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## **Original Research Article**

## Study on antipyretic property of the leaves of *Ligustrum robustum*

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#### **ABSTRACT**

**Background:** Thorough pharmacological experiments on various plants used in traditional medicines are in progress in order to establish their effectiveness and safety. But modern drugs or conventional medicines are often viewed as impersonal, emphasizing crisis intervention. Keeping in view the above idea, the present study is undertaken on the plant *Ligustrum robustum* to explore its antipyretic property in albino rats.

**Methods:** Healthy young albino rats weighing between 100-250gm were obtained for the study. The animals were divided into five groups with six animals in each group. Pyrexia was induced by subcutaneous injection of dried yeast in 2% gum acacia in normal saline at a dose of 20ml/kg body weight below the nape of the neck in albino rats. The antipyretic activity of the aqueous extract of *Ligustrum robustum* was tested by yeast induced method. The data were subjected to ANOVA followed by Dunnett's 't' test for statistical significance between different groups.

**Results:** *Ligustrum robustum* in doses of 100mg/kg, 200mg/kg and 400mg/kg significantly reduced the temperature (p<0.05 to 0.01) in the 3<sup>rd</sup> and 4<sup>th</sup> hour after drug administration.

**Conclusions:** Present study concludes that the aqueous extract of the leaves of *Ligustrum robustum* showed significant antipyretic property in the standard experimental animal models.

**Keywords:** Antipyretics, Albino rat, *Ligustrum robustum* 

#### INTRODUCTION

It is well known that traditional herbal medication existed since before the application of modern scientific method of health care, and today majority of world population depends on herbal care practices, particularly those living in villages. These drugs are invariable single plant extracts or from different plants extracts or fractions thereof or mixture of fraction/extracts from different plants.

The practices of using medicinal plants incorporated ancient beliefs and were passed on from one generation to another by oral and/or guarded literature. Although effective in the treatment of various ailments, very often these drugs are unscientifically exploited and/or improperly used. Therefore, these plants drugs deserve detailed studies in the light of modern science.<sup>3</sup> In the last decade WHO, recognizing the importance of herbal medicines, had passed many resolutions for improving the quality and efficacy of plant drugs.<sup>1</sup>

Fever (Pyrexia) is defined as an elevation of core body temperature above the level maintained by the individual, with a mean value of 98.6°F (37°C) the normal 'set point'.<sup>4</sup> A common feature of fever is the enhanced formation of cytokines such as IL-1 $\beta$ IL-6, interferon  $\alpha$  and  $\beta$  and TNF  $\alpha$ . The cytokines, increase the synthesis of PGE<sub>2</sub> in circumventricular organs in and near to the pre-optic hypothalamic area, and PGF<sub>2</sub>, via increases in cAMP

trigger the hypothalamus to elevate body temperature by promoting increase in heat generation and decrease in heat loss.<sup>5</sup>

Ligustrum robustum (Figure 1) is a common medium sized tree or shrub. A full-grown plant is about 30 feet high and 3 feet girth. Bark is quite smooth, pale brown in colour. Twigs are densely lenticelatte. Young shoots pubescent. Leaves 2-4 x 1-1.5 inches, ovate-lanceolate or elliptic, usually narrow at both ends, sometimes acuminate, glabrous; lateral nerves indistinct 5-8 pairs, with smaller ones in between.<sup>6</sup>



Figure 1: Leaves of Ligustrum robustum.

Ligustrum robustum is found abundantly in Manipur. It is also found scattered throughout the state of Tripura and distributed from Assam to Bangladesh, Myanmar and Malaysia. It is found abundant near the base of the hills. The plant Ligustrum robustum crushed leaves has been used for inflammatory gland swelling, skin infections. The leaves were boiled, and watery extract is given for treatment of acute gouty arthritis in Manipur.

The present study has been undertaken to evaluate the antipyretic action/property of the aqueous extract of the leaves of *Ligustrum robustum* on albino rat as compared to standard drugs.

### **METHODS**

The aqueous extract of Ligustrum robustum was prepared by the methods of Rao SK et al, and Khosla P et al, with slight modifications. <sup>7,8</sup> 50gm of powdered leaves were extracted with soxhlet apparatus with 500ml of distilled water till the eluent was colourless. The water extract was evaporated, scraped out, weighed and stored in a glazed porcelain jar for use. The yield was 18.83% and percentage of solubility of the extract was 0.6%.

On preliminary chemical investigation the aqueous extract of *Ligustrum robustum* was subjected to qualitative chemical test as described by Kokate CK, for the detection of phytoconstituents. Preliminary studies with 5% dilute ferric chloride, 25% basic lead acetate solution and

Wagner's reagent, showed the presence of flavonoids, phenolic compounds and tannins in the extract.

Healthy albino rats were obtained from the Central Animal House, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, India for the study. Ethical clearance was obtained from Ethical Committee.

The antipyretic activity of the aqueous extract of *Ligustrum robustum* was tested by yeast induced method of Brownlee as described by Burn JH et al.<sup>10</sup>

#### Materials

Albino rats were used in the study. Drugs which were used, Aspirin (manufactured by USV LTD, Mumbai), test drug (*Ligustrum robustum* was prepared by the methods of Rao SK et al, and Khosla P et al, dried yeast, distilled water, gum acacia present in department of Pharmacology, RIMS were used for the study.<sup>7,8</sup> Digital clinical thermometer, feeding tube, syringe, rat holder, marking pen.

Healthy young albino rats of either sex weighing between 100-250gm with a normal temperature of 98-99.6°F (constant for 7 days observation) were used for the study. The animals were maintained on a standard laboratory diet until approximately 2 hours before the administration of the drug, food was withdrawn but the animals had access to water ad libitum. The temperature of the room during the study was 22-25°C. After measuring the basal rectal temperature, animals were given subcutaneous injection of 2% gum acacia in normal saline at a dose of 20ml/kg below the nape of the neck.

After 19 hours of yeast injection, animals were restrained in individual cages for recording their rectal temperatures. Rectal temperatures were measured by inserting a digital clinical thermometer to a constant depth of 3cm. After recording the temperature, the animals were grouped into five groups of six animals each (Table 1).

Table 1: Grouping of animals (control, test and standard) and drug administration respectively.

Group	Drug
Control	Normal saline
Test A	L. robustum (100mg/kg)
Test B	L. robustum (200mg/kg)
Test C	L. robustum (400mg/kg)
Standard	Aspirin (100mg/kg)

The drugs were suspended in 2% gum acacia and administered orally. The volumes of medicaments were kept constant at 10ml/kg body weight of the animals.

Temperatures were recorded at hourly intervals up to 23 hours after yeast injection. The data were subjected to ANOVA followed by Dunnett's 't' test for statistical significance between different groups.

#### RESULTS

Table 2 shows the anti-pyretic effect of the aqueous extract of *Ligustrum robustum* leaves on dried yeast induced pyrexia in albino rats. There was no significant difference (p >0.05) between mean initial basal temperatures of different groups. After 19 hours of the injection of yeast subcutaneously, there was significant rise of temperature in

the Control group  $101.06\pm0.24$  (p >0.00.1), Test A  $100.50\pm0.20$  (p <0.001), Test B  $100.50\pm0.54$  (p <0.001), Test C  $100.07\pm0.14$  (p <0.001) and the Standard group  $100.50\pm0.15$  (p <0.001) respectively in comparison to the initial basal temperature in each group (Figure 2). However, there was no significant difference between the mean temperatures (p <0.05) in between the groups.

Table 2: Antipyretic activity of aqueous extract of *Ligustrum robustum* on dried yeast induced pyrexia in albino rats.

	Dose	Initial basal	Temp. after	Temperature after treatment (°F) (Mean ± SEM)			
Group	mg/kg, p.o. 10ml/kg	Rectal temp. (°F) (Mean±SEM)	19hrs of induction (°F) (Mean±SEM)	1 <sup>st</sup> Hr.	2 <sup>nd</sup> Hr.	3 <sup>rd</sup> Hr.	4 <sup>th</sup> Hr.
Control	10ml	99.05±0.13	101.06±0.24	101±0.22	100.9±0.3	100.6±0.3	100.9±0.27
A (Test)	100	98.70±0.08	100.50±0.20	100.5±0.18	100.1±0.06	99.9±0.06*	99.8±0.08⊥
B (Test)	200	98.90±0.10	$100.50\pm0.54$	$100.5 \pm 0.54$	100.3±0.11	99.8±0.03*	99.7±0.04⊥
C (Test)	400	99.25±0.05	100.07±0.14	100.07±0.14	100.3±0.21	99.8±0.11*	99.6±0.06⊥
Standard	100	99.00±0.15	100.50±0.15	100.50±0.20*	99.9±0.14*	99.8±0.13*	99.6±0.14⊥
One-way ANOVA	F(df)	2.34(4,25) NS	1.698(4,25) NS	2.87(4,25)* <0.05	3.61(4,25)* <0.01	8.56(4,25)* <0.001	12.72(5,25)* <0.0001

Values are mean  $\pm$ SEM; n=6 in each group; \*p <0.05, when compared to control at that particular hour;  $\pm$ p <0.01, when compared to control at that particular hour

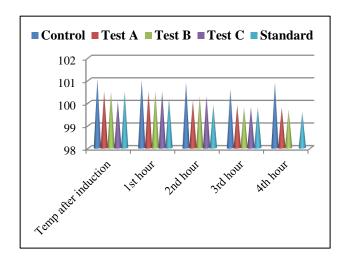


Figure 2: Anti-pyretic effect of the aqueous extract of Ligustrum robustum leaves on dried yeast induced pyrexia in albino rats.

The reduction of the mean temperature in aspirin treated group at  $1^{st}, 2^{nd}, 3^{rd}$  and  $4^{th}$  hour was  $100.5\pm0.20$  (p <0.05),  $99.9\pm0.14$  (p <0.01),  $99.8\pm0.13$  (p<0.05),  $99.6\pm014$  (p <0.01) respectively when compared to values of the control group at corresponding hours (Table 2).

The temperatures recorded with the test A drug (100 mg/kg p.o.) at  $1^{\text{st}}$ ,  $2^{\text{nd}}$ ,  $3^{\text{rd}}$  and  $4^{\text{th}}$  hours were  $100.5 \pm 0.18$ ,  $100.1 \pm 0.06$ ,  $99.9 \pm 0.06$ ,  $99.8 \pm 0.08$  (p<0.01) respectively (Figure 2, Table 2). The mean temperature for the test B drug (200 mg/kg, p.o) at the  $1^{\text{st}}$ ,  $2^{\text{nd}}$ ,  $3^{\text{rd}}$  and  $4^{\text{th}}$  hours were

100.5±0.04, 100.3±0.11, 99.8±0.03 (p <0.05), 99.7±0.04 (p <0.01) respectively (Table 2, Figure 2).

In the test drug C (400mg/kg, p.o.), mean temperatures were found to be  $100.5\pm0.14$ ,  $100.3\pm0.21$ ,  $99.8\pm0.11$  (p<0.05),  $99.6\pm0.06$  (p<0.01) at  $1^{st}$ ,  $2^{nd}$ ,  $3^{rd}$  and  $4^{th}$  hour respectively (Figure 2). The figures within parenthesis show the degree of significance when compared to values of the control group at the respective hours (Table 2).

#### **DISCUSSION**

The antipyretic activity of the aqueous extract of *Ligustrum robustum* leaves was studied by the yeast induced method of Brownlee et al, with slight modification. <sup>10</sup> In the present study, subcutaneous injection of 2% aqueous suspension of dried yeast in gum acacia was used at a dose of 20ml/kg below the nape of the neck of the albino rats. <sup>11</sup>

The initial basal temperature of various group of pyretic rats in present study ranged from 98.7±0.08 to 99.2±0.05°F which is in conformity with the findings of Gupta MB et al. 12 The rise in temperature after 19 hours of induction was between 100.5±0.15 to 101.06±0.24°F which is similar to the findings of Mukherjee PK et al. 13 There was no significant difference between the mean temperature of the different groups and the mean temperature after 19 hours of pyrexia (Table 2). The test drug *Ligustrum robustum* in concentrations of 100mg/kg, 200mg/kg and 400mg/kg did not reduce the body temperature of pyretic rats till the 2<sup>nd</sup> hour. But significant reduction of temperature was observed at 3<sup>rd</sup> hour and 4<sup>th</sup> hour (p<0.01) respectively.

Aspirin (100mg/kg) lowered the rectal temperature of pyretic rats significantly from the 1<sup>st</sup> hour to 4th hour (p <0.05 to 0.01). In the control group, the mean rectal temperature of the pyretic rats was more or less maintained throughout the study period (Table 2).

The results of the present study show that the aqueous extract of *Ligustrum robustum* possesses antipyretic activity in dried yeast induced elevation of body temperature in rats. No signs of adverse effects were noticed following treatment with aqueous *Ligustrum robustum* at doses of 100, 200 and 400mg/kg in rats.

Trease GE et al, and Rajnarayana K et al, reported that some flavonoids are predominant inhibitors of either cyclooxygenase or lipooxygenase. 14,15 The antipyretic effect of the aqueous extract of Ligustrum robustum could be due to the presence of flavonoid compounds. Hajare SW et al, demonstrated the antipyretic activity of Dalbergia sissoo leaves, fever was induced by injecting 20ml/kg s.c of 20% suspension of Brewer's yeast in normal saline below the nape of neck of albino rats.<sup>11</sup> Mutalik S et al, demonstrated the antipyretic effects of Solanum melangena Linn, pyrexia was induced by injecting 20% (w/v) aqueous suspension of Brewer's yeast. 16 Aspirin is a non-steroidal anti-inflammatory drug (NSAID) reset the thermostat. The mechanism of the antipyretic action of the NSAIDs is thought to be largely due to inhibition of prostaglandin production in the hypothalamus.<sup>17</sup>

#### **CONCLUSION**

Ligustrum robustum exhibited significant antipyretic effect upto 4<sup>th</sup> hour of drug administration in albino rats. Aqueous extract of Ligustrum robustum showed the presence of flavonoids, phenolic compounds and tannins in the extract. The antipyretic effect of the aqueous extract of Ligustrum robustum is due to the presence of flavonoid compounds.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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