

## Analgesic Activity of *Mesua ferrea* Linn.

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*Mesua ferrea* Linn. (Bengali name-Nageswar; English name-Cobra's Saffron) belongs to the family Guttiferae.<sup>1</sup> A number of biogenetically related constituents, viz., coumarins, xanthenes, flavonoids, a few terpenoids and steroids have been isolated from various parts of the plant.<sup>1</sup> Venom antidote property<sup>2</sup> with plant extracts and antimicrobial<sup>3</sup> activity of the whole flower extracts have been published. The antibacterial component 4-Alkyl- and 4-phynylcoumarins has been isolated from blossoms.<sup>4</sup> The plant extensively grows in the hills and planted in gardens in many parts of the country.<sup>1</sup> As a part of our continuing studies on the medicinal plants of Bangladesh the study was done to evaluate the analgesic activity using acetic acid induced writhing test in mice models.

The plant leaf of *Mesua ferrea* (MF) was collected from Dhaka University campus during the month of April 2004 and taxonomically identified by the taxonomist of Dhaka University Herbarium. The pulverized coarse powder (250 gm) of the plant leaf was successively extracted by methanol (1 L). The extracts were filtered and concentrated with a rotary evaporator at low temperature (40 - 50°C) and reduced pressure and was subsequently defatted<sup>5</sup> to get the dried methanol (MF) extracts (28.22 g). The methanol extract was fractionated with *n*-hexane and

ethyl acetate and the extracts were 5.82, 6.24 and 12.36 g for *n*-hexane (MFH), ethyl acetate (MFE) and methanol fraction (MFM), respectively.

Swiss albino mice (20 - 24 g) of both sex, aged 4-5 weeks were purchased from the Animal Research Branch of the International Centre for Diarrhoeal Diseases and Research, Bangladesh (ICDDR,B). The animals were kept in polyvinyl cages (BIK industries, India) at room temperature under condition of natural light and dark schedule and supplied with ICDDR,B formulated food pellets and water *ad libitum*. To keep the hydration rate constant, the food and water were withdrawn 12 hours before the experiments.

For the preparation of the test material at a dose of 250 and 125 mg/kg body weight 250 and 125 mg of all the extracts were triturated by the addition of small amount of Tween-80. After proper mixing of the extracts and Tween-80, distilled water was slowly added and the final volume of the suspension of each extract was adjusted to 10 ml. For the preparation of standard, 12.5 mg of aminopyrine (AMP, Sigma, USA) was taken and suspension of 2.5 ml was made with Tween-80 and distilled water.

The peripheral analgesic activity of different crude extracts of GF was studied by the acetic acid induced writhing method<sup>6</sup> using Aminopyrine as standard given orally at a dose of 50 mg/kg. Acetic acid (0.7%) at a dose of 0.1 ml/10g was administered intraperitoneally to create pain sensation. Five minutes after the administration of acetic acid, number of squirms or writhing were counted for each mouse for fifteen minutes.

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The results were analyzed for statistical significance using SPSS software followed by Student's t-test. *P* value <0.05 was considered significant.

In acetic acid induced writhing model the *n*-hexane, methanol and ethyl acetate partition fractions at a dose of 125 mg/kg body weight produced

36.08%, 16.33% and 10.21% (Table 1) reduction of writhing response. In case of *n*-hexane extract the results were found to be highly significant (*P*<0.0001) in comparison to the control. The extracts also produced 42.21, 19.63 and 17.06% reduction of writhing response at a dose of 250 mg/kg body weight, respectively.

**Table 1. Effects of crude extracts<sup>a</sup> on acetic acid induced writhing response in mice.**

Treatment	Dose (mg/kg, p.o)	Writhings <sup>b</sup>	% Inhibition
Control (Vehicle, 1% Tween)	-	100 ± 0.656	-
MFH	125	63.92 ± 0.364**	36.08
	250	57.79 ± 0.329**	42.21
MFM	125	83.67 ± 0.643	16.33
	250	80.37 ± 0.524	19.63
MFE	125	89.79 ± 0.482	10.21
	250	82.94 ± 0.528	17.06
AMP	50	36.66 ± 0.271**	63.39

<sup>a</sup>1hr after treatment, mice were injected i.p. with 0.7%(v/v) acetic acid (0.1ml/10g); 5 minutes after the injection, the number writhing was counted for 15 min. <sup>b</sup>Values are mean ± SEM (n = 6); \*\**P*<0.01, \**P*<0.05 compared to control. AMP: Amino Pyrine.

The results of the present study show that the *n*-hexane extract of MF administered orally to mice, produces significant antinociceptive action against chemical (acetic acid-induced visceral pain) models of nociception in mice. The abdominal constriction response induced by acetic acid is a sensitive procedure to evaluate the potential analgesic activity of drugs. Mechanical, chemical, or thermal threats to tissue integrity cause nociceptive neurons to increase their discharge rate.<sup>7</sup> It has been suggested that acetic acid acts by releasing endogenous mediators that stimulate the nociceptive neurons.<sup>5</sup> It is sensitive to non-steroidal anti-inflammatory drugs (NSAIDs) and to narcotics and other centrally acting drugs.<sup>8,9</sup> Recently, it was found that the nociceptive activity of acetic acid may be due to the release of cytokines, such as TNF- $\alpha$ , interleukin-1 $\beta$  and interleukin-8, by resident peritoneal macrophages and mast cells.<sup>10</sup> Thus, the present study presented here might indicate that the antinociceptive action of *n*-hexane fraction in the acetic acid-induced writhing test could be due to inhibition of the release of TNF- $\alpha$ , interleukin-1 $\beta$  and interleukin-8 by resident peritoneal cells. However,

this possibility remains to be tested in future studies. From the study it may also be said that traditional uses of *Mesua ferrea* Linn. for the treatment of various types of pain conditions has got definite basis. However further investigations are required to identify the active constituent(s) and to verify the therapeutic merits of the active constituent(s).

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