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DIURETIC ACTIVITY OF *TECTONA GRANDIS* LEAVES AQUEOUS EXTRACT IN WISTAR RATS

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ABSTRACT

Objectives: Present investigation was carried out to evaluate the acute diuretic activity of an aqueous extract of Leaves of *Tectona grandis* (Verbanaceae) in Wistar rats.

Methods: The aqueous extract of *Tectona grandis* leaves was administered at three doses (250, 500, and 1000 mg/kg, p.o.) to wistar rats in acute diuretic model. Furosemide and Hydrochlorthiazide, a standard diuretics were used as reference drugs. Urine volume and urine electrolyte level were determined.

Results: the aqueous extract of *Tectona grandis* leaves increased urine volume and urine electrolytes excretion in a dose dependant way which giving significant results at doses 500 mg and 1000 mg/kg in acute diuretic model.

Conclusion: The aqueous extract of *Tectona grandis* leaves possesses the acute diuretic activity, thus, validating the traditional use of this plant as diuretic. However, further studies are necessary to isolate and characterize the phytoconstituents responsible for diuretic action and to explore the exact underlying mechanism of *Tectona grandis*

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Key Words

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INTRODUCTION

Diuretics, either alone or in combination with other drugs, are valuable in the treatment of hypertension, congestive cardiac failure, ascites and pulmonary edema. Two widely used diuretics, thiazides (hydrochlorothiazide) and the high ceiling loop diuretics (furosemide), are associated with number of adverse effect such as electrolyte imbalance, metabolic alteration, development of new onset diabetes, activation of rennin-angiotensin-neuroendocrine system, and sexual dysfunction. Hence there is need of diuretics with lower potential for adverse effects such as the plant-based substances which are considered to be relatively safe¹.

T. grandis is known as *saka* in Sanskrit, *sagun* in Hindi, *sagwan* in Marathi and teak tree in English. Lapachol, a naphthaquinone isolated from the roots of *T. grandis*, has an antiulcerogenic effect in rats and guinea pigs². *T. grandis* has been investigated for wound healing activity in rats³. *T. grandis* has also been described to be useful as a hypoglycemic agent⁴.

According to Ayurveda, *T. grandis* wood is acrid, cooling, laxative, sedative to gravid uterus and useful in treatment of piles, leukoderma and dysentery. The roots are useful in anuria and retention of urine. The flowers are acrid, bitter dry and cure bronchitis, biliousness, urinary discharge, etc. According to the Unani system of medicine, the oil is useful in scabies, whereas wood is used for headache, biliousness, burning pains and pain, liver problems. It allays thirst, and acts as anthelmintic, expectorant and anti-inflammatory. The bark is astringent, acrid, cooling, constipating, anthelmintic and depurative. It is useful in bronchitis, hyperacidity, vitiated conditions of *pitta*, dysentery, verminosis, diabetes, leprosy and skin diseases⁵.

Tectona grandis Leaves contains Quinones such as Tectoquinone, lapachol, deoxylapachol and its isomer, tectoleafoquinone, anthraquinone – naphthaquinone pigment, Steroidal compounds such as Squalene, poly isoprene- α -tolyl methyl ether, betulinic acid, tecto grandone, monoterpene, Apocarotenoids such as Tectoionols-A, Tectoionols-B, Glycosides such as Anthraquinone glycosides, Phenolic acids such as Tannic

acid, Gallic acid, Ferulic acid, Caffeic acid and ellagic acid, Flavonoids such as Rutin and Quercetin⁶.

Tectona grandis. Linn leaf also reported to contain carbohydrates, alkaloids, tannins, sterols, saponins, proteins, calcium, phosphorus, crude fiber and also contain dye^{3,7,8}.

Besides its traditional claim as a diuretic, its diuretic activity remained unclear. Hence the present study was undertaken to explore diuretic properties of TG.

MATERIALS AND METHODS

Plant materials and extraction:

The leaves of TG were collected from Bhor region, Maharashtra, India in September-October 2009. The leaves were authenticated by Dr. Chakraborty T., Joint Director, Department of Botany, Botanical Survey of India, Pune and herbarium was deposited with voucher specimen No.: BSI/WRC/Tech/2011/JAPTEG1.

The leaves were dried under shade and powdered by using grinder mixer. The powdered material (1000 g) was taken and it was macerated with water, then the extract was collected. The obtained extract was transferred to a petri dish and evaporated to dryness at 60 °C on water bath, yielding a reddish coloured dry 180 g mass of preparation of aqueous extracts of TG leaves (ATG) (18 % w/w). ATG was preserved in desiccator⁹. ATG was suspended in 0.5 % CMC in distilled water and administered 5 ml/kg, per orally (p.o.)

Preliminary phytochemical evaluation of ATG:

The qualitative analysis of ATG was carried out for the evaluation of the presence of various phytoconstituents by using the standard phytochemical tests¹⁰, which revealed the presence of carbohydrates, saponins, tannins, and flavonoids in ATG.

Experimental animals:

Male Wistar rats (150-250 g) and female Swiss albino mice (20-30 gm) procured from the Yash Farm and National Toxicological Centre, Pune were used for the study. Animals had free access to standard pellet rodent diet (Lipton India Ltd., Mumbai, India) and water was provided *ad libitum*. The experimental protocol was approved by the IAEC of R. D.'s College of Pharmacy,

Bhor, India constituted as per the rules and guidelines provided by the CPCSEA, Chennai, India (RDCOP/IAEC/10/3).

Acute Oral toxicity (AOT) studies:

Healthy adult female Swiss albino mice (20-30 gm) were subjected to AOT studies as per OECD guidelines 2001 (AOT-423). Animals were observed individually after dosing at least once during the first 30 min, periodically during the first 24 h, with special attention given during the first 4 h, and daily thereafter, for a total of 14 days. The changes in skin, fur, eyes, mucous membranes, respiratory, circulatory, autonomic, central nervous system, somatomotor activity and behaviour pattern were noted.

The animals treated with ATG did not show any sign of toxicity and mortality during the 14 days of observational period after the administration of a limit dose of 5000 mg/kg, po. Hence for the further pharmacological studies doses of ATG selected were 250, 500, and 1000 mg/kg, p.o.

Acute diuretic activity^{11,12}:

The rats were randomly divided into seven groups (n=6) and treated once as follows: **Normal control**: 0.5 % CMC in distilled water (5 ml/kg, p.o.); **Urea 1000**: Urea (1 g/kg, p.o.); **FUR 20**: Furosemide (20 mg/kg, p.o.); **HTZ 10**: Hydrochlorothiazide (10 mg/kg, p.o.); **ATG 250, 500, and 1000**: ATG (250, 500, and 1000 mg/kg, p.o.). The rats were placed individually in metabolic cages at std environmental conditions. Urine was collected after 5 h and 24 h of the treatments and

urine volume and electrolyte content of the urine were analysed using commercially available kits.

Statistical analysis:

The data was expressed as mean±SEM for each experimental group. The results were analyzed for statistical significance using Student's t- test, one-way ANOVA followed by Dunnett's test. * $p < 0.05$, ** $p < 0.01$ were considered as statistically significant.

RESULTS

Evaluation of ATG for acute diuretic activity at 5 h.

Urine Volume:

The administration of ATG (500 and 1000 mg/kg) showed significant ($p < 0.05$ and $p < 0.01$ respectively) increase in urine volume as compared to normal control group. Whereas, ATG 250 was not significant in this regards. Further urea, furosemide and HTZ showed significant ($p < 0.01$) increase in urine volume with respect to normal control group (Table 1)

Electrolyte Content:

The administration of ATG (500 and 1000 mg/kg) showed significant increase in sodium ($p < 0.05$), potassium ($p < 0.05$) and chloride ($p < 0.05$ and $p < 0.01$ respectively) content of urine as compared to normal control group. Whereas, ATG 250 was not significant in this regards. Further urea, furosemide and HTZ showed significant ($p < 0.05$, $p < 0.01$ and $p < 0.05$ respectively) increase in sodium as well as significant ($p < 0.05$, $p < 0.01$ and $p < 0.01$ respectively) increase in potassium and chloride electrolyte content of urine with respect to normal control group (Table 1).

Table 1: Effect of ATG on total urine volume and electrolytes content of urine at 5 h.

Treatments	Urine Volume (ml)	Sodium (mmol/l)	Potassium (mmol/l)	Chloride (mmol/l)
Normal control	1.1± 0.28	102.00±1.14	40.16± 2.57	229.10 ± 3.45
Urea 1000	3.3± 0.20**	129.90±1.56 *	54.03±2.78 *	257.60± 4.12 *
FUR 20	5.7± 0.26**	542.90±3.97**	107± 2.85**	475.70±6.89 **
HTZ 10	4.3± 0.18**	260.60±3.75 *	78.63± 1.51**	337.70± 3.78 **
ATG 250	0.8± 0.17	107.10±1.14	44.72± 2.15	237.30±5.29
ATG 500	2.5± 0.15*	180.30±2.54 *	56.27± 2.57*	254.90±3.75 *
ATG 1000	3.7± 0.27**	226.30±2.18 *	65.02± 2.57*	286.00±4.39 **

Data was expressed as mean ± S.E.M. (n=6); * $p < 0.05$ and ** $p < 0.01$ as compared to normal control (one way ANOVA followed by Dunnett's test).

Evaluation of ATG for acute diuretic activity at 24 h.**Urine volume:**

The administration of ATG (500 and 1000 mg/kg) showed significant ($p < 0.05$ and $p < 0.01$ respectively) increase in urine volume as compared to normal control group. Whereas, ATG 250 was not significant in this regards. Further urea, furosemide and HTZ showed significant ($p < 0.05$, $p < 0.01$ and $p < 0.01$ respectively) increase in urine volume with respect to normal control group (Table 2).

Electrolyte content:

The administration of ATG (500 and 1000 mg/kg) showed significant ($p < 0.05$) increase in sodium, potassium, and chloride content of urine as compared to normal control group. Whereas, ATG 250 was not significant in this regards. Further urea, furosemide, and HTZ showed significant ($p < 0.05$, $p < 0.01$ and $p < 0.05$ respectively) increase in sodium, potassium and chloride electrolyte content of urine with respect to normal control group (Table 2).

Table 2: Effect of ATG on total urine volume and electrolytes content of urine at 24 h.

Treatments	Urine Volume (ml)	Sodium (mmol/l)	Potassium (mmol/l)	Chloride (mmol/l)
Normal control	3.3±0.26	103.30 ±0.62	41.23±3.53	229.10±4.26
Urea 1000	6.0± 0.29*	135.40 ±0.89*	52.36± 3.82*	291.30±5.16 *
FUR 20	11.4±0.37**	570.00 ±0.724**	151.7± 3.57**	552.90 ±3.15 **
HTZ 10	9.1±0.25**	270.10 ±15.5 *	101.4± 3.05 *	383.10±6.57 *
ATG 250	4.7±0.27	113.90 ±2.48	49.56± 3.02	233.30±6.07
ATG 500	7±0.25*	200.80 ±2.46 *	73.39± 2.84*	287.40±3.73*
ATG 1000	8.2±0.31**	266.40 ±1.84 *	87.39± 3.18*	340.80±6.30 *

Data was expressed as mean ± S.E.M. (n=6); * $p < 0.05$ and ** $p < 0.01$ as compared to normal control (one way ANOVA followed by Dunnett's test).

DISCUSSION

Administration of ATG (500 and 1000 mg/kg) showed significant increase in urine volume after 5 h and 24 h. ATG (500 and 1000 mg/kg) showed significant increase in urinary excretion of sodium, potassium, and chloride and the effect was equipotent to that of hydrochlorothiazide (HTZ).

Furthermore results collaborate the ethnopharmacological application of ATG as diuretic as that of thiazide diuretics, as such action was hypothesized for some plant like *Smilax canariensis*¹³, *Tanacetum vulgare*¹ and *Withania aristata*¹⁴.

There are several phytochemicals which could be responsible for diuretic effect such as flavonoids^{1,9,13,14,15,16} saponins^{1,9,14,17} and other polar compounds^{13,16}.

The preliminary phytochemical studies have confirmed the presence of carbohydrates, saponins, tannins and flavonoids in ATG. Hence the diuretic effects of aqueous extract of *Tectona grandis* leaves may be due to presence of saponins, tannins and flavonoids which may act individually or in combination.

The result of present study revealed that aqueous extract of *Tectona grandis* leaves (500 and 1000 mg/kg) has diuretic property equipotent to HTZ at higher dose tested. The diuretic action of aqueous extract of *Tectona grandis* leaves may be due to inhibition of $\text{Na}^+\text{-Cl}^-$ symport in the distal convoluted tubule or modulation of the activity of high affinity thiazides receptors in renal cortex.

However, further studies are necessary to isolate and characterize the phytoconstituents responsible for

diuretic action and to explore the exact underlying mechanism of *Tectona grandis*.

CONCLUSION

The aqueous extract of *Tectona grandis* leaves possesses the acute diuretic activity, thus, validating the traditional use of this plant as diuretic. However, further studies are necessary to isolate and characterize the phytoconstituents responsible for diuretic action and to explore the exact underlying mechanism of *Tectona grandis*.

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