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Evaluation of Antipyretic Potential of *Aegle marmelos* (L.) Correa Leaves

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ABSTRACT

Aegle marmelos (Bael) is a popular medicinal plant in the Ayurveda and Siddha systems of medicine and folk medicines used to treat various disease and disorders including fever. The present study was undertaken to evaluate the antipyretic property of *Aegle marmelos* (L.) Correa leaves (Family: Rutaceae) on Brewer's yeast-induced pyrexia in albino rats. It reveals that the ethanolic extract, at dose of 200 mg kg^{-1} body wt. and 400 mg kg^{-1} body weight, produced significant ($p<0.001$) reduction in elevated body temperature in a dose dependent manner followed by aqueous extract. The antipyretic effect of extracts was comparable to that of paracetamol (100 mg kg^{-1} body weight, p.o.), a standard antipyretic agent.

Key words: *Aegle marmelos*, Ayurveda, Folk medicine.

INTRODUCTION

Aegle marmelos (L.) Corr., (Rutaceae) is a popular medicinal plant in the Ayurvedic and Siddha systems of medicine and folk medicines used to treat a wide variety of ailments. The Bael tree is considered as a sacred tree by the Hindus. They offer its leaves to Lord Shiva during worship. The plant, popularly known as the Bael tree, is native to the Indo-Malayan region[1] and is currently cultivated in India, Pakistan, Bangladesh, Sri Lanka, Burma, and Thailand[2]. The tree is a slender, aromatic perennial, 6.0–7.5 m tall and 90–120 cm in girth. It flowers from May to July and yields an annual average of 300–400 fruits (200–250 kg) per tree. The plant is rich in alkaloids, among which aegline, marmesin, marmin, and marmelosin are the major ones. Leaves of A. marmelos contain an alkaloidal-amide, Aegeline 2[2]. The leaves also contain Scopoletine (7-Hydroxy-6-methoxy coumarin)[3] having antithyroid activity. A. marmelos extract contains a triterpinoid, lupeol[4] which is capable of inhibiting cell proliferation. The leaves contain inorganic trace elements such as Cu, Ni, Zn, K and Na where as Fe, Cr and V levels found in marginal levels[5]. A new 7-geranyloxy coumarin [7-(2, 6- dihydroxy -7 –methoxy -7- methyl -3 –octa enyloxy) coumarin] named marmenol[6] has been isolated from the leaves of methanolic extract of A. marmelos. In addition to marmenol, several known

compounds, praealtin D, trans-cinnamic acid, valencic acid, 4 methoxy benzoic acid, betulinic acid, cis and transcoumaroyltyramine, montanine and rutaretin have also been obtained from the extract. Lampronti *et. al.,*[7] identified three derivatives, butyl-ptolylsulphide, 6-methoxy-4-chromanone and butylated hydroxyanisole from the extract exhibiting strong inhibitory activity on in Vitro growth of human k562 cells. Graded hydrolysis of purified bael gul afforded three natural and two acidic oligosaccharides[8], together with monosacchrides. The natural oligosacchrides were charecterised as 3-o-beta-Dgalactopyranosyl-L-arabinose, 5-o-beta-D-galactopyranosyl-Larabinose and 3-o-beta-D-galactopyranosyl-D-galactose and the acidic oligosaccharides as 3-o-(beta-Dgalactpyranosyluronic acid) -D-galactose and 3-o-(beta-Dgalactopyranosyluronic acid)-3-o-beta-D-galactopyranosyl-Dgalactose. All parts of the tree, including the fruit, possess medicinal properties. Aqueous leaf extract and methanolic extract of the root and bark of *A. marmelos* showed preventive effects on myocardial diseases. Unripe fruit is useful for treating diarrhoea, dysentery and stomachalgia. The aqueous extracts of the stem, root, and bark are used to treat malaria, jaundice, and skin diseases such as ulcers, urticaria, and eczema[4]. In pharmacological trials, both the fruit and root showed antiamoebic and hypoglycaemic activities. The leaves are made into a poultice and used in the treatment of opthalmia. The leaf part of the plants have been claimed to be used for the treatment of inflammation, asthma, hypoglycemia, febrifuge, hepatitis and analgesic[9-12]. The roots and the bark of the tree are used in the treatment of fever by making a decoction of them. Thus, an effort has been made to evaluate antipyretic activity of *Aegle marmelos* leaves.

MATERIAL AND METHODS

Plant materials

Fresh leaves of *Aegle marmelos* were collected from Sanjivani Udyan (Herbal Garden) Bhopal (M.P.), India in July 2008 and identified by Professor (Dr.) H. S. Chatree [Retd. Botanist and Taxonomist, Govt. Agriculture College Mandsaur (M.P.)] and a voucher specimen (BITSP/007/2007) was deposited for reference to Department of Pharmacognosy, BITS-Pharmacy. The material was dried under controlled temperature, powdered and passed through a # 40 mesh sieve and stored in decicator until extraction.

Extraction

Ethanolic and aqueous extract was prepared by soxhletation and cold maceration method respectively and filtered twice through filter paper. The obtained extract was dried by evaporation (yield was 9.8% and 15.6% respectively as compare to powdered material). The extract was stored in refrigerator and weighed quantity was suspended in 2% Tragacanth solution for the experiment.

Phytochemical Screening

The chemical constituents of the Ethanolic extract of *Aegle marmelos* leaves (L.) Correa (EACL) and aqueous extract of *Aegle marmelos* (L.) Correa leaves (AACL) were identified by qualitative analysis and confirmed by thin layer chromatography for the presence of flavonoids, tannins, steroids and saponins.

Animal used

Wistar albino rats (150 ±20 g) were used for the antipyretic study. Albino mice weights about 25±5 g were used for the acute toxicity studies of the crude extracts. Institution Animal Ethics Committee has approved the project (919/ac/08/CPCSEA). The animals were kept in departmental animal house in well cross ventilated room at 27±2^{0}C, relative humidity 44–56% and light and dark cycles of 10 and 14 h respectively for 1 week before and during the experiments. Animals were provided with standard diet (Lipton, India) and the food was withdrawn 18–24 h before the start of the experiment and water *ad libitum.*

Acute Toxicity Studies

The acute toxicity of the extracts was determined in albino mice, maintained under standard conditions. The animals were fasted overnight prior to the experiment. Fixed dose (OCED Guideline No. 420) method of CPCSEA was adopted for toxicity studies.

Induction of yeast-induced pyrexia

Rats were divided into five groups of six rats each. The normal body temperature of each rat was measured rectally at predetermined intervals

and recorded. Hyperexia was induced in rats by 20 ml/kg administration of 20 % aqueous suspension of brewer's yeast subcutaneously. The animals were then fasted for the duration of study (approx 24 hrs), but water was made available *ad libitum*. Control body temperature was taken 24h after the injection to determine the pyretic response to the yeast. Body temperature was taken 1h prior to drug administration in fevered animal served as pre drug control. Extracts were given in dose 200 mg kg^{-1} body wt. and 400 mg kg^{-1} body wt., orally. Paracetamol was taken as standard drug (100 mg kg^{-1} body wt.)[13].

Statistical Analysis

The data are expressed as mean ± S.E.M. The difference among means has been analyzed by one-way ANOVA. A value of $P < 0.05$ was considered as statistically significant.

RESULTS

Phytochemical Screening

The EACL and AACL ware tested positive for terpenoids and alkaloids in preliminary phytochemical tests. Saponin glycoside identified by phytochemical tests.

Acute Toxicity Studies

In the LD_{50} value determination, we observed that the EACL and AACL was safe to use in animals and showed no mortality on 2000 mg kg^{-1} body wt. Therefore 2000 mg kg^{-1} dose was considered as a safe dose, $1/5^{th}$ and $1/10^{th}$ (400 and 200 mg kg^{-1} body wt. respectively) of that was selected for all in vivo experiments as maximal dose (Table 1).

Antipyretic Activity

Effect on Brewer's yeast induced pyrexia

The effect of the ASC on Brewer's yeast induced pyrexia in rats is presented in Table 2.

The subcutaneous injection of a yeast suspension elevated the rectal temperature markedly after 24 h of administration. Treatment with the EACL and AACL at doses of 200 mg kg^{-1} body wt. and 400 mg kg^{-1} body wt. decreased the rectal temperature of the rats in a dose-dependent manner. The antipyretic effect started as early as 1 h, and the effect was maintained for 4 h, after its administration. The standard drug paracetamol (100 mg kg^{-1} body wt.) reduced the yeast-provoked elevation of body temperature significantly. The present results show that the *Aegle marmelos* (L.) Correa possesses a significant antipyretic effect in yeast-provoked elevation of body temperature in rats, in which EACL more significant followed by AACL and its effect is comparable to that of paracetamol (standard drug).

DISCUSSION

We aimed our study for screening antipyretic activity of different extract of *Aegle marmelos* (L.) Correa leaves and observed it possesses a significant antipyretic effect in yeast-provoked elevation of body temperature in rats in a dose-dependent manner up to 4 h after its administration. Fever was induced as described by Abena, A. A, et al. (2003). Fever may be a result of infection or one of the sequelae of tissue damage, inflammation, graft rejection, or other disease states. Antipyretic are drugs, which reduce the elevated body temperature. Regulation of body temperature requires a delicate balance between production and loss of heat, and the hypothalamus regulates the set point at which body temperature is maintained[14].

Results of effect on hyperexia induced in rats by brewer's yeast are given in table 2. It revealed that ethanolic extracts as well as aqueous extracts of *Aegle marmelos* (L.) Correa leaves (200 mg kg^{-1} body wt. and 400 mg kg^{-1} body wt.) showed a

Table 1: Acute Toxicity Study (CPCSEA guideline)

Treatments	Dose(Mg kg^{-1} body wt.)	No. of Animals used	No. of Death	% Death
EACL	2000	3	0	0
AACL	2000	3	0	0

Table 2: Effect of tested samples on Hyperexia induced in rats by Brewer's Yeast

Groups	Samples	Normal body temp. at 0 hr (ºc)	Body temp. after 24 hr after administration of yeast suspension (ºc)	Body temp. after 1 hr. after drug administration (ºc)	Body temp. after 2 hr. after drug administration (ºc)	Body temp. after 3 hr. after drug administration (ºc)	Body temp. after 4 hr. after drug administration (ºc)
1	Control	38.29 ±0.22	39.41 ± 0.57	39.49 ± 0.50	39.61 ± 0.47	39.51 ± 0.55	39.44 ± 0.44
2	EACL (200 mg kg^{-1})	38.26 ± 0.41	39.36 ± 0.57	38.27 ± 0.49***	38.07± 0.45***	37.61± 0.48***	37.42± 0.47***
3	EACL(400 mg kg^{-1})	38.33±0.21	39.46±0.39	38.71±0.49***	38.01±0.47***	37.61±0.42***	37.01±0.43***
4	AACL(200 mg kg^{-1})	38.46±0.41	39.50±0.57	38.30±0.49***	37.56±0.45***	37.51±0.48***	37.32±0.49***
5	AACL(400 mg kg^{-1})	38.13±0.21	39.46±0.39	38.31±0.49***	38.09±0.45***	37.58±0.49***	37.11±0.49***
4	Paracetamol (100 mg kg^{-1})	38.06±0.21	39.3±0.35	38.18±0.35***	37.48±0.30***	37.04±0.36***	36.74±0.36***

All values are given as mean ± SEM, N=6.

****P*<0.001 compare to yeast suspension treated animals (after Administration of 24 h).

Control = 2% Tragacanth sol^{n}

significant antipyretic effect in yeast-provoked elevation of body temperature in rat. It has been observed that ethanolic extracts more effective against elevated body temperature in rats in comparison to aqueous extract in dose dependent manner. In both the cases, the extracts caused a significant lowering of body temperature, with the effect being comparable to that of paracetamol. The present pharmacological study confirms the therapeutic value of *A. marmelos*. However, there are several area on explored. Very less information is available regarding the chemical constituents of leaves of this plant. The standardization of the extracts, identification and isolation of active principles and pharmacological studies of isolated principle may be considered for detail studies. Further, synthesis of the active principle can lead to developments of promising pharmacological actions.

REFERENCES

1. Indian Herbal Pharmacopoeia. *Indian Drug Manufacturer Association*, Mumbai (2002).
2. Narendra T., Sweta S., Tiwari P., Papi Reddy K, Kholiq T., prathipati P., Puri A., Srivastav A. K., Chandra R., Agrawal S. C. and Raj K., *Bioorg Med Chem.,* **17**: 1808-1811 (2007).
3. Panda S. and Kar A., *Phytother Res.,* **20**: 1103-1105 (2006).
4. Lambertini E., Lampronti I., Penolazzi L., Khan M. T., Ather A., Georgi G., Gambhir R. and Piva R., *Oncol Res*., **15**: 69-79 (2005).
5. Narendhirakannan R. T., subramanian S. and Kandaswamy M., *Biol Trace Elem Res.,* **103**: 109-115 (2005).
6. Ali M. S. and Perrez M. K., *Nat Prod Res*., **18**: 141-146 (2004).
7. Lampronti I., Martello D., Bianchi N., Borgatti M., Lambertini E., Piva R., Khan M. T., Gambhir R. and Choudhuri M. S., *Phytomedicine.,* **10**: 300-308 (2003).
8. Roy, A. K. Mukherjee and C. V. Rao. Graded hydrolysis studies on bael gum. *Carbohydr Res.,* 41, 219-226 (1975).
9. Ponnachan P.T.C., Paulose C.S., Panikar K.R., *Indian J. Exp. Biol.,* **31:** 345-7 (1993).
10. Kamalakkannan N. and Prince P.S., *J. Herb. Pharmacother*., **5**: 87-96 (2005).
11. Kakiuchi N., Senaratne L.R., Huang S.L.,Yang X.W., Hattori M., Pilapitiya U. and Namba T., *Planta. Med*., **57**: 43-46 (1991).
12. Prince P.S. and Rajadurai M., *J. Pharm. Pharmacol*., **57**: 1353-7 (2005).
13. Abena A. A., Deatewa M., Gacosso G. and Ouamba J. M., *fitoterapia*, **71**: 231-236 (2003).
14. Goodman SL and Gilman A, The Pharmacological Basis of Therapeutics, 5 ed, Macmillan Publishing Co Inc, New York, 992 (1996).