) comparable to the standard drug Metformin. The results obtained provide a support for the use of this plant in traditional medicine and its further investigations.

KEY WORDS

Lannea Coromadelica, antihyperglycemic, flavonoids, rats.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disease caused by inherited and/or acquired deficiency in production and improper functioning of insulin [(1)].The development of diabetes-associated complications is primarily due to the increased glucose concentration and increased polyol pathway activity. In addition, hyperglycemia is involved in most diabetic complications through excessive production of reactive oxygen species [(2)]. Traditionally, medicinal plants were known to have valuable therapeutic effects, in modern medicine. Lannea coromandelica Houtt. Family Anacardiaceae), is located in tropical Asia. It is commonly known as wodier or Indian ash tree [(3)]. *L. coromandelica* contains polyphenols including tannins like ellagic acid and Gallic acid; flavonoids like quercetin, kaempferol, isoquercetin; flavonols like physicion, leucocyanidine, and leucodelphidin; gums and mucilage. In addition, the tree also contains some sterols [(4)]. *L. coromandelica* have been reported to have potential as anti-inflammatory[(5)], anti-microbial, wound healing[(6)], hypotensive and aphrodisiac activities[(7)], ulcerative stomatitis, dyspepsia, general debility, gout, cholera, diarrhoea, dysentery[(8)], sore eyes, leprosy, sprains,bruises[(9)], elephantiasis[(10)].

Additionally, the plant gum is used in sprains, asthma and as a cordial to women during lactation[11] [12]. There is no study reported on antihyperglycemic effect of leaf extract of *L. coromandelica*. Thus, the present study was undertaken to evaluate the antidiabetic activity of ethanolic extract of *L. coromandelica* leaves in alloxan induced diabetic rats.

MATERIALS AND METHODS

PLANT COLLECTION AND IDENTIFICATION:

The leaves of the plant material used in the current study were collected from Guntur, Andhra Pradesh. The plant material was identified and authenticated by Dr. S.M. Khasim, Botanist, Acharya Nagarjuna University, Guntur, Andhra Pradesh.

PREPARATION OF THE PLANT MATERIAL EXTRACT

The leaves of *L. coromandelica* were cleaned, shade dried and made to fine powder. The powdered plant material was extracted with ethanol (95%) by Soxhlet extraction process. The solvent was recovered by distillation after completion of the extraction. The extracts were subjected to qualitative tests for the identification of various phenols and flavonoids[13][14].

PREPARATION OF DRUG SOLUTION

The ethanolic *extract* of *L. coromandelica* and standard metformin were dissolved in 0.9% sodium chloride in water and administered orally to the animals with the help of an intragastric catheter.

EXPERIMENTAL ANIMALS

All protocols and experiments used in the present study were approved by the Institutional Animal Ethics Committee (IAEC). Healthy, adult male Wistar rats (180-250 g) were housed in poly propylene cage group of 6 animals per cage. All rats were maintained under standardized laboratory conditions (12hr light/dark cycle, 24°C) and provided free access to balanced pellet diet and purified drinking water *ad libitium* throughout the experimental period . The animals were randomly distributed into 4 groups with 6 animals in each group.

ORAL GLUCOSE TOLERANCE TEST

The oral glucose tolerance test (OGTT)[15] was performed in overnight fasted (18 hours) normal rats. Rats were divided into four groups, each consisting of six animals each. Group I animals received only vehicle (0.9% w/v saline *p.o.)* in a volume of 0.5 ml/kg and served as a control. Group II received metformin (250 mg/kg, *p.o*) as a reference drug suspended in vehicle. The *L. coromandelica* extract, suspended in vehicle, was administered at doses of 100 and 200 mg/kg, *p.o.,* to the animals of groups III and IV, respectively.Glucose (3g/kg) was fed 30 min after the administration of the extract. Blood was withdrawn by tail vein puncture method at 0, 30, 60, 90 and 120 min of glucose administration and blood glucose level was estimated by glucose oxidase-peroxidase method [16].

HYPOGLYCEMIC ACTIVITY

Fasted rats were divided into four groups of six animals each. Group I animals received only vehicle (0.9% w/v saline *p.o.)* in a volume of 0.5 ml/kg and served as a control. GroupII received metformin (250 mg/kg, *p.o*) as a reference drug suspended in vehicle. The *L. coromandelica* extract, suspended in vehicle, was administered at doses of 100 and 200 mg/kg, *p.o.* to the animals of groups III and IV, respectively. Blood samples were collected by tail vein puncture method at 0, 30, 60, and 120 min for glucose estimation and blood glucose

level was estimated by glucose oxidase-peroxidase method after dosing [17].

EXPERIMENTAL INDUCTION OF TYPE 2 DIABETES IN RATS

The animals were provided with free access to water for 16-18 hours prior to the induction of diabetes. Induction was carried out by single intraperitoneal administration of Alloxan monohydrate (Sigma St Lous, M.O., USA) dissolved in sterile normal saline to overnight fasted animals at a dose of 120 mg/kg body weight . Alloxan produces fatal hypoglycemia as a result of massive pancreatic insulin release. The fasting blood glucose level was assessed after 72 hours of alloxan injection. The rats with blood glucose level above 200mg/dl were then selected for the study. The diabetic animals were allowed free access to tap water, pellet diet, and were maintained at room temperature in plastic cages.

STUDY DESIGN

Fasted rats were divided into four groups of six animals each and were treated with single dose/day (*p.o*) of standard drug and extracts of *L .coromandelica* .

Group I: Received normal saline 0.9% w/v *p.o.* served as control.

Group II: Rats were treated with metformin (250mg/kg, *p.o*) as a reference drug, suspended in vehicle.

Group III: Rats were treated with *L. coromandelica* extract (100mg/kg, *p.o.)*

Group IV: Rats were treated with *L. coromandelica* extract (200mg/kg, *p.o.)*

Blood samples were collected by tail vein puncture at 0, 30, 60, and 120 min for glucose estimation after dosing [17].

STATISTICAL ANALYSIS

All values were expressed as mean ± S.E.M. Statistical analysis was performed by one-way analysis of variance (ANOVA) followed by Dunnett's t-test for multiple comparisons. The results were considered statistically significant if $P < 0.05$.

RESULTS

EFFECT OF *L. coromandelica* ETHANOL EXTRACT ON ORAL GLUCOSE TOLERANCE TEST

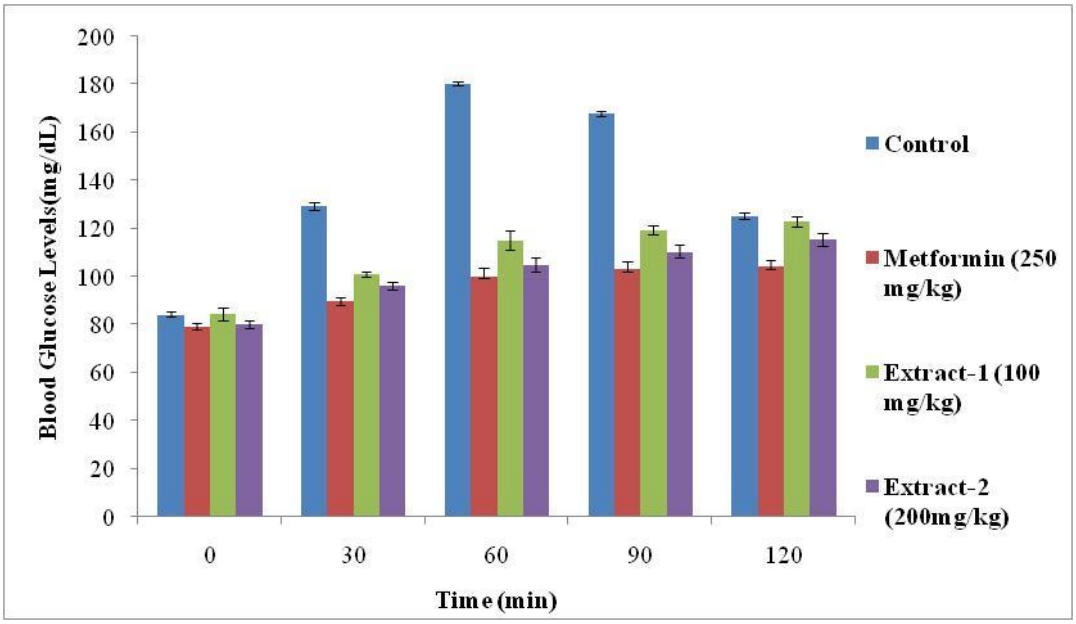
The blood glucose levels of normal rats reached high levels at 60 min after the oral administration of glucose (3g/kg) and gradually decreased to 125 mg/dl in 2 hours as shown in Table I. The pretreated groups with ethanol extract of *L. coromandelica* (100 and 200 mg/kg) and metformin (250 mg/kg) elicited decreased blood glucose level significantly ($P < 0.05$) as compared to the control group.

Table I: **Effect of ethanol extract of *L. coromandelica* on OGTT**.

S.No	Time (min)	Blood glucose (mg/dL)levels			
		Control	Metformin (250 mg/kg)	Extract-1 (100mg/kg)	Extract-2 (200mg/kg)
1	0	84±1.2	79±1.4	85±2.6	80±1.4
2	30	129±1.4	90±1.7	101±1.1	96±1.6
3	60	180±0.8	100±3.3	115±4.1	105±2.9
4	90	168±1.2	103±3.2	119±1.7	110±2.7
5	120	125±1.3	104±2.8	123±2.2	115±2.6

Values are given as mean ± S.E.M (n=6), P<0.001.

Figure I: Effect of ethanol extract of *L. coromandelica* on OGTT.



Values are given as mean ± S.E.M (n=6), P<0.001.

EFFECT OF *L. coromandelica* ETHANOL EXTRACT IN FASTED NORMAL RATS

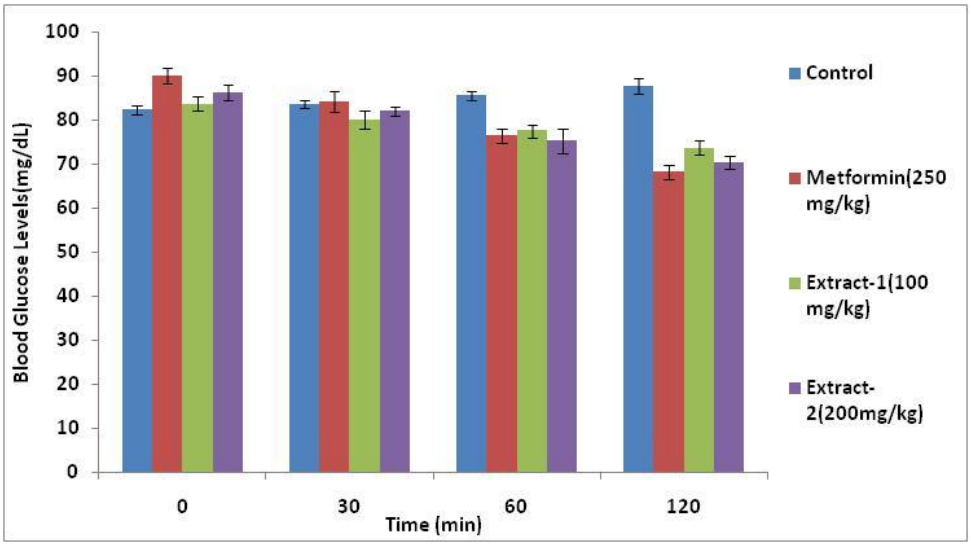
The *L. coromandelica* ethanol extract was subjected to hypoglycemic activity at two dose levels (100 and 200 mg/kg), based on the anti hyperglycemic activity in OGTT as shown in Table II. The ethanol extract of *L. coromandelica* did not shown any hypoglycemic activity.

Table II: Effect of ethanol extract *L. coromandelica* extract in fasted normal rats.

S.No	Time (min)	Blood glucose (mg/dL)levels			
		Control	Metformin (250 mg/kg)	Extract-1 (100 mg/kg)	Extract-2(200mg/kg
1	0	82 ± 1.0	90±1.7	84±1.6	86±1.8
2	30	84±0.8	84±2.4	80±2.0	82±1.0
3	60	86±1.1	76±1.6	78±1.5	75±2.7
4	120	88.2±1.9	68±1.5	74±1.7	70±1.4

Values are given as mean ± S.E.M (n=6), P<0.05.

Figure II: Effect of ethanol extract of *L. coromandelica* on fasting blood glucose level in alloxan induced diabetic rats.



Values are given as mean ± S.E.M (n=6). P<0.05

DISCUSSION

Diabetes mellitus is the metabolic, endocrine disorder that is seen due to insufficient production and improper functioning of the insulin. Diabetes mellitus is further associated with chronic complications including microvascular, macrovascular, and neuropathic disorders[18]. The currently available antihyperglycemic drugs have their own limitations and adverse effects in the treatment of diabetes. However, traditional medicinal plants were well known for their safe and effective usage, cost effectiveness, reduced limitations and less adverse effects [19]. The bark extract of *L. coromandelica* plant reported to show antidiabetic activity in mice [20]. Inaddition, the present study results indicated that *L. coromandelica* leaf extract (100 and 200 mg/kg b.w.) also significntly reduced glucose level in glucose loaded animals and in alloxan induced diabetic animals as compared to the normal rats as shown in Figure I. Alloxan reported to cause massive reduction in the insulin release by the destruction of β-cells of the pancreas, thereby inducing hyperglycaemia[21]. Alloxan induced free radical production and caused damage to the tissues [22]. Phytochemical studies of ethanolic leaf extract of *L. coromandelica* revealed the presence of phenolic and flavonoid compounds [23] [24]. However, it is reported that flavonoids constitute active biological principles of most medicinal plants that show antidiabetic properties [25]. Thus, flavonoids present in this plant may be responsible for the antidiabetic effect of the *L. coromandelica* extract. Recently, reported in silico docking studies of *L. coromandelica* leaf indicated that 2 Tropylpropanaltosylhydrazone, a Cyclin dependent kinase 5 (Cdk5) inhibitor could be a potential leading compound for the treatment of diabetes [26]. All the supported studies reported on leaf extract indicate that plant could play a promising role in the treatment of diabetes in future.

CONCLUSION

L. coromandelica Linn. plant used for the study is having traditional medicinal values. The present study results indicated that ethanolic leaf extract *L. coromandelica* possess significant antidiabetic

activity in alloxan induced diabetic rats. Further pharmacological investigations are needed to elucidate the mechanism of the shown antihyperglycemic effect.

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Conflict of interest

Conflict of interest declared none

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