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Hypoglycemic activity of methanolic extract of *Tectona grandis* linn. Root in alloxan induced diabetic rats

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ABSTRACT

This research aims to investigate the hypoglycemic activity of methanolic extract of *Tectona grandis* root in alloxan induced diabetic albino rats. A comparison was made between the action of *Tectona grandis* methanolic extract and a known antidiabetic drug glibenclamide (0.5mg/kg p.o). The methanolic extract of *Tectona grandis* linn. root was administered orally at different doses to normal rats. The methanolic extract at 500 mg/kg dose level exhibited significant ($p < 0.05$) hypoglycemic activity.

Key words: Alloxan , antidiabetic ,T.grandis, blood glucose

INTRODUCTION

Diabetes mellitus (DM) is a chronic disease with long-term macrovascular and microvascular complications, including diabetic nephropathy, neuropathy, and retinopathy (David A et al, 2009). The term *diabetes mellitus* is actually derived from the Greek words meaning “to run through.” Diabetes mellitus is a serious complex chronic condition that is a major source of ill health worldwide. This metabolic disorder is characterized by hyperglycemia and disturbances of carbohydrate, protein and fat metabolisms, secondary to an absolute or relative lack of the hormone insulin. Besides hyperglycemia, several other factors including dislipidemia or hyperlipidemia are involved in the development of micro and macrovascular complications of diabetes, which are the major causes of morbidity and death. The hyperglycemia is the result of a deficiency of insulin secretion caused by pancreatic β -cell dysfunction or of resistance to the action of insulin in liver and muscle, or a combination of these (Sikarwar MS et al, 2009). Hyperglycemia is closely associated with increased production of free radical species and increased oxidative stress (Banerji MA et al, 2001). Herbs have recently attracted attention as health beneficial foods and as source materials for drug development. Herbal medicines derived from plant extracts are being increasingly utilized to treat a wide variety of clinical diseases including liver disease (Chattopadhyay RR, 2003), ischemia, perfusion injury, atherosclerosis, acute hypertension, hemorrhagic shock, diabetes mellitus and cancer with relatively little knowledge regarding their modes of action (Jeong HG et al, 2002).

Tectona grandis Linn. (Verbenaceae) is a large deciduous tree. Branchlets are quadrangular, channeled and stellately tomentose. The tree is growing in higher situations, native to central India, Konkan, Western Deccan peninsula, South India and Burma. It is commonly known as sagwan (Hindi), saka (Sanskrit) and teak tree (English). Teak is a hardwood species of worldwide reputation. Root contains lapachol, tectol, tectoquinone, β -sitosterol and a diterpene,

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tectograndinol (D.V. Goswami et al, 2009). Traditionally roots are used in the treatment of anurea and urine retention (C.P. Khare, 2004). The principle rationale behind the use of this plant for the study of different pharmacological effects is that the trival community of Dhule district of Maharashtra is being using the root extract for their common diseases. It is used as anti-inflammatory, anti-bacterial, cytotoxic, antianaemic, anti ulcer, anti viral, wound healing. Lapachol is the main chemical constituent which is reported in plant. The present paper involves the hypoglycemia activity of the methanolic extract of *T.grandis* in alloxan induced diabetic rats.

MATERIAL AND METHODS

Animals

Albino wistar male rats weighing 150-200g was used for the present study. They were maintained in the animal house of School of pharmacy, SGVU, Jaipur for experimental purpose. The animals were maintained under controlled conditions of temperature ($23 \pm 2^\circ\text{C}$), humidity ($50 \pm 5\%$) and 12-h light-dark cycles. All the animals were acclimatized for seven days before the study. The animals were randomized into experimental and control groups and housed individually in sanitized polypropylene cages containing sterile paddy husk as bedding. They had free access to standard pellets as basal diet and water ad libitum. Animals were habituated to laboratory conditions for 48 hours prior to experimental protocol to minimize if any of non-specific stress. All the studies conducted were approved by the Institutional Animal Ethical Committee (IAEC) of School of pharmacy, SGVU, Jaipur. According to prescribed guidelines of CPCSEA, Government of India.

Plant Material

Roots of the plant *T.grandis* (Linn.) were obtained and identified from authentic sources. The roots of the plant *Tectona grandis* were collected from Haridwar and authenticated by Rajasthan University; Jaipur. A voucher specimen (RUBL20633) has been kept in herbarium in Department of Botany, University of Rajasthan, Jaipur. The collected roots were dried in shade, crushed to coarse powder and used for further studies.

Preparation Of Extract

50g root powders were extracted with 400ml of methanol for 18h by hot continuous extraction method. The methanolic extract was filtered and partitioned by using petroleum ether to remove impurities. The solvent was evaporated under reduced pressure and dried in vacuum. The dried extract of *Tectona grandis* thus obtained was used for the assessment of hypoglycemic activity. The extracts were subjected to preliminary qualitative tests (Khandelwal KR, 2000) to identify the various phytoconstituents present in roots.

LD₅₀

The extract of *T.grandis* root was found to be safe for further biological studies as no toxic effect and lethality was observed up to 3000 mg/kg per oral in rat. Only the consumption of food was

increased by 20% in the dose of 2000 and 3000 mg/kg during 4h but remaining normal afterwards.

Hypoglycaemic activity in normal rats

Twenty-four albino rats weighing 150-200g were fasted for 18h and were divided into four groups of six animals in each. The groups included **i) (vehicle control)** received 5% gum acacia in normal saline, 1ml/200g rat. **ii) (Test drug I)** received 250mg/kg, p.o. 5% w/v, and 1ml/200 g rat. **iii) (Test drug II)** received 500 mg/kg, p.o. 10% w/v, and 1ml/200 g rat. **iii) (Standard)** received Glibenclamide (0.5 mg/kg p.o. 10% w/v, 1ml/200 g rat). One milliliter of blood from the tail of each rat was collected at '0' hour. At two hours of treatment, blood samples were collected again from the treated animals and blood glucose was estimated by glucose estimated method (Barham D et al, 1972).

Hypoglycaemic activity in diabetic rats

Albino rats (n=44) were fasted for 48h. Diabetes was inducing by administering (Kokate CK 1994, Anturlikar SD et al 1995, Goel RK et al 1987) freshly prepared alloxan monohydrate 2.4% in normal saline subcutaneously at a dose of 120 mg/kg, body weight as single dose (Shoka AA, 1992). After 72h of alloxan, 18 h fasting blood was collected from those that survived (n=34) (Geetha BS, 1994) sugar estimated by glucose oxidase method. Twenty four diabetic rats with blood glucose level of 300-500 were selected and were divided into four groups of six each. The selected groups were treated with vehicle (5% gum acacia, 1ml/200g), test drug (250mg/kg, p.o.), test drug (500 mg/kg, p.o.) and glibenclamide (0.5 mg/kg, p.o.), respectively four seven days (Singh N, 1989). On the eighth day blood samples were collected after 18h of fasting and blood glucose was estimated again.

Statistical analysis

Results are expressed as mean \pm SD. The differences between experimental groups were compared by one-way Analysis of Variance (ANOVA) followed by Bonferroni's test. The results were considered statistically significant when $P < 0.05$.

RESULT

The plant extract of *Tectona grandis* roots methanolic extract showed hypoglycemic activity by reducing blood glucose level significantly. It is also much effective when compare with the standard drug Glibenclamide. It reduces blood glucose level after seven days at the 500 mg/kg in rats compare with standard drug. We found that methanolic extract of plant *Tectona grandis* roots is more effective in reducing the blood glucose level compare to the standard drug (Glibenclamide).

The hypoglycemic activity of methanolic extract of *Tectona grandis* root in normal (non diabetic) and diabetic rats is shown in Table. The test drug, at a dose of 500 mg/kg, p.o. significantly lowered the blood, at 2h. However, the activity of the

standard drug, glibenclamide (0.5mg/kg/day), was more pronounced ($P<0.001$). In alloxan induced diabetic albino rats, *Tectona grandis* at a dose of 250 and 500 mg/kg/day and standard drug glibenclamide (0.5mg/kg/day) for seven days was highly significant ($P<0.001$) in comparison with control group (Figure 1 and 2). However, in diabetic rats the hypoglycemic effect of the test drug at 250 mg/kg was significantly less than the standard drug glibenclamide.

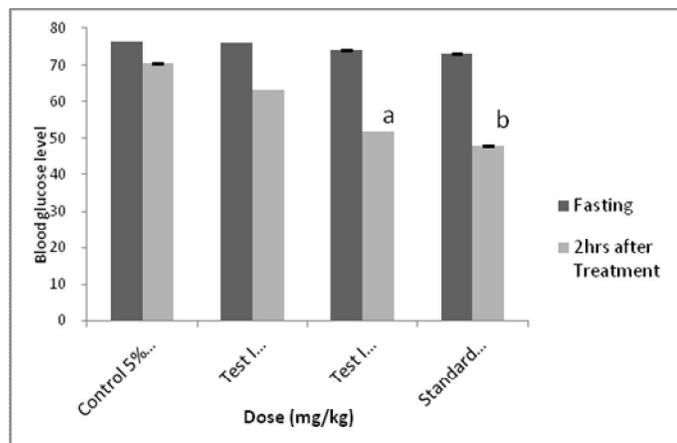


Fig 1: Blood Glucose Level in Normal Rats. a= $p<0.001$ Vs Control and b= $p<0.001$ Vs Control

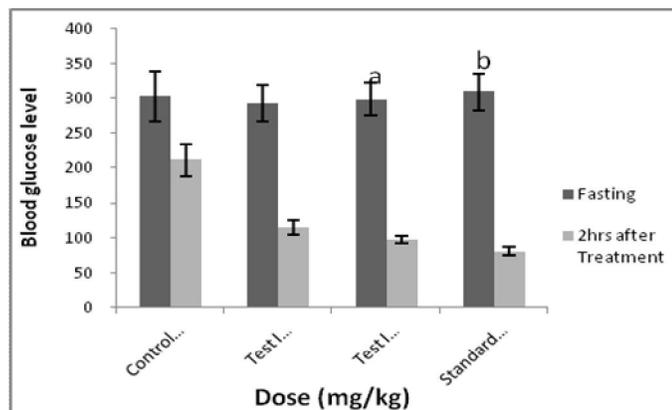


Fig 2: Blood Glucose Level in Diabetic Rats

a= $p<0.001$ Vs Control
b= $p<0.001$ Vs Control

DISCUSSION

Results of present study shows that methanolic extract of *Tectona grandis* roots (500 mg/kg) significantly decreases fasting glucose levels of normal rats ($P<0.001$). However, the reduction was found to be less effective than that of glibenclamide. [Table] The blood glucose levels in normal and diabetic albino rats before administration of the drugs correspond well with the findings of previous workers.

The test drug at doses of 250 and 500 mg/kg/day for seven days reduced the blood glucose level of diabetic rats significantly ($P<0.001$). Effect of the tests drug at doses of 250 and 500 mg/kg, orally, on blood glucose level was comparable with that of standard drug, glibenclamide. This antihyperglycemic effect

may be due to lapachol (a naphthoquinone), lapachonone (Goel RK et al 1987, Mowrey DB, 2007) deoxylapachol and tectoquinone (Sumthong P, 2006) which have been reported to be the constituents of *T. grandis* (Goel RK et al 1987).

The hypoglycemic effect of *Tectona grandis* may be due to presence of flavonoid compound is reported to promote regeneration of β cells of Islets of Langerhans. The mechanism of alloxan diabetes has been the subject of many investigations and it is now generally accepted that free radicals are selectively involved in the initiation of the damage that ultimately leads to β cells death (Minami T et al, 1999). Therefore, the pancreas is especially susceptible to the action of alloxan induced free radical damage. Many substances have been shown to ameliorate the diabetogenicity of alloxan in animals, which protect by reacting with free radicals formed from alloxan during its interaction with β cells, or prevent radical formation (Jorn et al, 1999). Recently, it was reported that the *Tectona grandis* extract, exhibited significantly radical scavenging activity and thus antioxidant activity and the present finding indicates that administration of *Tectona grandis* root confirms the possibility that the major function of the extract is on the protection of vital tissues including the pancreas, thereby reducing the causation of diabetes in these animals.

Therefore, protective effect of *Tectona grandis* extract on pancreas of alloxan induced diabetic rats could be attributed directly to scavenging activity and for more extent to the regenerative properties of the extract.

CONCLUSION

Our study indicates that *Tectona grandis* methanolic extract produced antihyperglycemic effects in experimental diabetes by providing a regenerative modification against damaged caused by alloxan to endocrine cells of the pancreas.

However, methanolic extract of *Tectona grandis* may exert its hypoglycemic action by mechanisms such as stimulation of glucose uptake by peripheral tissue, inhibition of insulinase activity in both liver and kidney, inhibition of endogenous glucose production or inhibition of renal glucose reabsorption.

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Table 1: Hypoglycemic activity of *Tectona grandis* in normal and diabetic rats

Group	Blood glucose –in normal rats		Blood glucose –in diabetes rats	
	Fasting	2h after treatment	Fasting	2h after treatment
Control (5% gum acacia)	76.05 ± 0.06	70.73 ± 0.05	302.5 ± 35.53	211.16 ± 23.06
Test I <i>T. grandis</i> (250mg/kg)	75.95 ± 0.05	62.86 ± 0.07*	292.66 ± 25.46	114.33 ± 9.85**
Test II <i>T. grandis</i> (500mg/kg)	73.86 ± 0.06	51.78 ± 0.07 **	297.83 ± 23.15	96.83 ± 5.14**
Standard Glibenclamide (0.5mg/kg)	72.76 ± 0.26	47.85 ± 0.04**	308.66 ± 26.32	80.5 ± 5.88**

Values are mg (%), mean ± SD, n=6 in each group, *p<0.01, **p<0.001 as compare to respective control.

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