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Full Length Research paper

Analgesic activity of bark of *Murraya paniculata*

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Murraya paniculata **is a common plant widely available in Bangladesh. Different parts of the plant have been used extensively in various traditional formulations in South Asian countries. In order to rationalize the traditional use of the bark of *M. paniculata*, extract of equal proportions of petroleum ether, ethyl acetate and methanol was subject to mice, to evaluate its analgesic activities. The extract of the bark of *M. paniculata* obtained by cold extraction at an oral dose of 200 and 400 mg/kg body weight significantly and dose dependently reduced the frequency of acetic acid induced writhing and prolonged the tail flicking latency in mice. At the given doses, the extract showed 37 ($p<0.001$) and 45% ($p<0.001$) inhibition of writhing respectively. In radiant heat tail-flicking method the crude extract produced 56 ($p<0.001$) and 73% ($p<0.001$) elongation of flicking time after 30 min and 30 ($p<0.01$) and 41% ($p<0.001$) elongation of flicking time 60 min after oral doses of 200 and 400 mg/kg body weight respectively. On the other hand, the bark extract exhibited 19% ($p<0.05$) elongation of flicking time after 120 min.**

Key words: *Murraya paniculata,* whole extract, acetic acid induced writhing, tail flicking test, analgesic activity.

INTRODUCTION

Nature is the best source of medicinal constituents. From the vast natural resources, the plants are being used for therapeutic purposes from the beginning of the civilization (Kirtikar and Basu, 1980). Plants are considered as natural chemical factory. Many constituents of natural origin are now being used in modern medicines. The list of plant- derived medicinal substances occurring in the modern medicine is very long. About 100 such drugs of defined structures are in common use today throughout the world and about half of them are accepted as useful drugs in the industrialized countries (Ghani, 2003). It is estimated that more than 25% of all prescription drugs used in the industrialized countries contain active principles that are still extracted from plants. Medicinal plants synthesize a large number of chemical substances, some of which produce important pharmacological effects on various physiological systems of animals (Ghani, 2003). Most of these plants are also rich sources of bioactive compounds and often serve as important raw materials for drug development. So systematic research on medicinal plants may open the door of many unknown therapeutic tools.

Murraya paniculata, known as cosmetic bark tree, is distributed throughout India, Bangladesh, tropical and subtropical Asia and Africa. They are armed shrub or small tree, leaves are 3 to 7 foliolate, and flowers are inflorescence, corymbose, fragrant. Traditionally most of the plant parts are used therapeutically in treatment of various diseases. The plant is known to have emetic, antipyretic (Chopra et al., 1982), carminative, anti-inflammatory (Calixto et al., 2000), analgesic (Chevallier, 1996) and antiulcer activities. The present study was designed to investigate analgesic activity by acetic acid induced writhing and radiant heat time flicking method in Swiss-albino mice (Koster et al., 1959).

MATERIALS AND METHODS

The bark of the plant *M. paniculata* was collected from the district of Tangail, Bangladesh in March 2006. The specimens of the plant were submitted to the Herbarium of Botany Department, University of Dhaka and taxonomically identified and authenticated by the experts. The collected stem barks were washed, cut into small pieces and dried in the sun for about a week before grinding to course powder. The coarse powder was extracted with a mixture

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Table 1a. Effect of bark extract of *M. paniculata* on acetic acid induced writhing count of mice.

Animal group	Writhing count of individual mouse						Mean	Writhing (%)
Control (1%Tween 80, 10 ml/kg, p.o.)	18	16.5	18	15	13.5	15	16.0	100
Aminopyrine	5.5	8	5	8	6	6.5	6.5	41
MP extract (200 mg/kg)	8	10	7.5	15	10	10	10.08	63
MP extract (400 mg/kg)	8	8	9.5	12	6	9	8.75	55

MP= *Murraya paniculata.*

Table 1b. Effect of bark extract of *M. paniculata* on acetic acid induced writhing inhibition in mice.

Treatment	Dose (mg/kg, p.o.)[a]	Writhing[b]	Inhibition (%)
Control (1%Tween-80, 10 ml/kg p.o.)	-	16.0 ± 091	0.00
Aminopyrine	50	6.5 ± 0.63*	59.37
MP extract	200	10.08 ± 1.33*	37.00
	400	8.75 ± 0.99*	45.31

[a] Administered 1 h before 0.7% acetic acid (0.1 ml/10 gm, ip), [b] Counted for 15 min, starting 5 min after acetic acid injection. Values are mean ± SEM, One way ANOVA ; n = 6, *P<0.001 vs control; MP= *Murraya paniculata.*

of solvents comprising of petroleum ether, ethyl acetate and methanol in equal proportions. Swiss-albino mice of either sex, aged 4 to 5 weeks, average weight 20 to 25 gm were used for the experiment taking six in each group. The mice were purchased from the Animal Research Branch of the International Centre for Diarrheal Diseases Research, Bangladesh (ICDDR, B). They were kept in standard environmental condition and fed ICDDR, B formulated rodent food and water *ad libitum*. Twenty four experimental animals were randomly selected and divided into four groups denoted as group-I, group-II, group-III and group-IV, consisting of 6 mice in each group. Each group received a particular treatment that is, control, positive control and the two doses of the extract. At zero hour two doses of test sample, control (1% Tween-80 solution in saline) and aminopyrine were administered orally by means of a long needle with a ball-shaped end. After 40 min acetic acid (0.7%) was administered intra-peritoneally (0.1 ml/ 10 gm of body weight) to each of the animal of all the groups. The 40 min interval between the oral administration of test materials and intra-peritoneal administration of acetic acid was given to assure proper absorption of the administered samples. Five minutes after the administration of acetic acid, number of squirms or writhing were counted for each mouse for 15 min (Whittle, 1964; Ahmed et al., 2001).

The analgesic activity was also determined by measuring drug-induced changes in the sensitivity of the pre-screened (reaction time: 2 to 4 s) mice to heat stress applied to their tails. A Medicraft Analgesiometer was employed for this experiment (D'Amour and Smith, 1941; Ahmed et al., 2000). Intensity of the current passing through the naked nicrome wire was 5 ampere. The distance between the heat source and the tail skin was 1.5 cm and cut-off reaction time was fixed at 10 s to avoid tissue damage. Morphine was used as the standard analgesic for comparing the tail-flick latencies of crude extract.

RESULTS

In acetic acid induced writhing model in Swiss-albino mice, bark extract of *M. paniculata* at doses of 200 and 400 mg/kg body weight caused significant inhibition of writhing by 37 ($p<0.001$) and 45% ($p<0.001$) respectively (Table 1b). In radiant heat tail-flicking method the bark extract produced 56 ($p<0.01$) and 73% ($p<0.001$) elongation of tail flicking time 30 min after oral doses of 200 and 400 mg/kg body weight respectively (Table 2b). Similarly the extract showed 30 ($p<0.01$) and 41% ($p<0.001$) elongation of flicking time 60 min after oral doses of 200 and 400 mg/kg body weight respectively. On the other hand, the extract exhibited only 19% ($p<0.05$) elongation of flicking time after 120 min. All other results were insignificant when compared with the control (Table 2a).

DISCUSSION

While the traditional use of herbal medicines is more or less obsolete today, it is still used for the remedy of diseases in a large number of patients throughout the world. Many plant metabolites are being successfully used in the treatment of variety of diseases. Even today many people of the world population rely upon the plant resources for their medication (Broneton, 1995). Bangladesh is a potential source of hundreds of medicinal plants. In continuation of our work on the isolation, purification, characterization and pharmacological activities of different bioactive molecules from different medicinal plants of Bangladesh, we investigated this time the bark of *M. paniculata* for its analgesic activities. To investigate for analgesic activities of the bark extract of *M. paniculata*, we used acetic acid induced writhing and radiant heat methods. Intraperitoneal administration of acetic acid (0.7%) causes localized inflammation in mice

Table 2a. Effect of bark extract of *M. paniculata* on tail flicking time in mice by radiant heat method.

Treatment	Dose(mg/kg)[a]	Reaction time (s)[c]		
		30 min	60 min	120 min
Control (vehicle,10 ml/kg, p.o.)	-	4.16±0.13	4.63 ± 0.29	5.05± 0.21
Morphine	2[b]	8.23±0.233***	7.21± 0.24***	6.13 ± 0.19**
MP extract	200[a]	6.5 ± 0.24***	6.0 ± 0.28**	5.71 ± 0.21
	400[a]	7.2 ± 0.29***	6.55 ± 0.18***	5.98± 0.29*

[a]per oral administration of vehicle and crude extract, radiant heat intensity was 5 amp; [b]sub-cutaneous administration; [c]Values are mean ± SEM (n = 6); One-way ANOVA; d.f=3.20, ***p<0.001, **p<0.01, *p<0.05 compared to control. MP= *Murraya paniculata.*

Table 2b. Effect of bark extract of *M. paniculata* on elongation time in mice by radiant heat method.

Treatment	Dose (mg/kg)	Elongation (%)		
		30 min	60 min	120 min
Control (vehicle, 10 ml/kg, p.o.)	-	0.00	0.00	0.00
Morphine	2[b]	97.60	55.70	21.40
MP extract	200[a]	56.00	29.50	13.20
	400[a]	72.80	41.40	18.50

[a]per oral administration of crude extract, radiant heat intensity was 5 amp; [b]sub-cutaneous administration; MP= *Murraya paniculata.*

mice due to the biogenesis of prostaglandins and leukotrienes. The biosynthetic prostaglandins, particularly prostacycline and prostaglandin-E have been reported to be responsible for the pain sensation due to intra-peritonial administration of acetic acid (Berkenkopf and Weichman, 1988). Aminopy-rine, like other non-steroidal anti-inflammatory drugs inhibits the biogenesis of prostaglandins thus inhibiting the writhing in experimental animals like mice. As the bark extract of *M. paniculata* inhibits the writhing in mice, it is possible that the extract acts through the same mechanism of action as that of aminopyrine.

Substance P is released in excessive quantities due to the stimulation of non myelinated C fibers of mouse's tail after the application of radiant heat. In case of acetic acid writhing model, prostacycline stimulates C fibers where as in radiant heat method C fibers are stimulated by radiant heat, serving as noxious stimuli. Narcotic analgesics like pethidine and morphine are potential agonist of μ, χ and δ receptors. These receptors are specific for endogenous narcotics like endorphins, enkephalins etc. After binding to these receptors narcotic analgesics antagonize the action of substance P in the CNS by producing post-synaptic inhibitory action on interneuron, which processes the nociceptive information to be transmitted to the CNS. As our bark extract of *M. paniculata* showed significant analgesic activity in radiant heat method, it can be assumed that the extract could act by a central anti-nociceptive mode like that of morphin.

In the present study, we investigated analgesic activity of two doses of extract of *M. paniculata* by acetic acid induced writhing method (Chakraborty et al., 2004; Hendershot and Forsaith, 1959). The study indicated that at doses of 200 and 400 mg/kg body weight the extract caused significant inhibition of writhing. It was observed from the study that percent of inhibition of writhing can be increased by increasing the dose. Results of two doses were also comparable with those of standard drug amino-pyrine. Similar analgesic activities were also observed in radiant heat method. The aforementioned doses of the bark extract significantly and dose dependently increased the elongation of tail flicking time in mice when compared to standard drug morphine.

These observations are also consistent with those of Chevallier A. (1996), when he observed significant analgesic activity in *M. paniculata.* It is evident from the study that the bark of *M. paniculata* extracted by equal proportions of petroleum ether, ethyl acetate and methanol exhibits significant analgesic effect in albino mice. We believe, further detailed advanced studies may be pursued in future to explore the analgesic activities of the plant as well as its active constituents.

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