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Anti-pyretic Activity of *Gmelina arborea* Roxb. Fruit extracts

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ABSTRACT

The plant *Gmelina arborea* has been traditionally used in India for several medicinal purposes like anthelmintic, diuretic, antibacterial, antipyretic, antioxidant and antidiabetic. The aim of the present study is to explore the antipyretic activity of *G. arborea* fruit extracts using ethanol, ethyl acetate, n-butanol and petroleum ether as solvents. The antipyretic activity was evaluated by inducing fever in experimental animals by injection of Brewer's yeastat single dose of 300 mg/Kg, b.w. All data are verified for statistically significant by using one way ANOVA at 1 % level of significance ($p < 0.01$). All extracts showed antipyretic activity at 300 mg/Kg b.w., and the activity is well comparable with the standard drug, Aspirin. Petroleum ether is more effective as compared to other solvent extracts.It could be concluded that *G. arborea* fruits possess antipyretic activity.

Keywords: *Gmelina arborea*, *Verbenaceae*, Brewer's yeast, pyrexia.

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INTRODUCTION

Pyrexia is the body's natural function caused by pro inflammatory mediators (cytokines, such as interleukin 1β, α, β, and TNF- α)[1,2], which increase the synthesis of prostaglandin E2 (PgE2) near hypothalamic area and thereby trigger the hypothalamus to elevate the body temperature.[3-5]

Gmelina arborea Roxb fruits are oval in shape, ¾ inches in length and are yellow in color. The fruits are sweet in taste and sometimes astringent.[6,7]The plant, *G. arborea* was reported to have several medicinal properties such as aphrodisiac, astringent, analgesic, antipyretic, antidiabetic, diuretic, anti-inflammatory and tonic characteristics.[8]

The literature survey reveals that fruits of *G. arborea* contain cardiac glycosides and steroids. The ethanol extract contains alkaloids, carbohydrates, anthraquinone glycosides, gums, mucilages, tannins, phenolic compounds and flavonoids. The ethyl acetate extract contains gums, mucilages, proteins and amino acids.The n-butanol extract contains alkaloids, anthraquinone glycosides, gums, mucilages, tannins, phenolic compounds, triterpenoids, saponins and flavonoids.The petroleum ether extract contains alkaloids, carbohydrates, anthraquinone glycosides, proteins, amino acids, triterpenoids and saponinns.[9]

The literature survey reveals that no such systematic scientific work has been carried out on the anti-pyretic activity of fruits extract of *Gmelina arborea* roxb.

MATERIALS AND METHODS

Drugs and Chemicals

Aspirin was procured as gift samples from Cadila Pharmaceutical Ltd., Ahmadabad, India. Brewer's yeast (Water soluble fraction of yeast autolysate standard material for culture media rich in B - Vitamins and growth factors), petroleum ether AR 40-60°C and n-butanol GR 80°C were procured from Loba Chemie Pvt. Ltd., Mumbai, India. The ethanol AR and ethyl acetate AR 60-80°C (Emsure® ACS) were procured from Merck Pvt. Ltd., Navi Mumbai, Maharashtra, India. All other chemicals and reagents used in present work were procured from authorized dealer.

Collection of plant materials, identification and size reduction

The fruits of *G. arborea* were collected from local area of Koraput district (India) in the month of April and May 2008. The plant was identified and authenticated by the BijuPatnaik Medicinal Plants Garden and Research Centre, Dr. M.S. Swami Nathan Research Foundation, Jeypore, Koraput (District), Orissa (Letter no. MJ/DBT (08)/1067, dated 05.09.2008). The fruits were shade dried under normal environmental conditions. The dried fruits were pulverized to form

coarse powder by using electrical grinder and stored in a closed air tight container for further use.

Preparation of solvent extracts

The coarse powder form of dried fruits was extracted by Soxhlation method by using ethanol, ethyl acetate, n-butanol and petroleum ether as solvents. A total amount of 1500 g coarse powdered fruits was extracted with 1200 ml of each solvent. For each solvent, 10 cycles were run to obtain thick slurry. Each slurry was then concentrated under reduced pressure to obtain crude extract. All crude extracts were kept in closed air tight containers under cool and dark place for further study.[10]

Acute toxicity studies

To study the toxic effect (if any) of *G. arborea* extracts, Albino mice of either sex (20-25 g) were used. The animals were kept in the standard polypropylene cages at 25±2°C/60% relative humidity in normal day and night photo cycle (12: 12 h). The animals were acclimatized for a period of 14 days prior to performing the experiments. Prior to the study, the experimental protocols were approved by the Institutional Animal Ethics Committee of Gayatri College of Pharmacy, GayatriVihar, Jamadarpali, Sambalpur, Odisha (Ethical Committee No 1339/ac/10/CPCSEA).[11]

Acute oral toxicity study was performed as per OECD–423 guidelines.[12,13] The animals were kept fasting overnight but allowed free access to water *ad libitum*. The fasted mice were divided into different groups of six animals each. Each solvent extract solution was administered orally at a dose of 10 mg/Kg b.w., using normal saline water as vehicle and mortality in each group was observed for 14 days. If mortality was observed in 2 out of 3 animals, then the dose administered was assigned as toxic dose. If mortality was observed in one animal, then the same dose was repeated again to confirm the toxic dose. If mortality was not observed, the same procedure was repeated in each group for each extract with higher doses such as 100, 300, 600, 1000, 2000 and 3000 mg/Kg b.w. One tenth of this lethal dose was selected as the therapeutic dose for the evaluation of anti-inflammatory and antipyretic activities.

Antipyretic activity

Healthy Wistar rats of either sex, weighing 180-250 g were used. They were housed in standard conditions of temperature (25±2 °C), relative humidity of 45-55 % in animal house at Gayatri College of Pharmacy, Sambalpur, Odisha. They were fed with a standard pellet diet and water *ad libitum*. All the animals were carefully monitored and maintained in accordance with CPCSEA guidelines (Control and experimental animals) for 15 days.

The antipyretic activity of plant extracts was evaluated by inducing fever in experimental animals by injection of Brewer's yeast.[14,15] In rats subcutaneous injection of Brewer's yeast suspension produces significant pyrexia which can be counteracted by clinically effective antipyretic drugs.

Wistar rats were divided into six groups (3 each). The animals of group (I) served as normal control (Vehicle) which received normal saline water (2 ml/Kg b.w., orally) only. The animals of group (II) served as standard control which received Aspirin (300 mg/Kg b.w., orally). Groups (III)to(XI) received ethanol, ethyl acetate, n-butanol and petroleum ether extracts respectively at a dose of 300 mg/Kg b.w., orally. The initial rectal temperaturesof Wistar rats were recorded at 60, 120 and 180 min by insertion of a thermocouple (BK4302 DigitalThermometer, Century Harvest Electronics Co., Limited, China) to a depth of 2 cm into the rectum. A 15% suspension of Brewer's yeast in 0.9% saline was injected subcutaneously in back below the nape of the neck in a dose of 10 ml/Kg. The site of injection was massaged in order to spread the suspension beneath the skin. The room temperature was maintained between 22 to 24°C. Immediate after the yeast injection, the food was withdrawn but free access to water *ad libitum*. At 18 h post challenge, the rise in rectal temperatures was recorded. The observations were repeated after 30 min. Only animals with a body temperature of at least 38°C were included in this test. The maximum reduction in average rectal temperature in comparison with the control hyperpyrexia group was calculated and the results were compared with the effect of a standard drug, Aspirin.

Statistical analysis

To determine the statistical significance, standard deviation, standard error mean and one way analysis of variance (ANOVA) at 1% level significance was employed followed by z-test. P values < 0.01 were considered significant.[14]

RESULTS AND DISCUSSION

Acute toxicity study revealed that no mortality was found with any solvent extract at any dose in Swiss albino mice. No significant symptoms and side effects were observed with any animal.

The result of acute toxicity study confirmed that *G. arborea* fruits extract would be non- toxic in living bodyand the LD_{50}values of the extracts were found to be 3000 mg/Kg body weight. One tenth of this lethal dose that is 300 mg/Kg b.w. was selected as the therapeutic dose for the evaluation of pharmacological activities.

All extracts exhibited antipyretic activities at 300 mg/Kgb.w. (Table 1). The antipyretic effects of the all the extracts of *G. arborea*are somewhat comparable with the standard drug, Aspirin (Fig 1). All the extracts showed lesser antipyretic activity than the standard drug, Aspirin but several

folds more active than the normal control. The antipyretic activity of the extracts were found in the order of petroleum ether> ethanol> n-butanol> ethyl acetate extract.By employing one-way ANOVA, all data were found to be statistically significant (*F value* < *F crit*) at 1% level of significant ($p < 0.01$ that is $p = 0.000020285$) followed by z-test.

The activities shown by all the extracts are of considerable importance and have justified their use in controlling the pyrexia as suggested in the folklore medicine. It will be worth mentioning that although different constituents were extracted in different solvents as per their polarities, the petroleum ether extract is more effective when compared to other solvent extracts

Table 1. Antipyretic activity of *G. arborea* fruits extracts on Brewer's yeast-induced pyrexia in rats.

Drugs/ Dose (mg/kg)	Rectal temperature in °C at time (h) (X±S.D.)				
	-18[a]	0[b]	1	2	3
Control 10 ml/kg	36.91±0.5	38.27±0.44 (+1.36)[c]	38.28±0.47	38.14±0.50	38.09±0.61
Aspirin (300) (Standard)	36.54±0.7	38.31±0.56 (+1.77)[c]	36.71±0.41	36.66±0.48	36.18±0.38
Ethanol extract (300)	36.85±0.8	38.45±0.90 (+1.69)[c]	37.28±0.77	36.83±0.67	35.22±0.71
Ethylacetatee xtract (300)	36.74±1.1	38.39±0.82 (+1.65)[c]	37.39±0.69	36.83±0.89	36.61±0.83
n-butanol extract (300)	37.28±0.9	38.78± 1.1 (+1.50)[c]	37.67±0.85	37.17±0.91	36.44±0.66
Pet. ether extract (300)	37.23±1.0	38.94±0.77 (+1.71)[c]	37.67±0.96	36.89±0.97	36.22±0.73

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	14.5697	4	3.64241	11.4501	0.000020285	2.7587
Within Groups	7.95282	25	0.31811			
Total	22.5225	29				

Control – Normal saline water. Each value is represented as mean ± standard deviation (n = 3). Standard error of mean < 0.635. *P<0.05, **P<0.01, ***P<0.001, when compared to control (Test of significance between two proportions by z-Test). a - temperature just after 18 h of Brewer's yeast injection, b - temperature just before drug administration and c - change in temperature following Brewer's yeast injection. Data are found to be significant (*F value* < *F crit*) by testing through one way ANOVA at 1% level of significance ($p < 0.01$ that is $p = 0.000020285$).

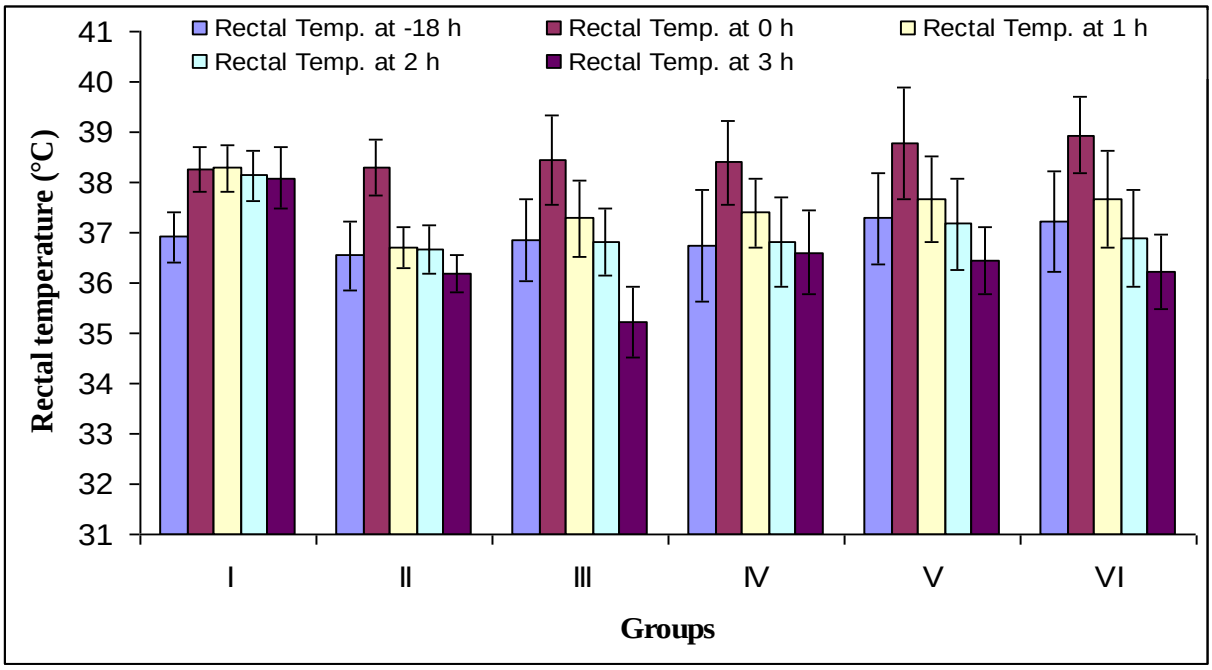

Figure 1. Comparative study on antipyretic activity of various *G. arborea* Roxb fruits extracts.

Each bar represented as mean ± standard deviation (n = 3). Group I – Control (Normal saline water), group II - Standard (Aspirin - 300 mg/kg b.w.), groups III to VI – ethanol, ethyl acetate, n-butanol& petroleum ether extract at 300 mg/kg b.w., respectively.

CONCLUSION

It can be concluded that the extracts of *G. arborea* fruits possess antipyretic activity. The petroleum ether and ethanol extracts showed better antipyretic activity. However, the components responsible for the antipyretic activity are currently unclear. Therefore, further investigation is needed to isolate and identify the constituents present in the fruits extracts.

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