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Antinociceptive activity of methanol extract of *Begonia thomsonii* A. DC. leaves

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ABSTRACT

The nature has provided abundant plant wealth for all the living creatures, which possess medicinal virtues. Therefore, there is a necessity to explore their uses and to ascertain their therapeutic properties. The present study was to investigate anti-nociceptive action of the methanol extract of *Begonia thomsonii* A.DC. leaves. The mice were submitted to acetic acid-induced writhing test and Formalin induced licking test to assess antinociceptive activities, respectively. Two doses 400 and 200 mg/kg were administered for testing. The methanol extract of *B. thomsonii* at both doses, exhibited a significant ($P < 0.001$) dose-dependent antinociceptive activity in acetic acid writhing test and Formalin test. In acetic acid-induced writhing test, oral administration of methanol extract of *B. thomsonii* (200 and 400 mg/kg) also decreased the writhing significantly while compared to control. The dose 400 mg/kg showed maximum percentage of pain inhibition (33.33%). Aspirin (10 mg/kg) was used as reference antinociceptive drugs. Methanol extract of *B. thomsonii* (200 and 400 mg/kg) significantly suppressed the licking activity in both phase of the formalin-induced pain in mice in a dose dependant manner. The reference analgesic drug Aspirin (10 mg/kg) also significantly inhibited the licking activity against both phases of formalin induced pain. The leaf extract has potential antinociceptive activity. The present study supports the use of *B. thomsonii* in different pain states.

Keywords: *B. thomsonii*, anti-nociceptive, Acetic acid writhing test, Formalin.

INTRODUCTION

Medicinal plants and their use by indigenous cultures is not only helpful for maintenance of traditions and biodiversity but also for community healthcare and drug development in the present and future. About 25% of prescribed drugs in the world are of plant origin [1]. Approximately 80% people rely on traditional plant based medicines for their initial health care needs in developing countries [2]. Therapies with synthetic tropical applications have many side effects and cannot be afforded by the people due to higher cost of the drug. For overcoming this problem plants growing around us are utilized without scientific validation. The use of higher plants and their extracts to treat infections is an age-old practice. Traditional medicinal practice has been known for centuries in many parts of the world. Herbal medicines are gaining interest because of their cost effective and eco-friendly attributes [3,

4].

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage [5]. By acting in the CNS or on the peripheral pain mechanism, analgesic compounds selectively relieves pain without significant alteration of consciousness. Actually analgesics are applied when the noxious stimulus cannot be removed or as adjuvant to more etiological approach to pain [6]. Analgesics relieve pain as a symptom, without affecting its cause [7]. Currently available analgesic drugs such as opiates and NSAIDs are not useful in all cases due to their side effect profile. Opiate analgesic such as morphine has strong addictive potential and other side effects including respiratory depression, drowsiness, decreased gastrointentinal motility, nausea and several alterations of endocrine and autonomic nervous system while NSAIDs are well known for their ability to produce gastrointestinal bleeding, ulceration etc [8, 9]. Therefore, search for new analgesic drugs with promising pharmacological actions has become an urgent need.

Begonia thomsonii is a species of plant of the family of the *Begoniaceae* [10]. The species is part of the *Platycentrum* section. Specially found in India and Bangladesh. The flowers are frequently showy and large, white, pink, scarlet or yellow in colour; they are monoecious, with unisexual male and female flowers occurring separately on the same plant, the male containing numerous stamens, the female having a large inferior ovary and two to four branched or twisted stigmas. Begonia houseplants species have been introduced, and there are numberless hybrids and variations . Because of the great number of interesting forms. These are also foliage begonias that are very nearly a hot house variety. They do best in a temperature of 70-75 F. (21-24 C.). The leaves are heart-shaped and are the most striking foliage producers. The leaves can be bright red, green, pink, silver, gray and purple in vibrant combinations and patterns. The leaves are slightly hairy and textured adding to the interest of the foliage. The flowers will tend to be hidden in the foliage. Seeds contain alkaloids, mucronatine, usaramine, nilgirine, mucronatinine and crotastriatine. Luteolin, vitexin, its O-xyloside and chrysoeriol-7-rutinoside have also been isolated from seeds. Vitexin, vitexin-4'-O-xyloside and apigenin have been isolated from leaves and stem bark. Most effective in cold and digestive diseases and cancer. Effective in burn, bronchitis, candidiasis, and anti-inflammatory hepato protective. Risk factors of diabetes, kidney problems, high blood pressure.

The purpose of this experiment was to test the antinociceptive activity of *B. thomsonii* on mice using Acetic acid writhing test and Formalin test.

MATERIALS AND METHODS

Experimental animals

Swiss albino mice, weighing about 25–30 g, were collected from Jahangir Nagar University, Savar, Bangladesh. The animals were provided with standard laboratory food and distilled water ad libitum and maintained at natural day-night cycle having proper ventilation in the room. All the experiments were conducted in an isolated and noiseless condition. The study protocol was approved by the P&D Committee, Department of Pharmacy, International Islamic University Chittagong, Bangladesh. The animals were acclimatized to laboratory condition for 10 days prior to experimentation

Plant material and preparation of extract

B. thomsonii was collected from a local village Sylhet, Bangladesh and authenticated by Dr. Shaikh Bokhtear Uddin (Professor, Department of Botany, and University of Chittagong, Bangladesh). The collected plant was washed thoroughly with water and air dried for a week at 35 to 40°C and pulverized in an electric grinder. For methanol extract, 500 g powder of leaves was soaked in 2 liter of methanol for 12 days. Subsequently, the mixture was filtered using Whatman filter paper. The filtrate was concentrated over the vapor of the water bath and dried.

Antinociceptive activity

Acetic acid induced writhing test

Mice were divided into four groups of both sexes containing five of each. For writhing test, 0.6% (v/v) acetic acid solution (10 mL/kg body weight) was injected intraperitoneally to each mice and the number of writhing and stretching was counted over 20 min. Group I served as control received normal saline 10ml/kg), Group II received Aspirin 10 mg/kg as a standard, Group III and Group IV treated with methanol extract of *B. thomsonii* (200 and 400 mg/kg) orally 30 min before acetic acid injection [11].

Formalin induced licking test

20 µL of 2.5% Formalin in saline was injected subcutaneously to a hind paw of the mice after 30 min administration of the Aspirin 10 mg/kg, methanol extract of *B. thomsonii* of 200 mg/kg and 400 mg/kg p.o to the Group II, III and IV respectively. Group I as control received only formalin (20 µL of 2.5%) during the experiment. The time spent licking and biting responses of the injected paw was taken as an indicator of pain response and

the data were expressed as total licking time in the early phase (0-5 min) and the late phase (15-30 min) after formalin injection [11].

Statistical analysis

The data was analyzed by one-way ANOVA followed by Dunnet's test to estimate significant differences between the test and control groups with GraphPad Prism Data Editor for Windows, Version 6.0 (GraphPad software Inc., San Diego, CA). Values were expressed as mean ± Standard error for mean (± SEM). $p < 0.05$ - 0.01 were considered as statistically significant.

RESULTS

Analgesic Activity

Acetic acid test

Treatment with methanol extract of *B. thomsonii* 200 mg/kg, p.o. and 400 mg/kg, p.o. significantly decreases the number of writhing after acetic acid induction in mice (Table 1 and Figure 1). Maximum analgesic activity (33.33%) was found at 400 mg/kg. Aspirin (10 mg/kg) shown 55.08% protection against acetic acid induced writhing in mice.

Table 1: Effect of *B. thomsonii* extract on acetic acid induced writhing response in mice.

Treatment	Writhing	% inhibition
Control(1% tween)	30 ± 0.40	-
Aspirin (10mg/kg)	13.25 ± 0.47[a]	55.08
MEBT (200mg/kg)	24.5 ± 0.28[a]	18.33
MEBT (400mg/kg)	20 ± 0.408[a]	33.33

MEBT =Methanol extract of *B. thomsonii;* *P<0.05, **P<0.01 as control.

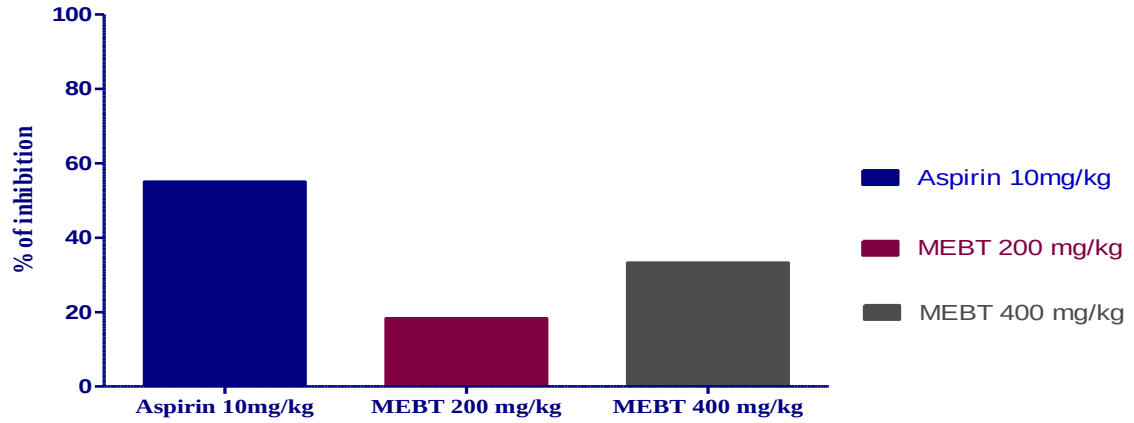

Figure 1: Effect of *B. thomsonii* leaves extract on acetic acid induced writhing response in mice.

Formalin test

The effect of ethanol extract of *B. thomsonii* in formalin test is shown in Table 2 and Figure 2. At both doses, there was dose dependent decrease of paw licking time in early phase but dose of 400 mg/kg significantly (P<0.05) reduced latency to discomfort in late phase compared to the late phase of the test control. In contrast, the reference Analgesic drug Aspirin (10 mg/kg) significantly reduced the licking activity against both phases of formalin-induced nociception.

Table 2: Analgesic profile of *B. thomsonii* leaves extract assessed by the formalin test in mice.

Treatment	Early Phase (1st 5	% inhibition	Late Phase (Last 15	% inhibition
Control (1% tween)	86±0.70	-	89.5±0.87	-
Aspirin (10mg/kg)	37±0.91[b]	56.98	28±0.71[b]	67.77
MECB (200mg/kg)	67.25±0.85[a]	21.80	70.5±0.29[b]	21.23
MECB (400mg/kg)	58.5±0.95[b]	31.98	59.25±0.85[b]	33.79

MEBT=Methanol extract of *B. thomsonii*; [a]P<0.05, [b]P<0.01 as control.

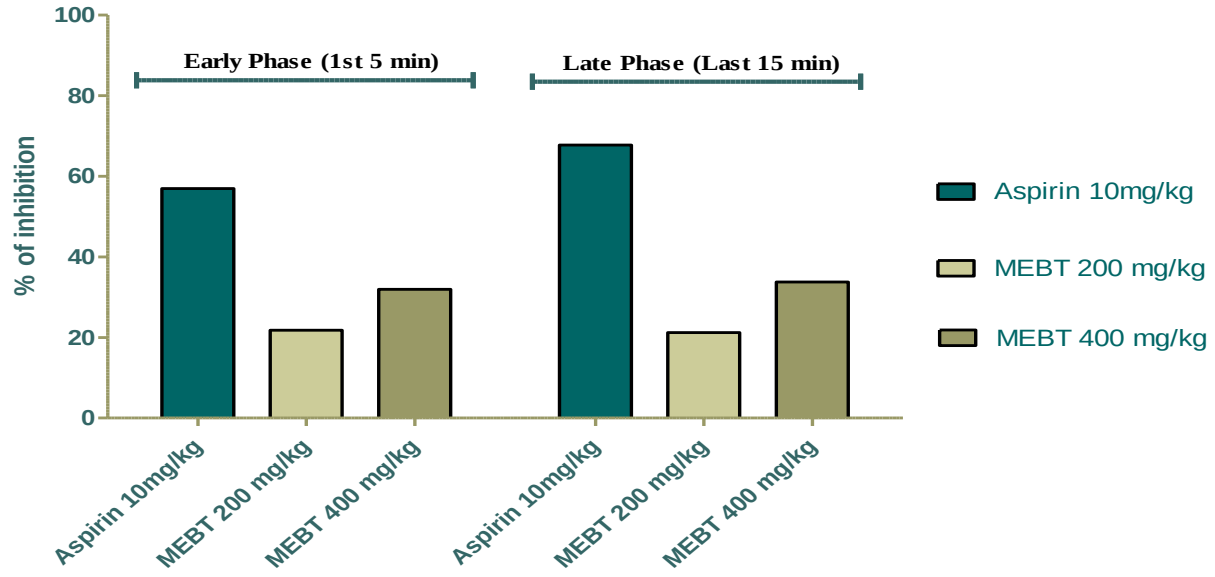

Figure 2: Effect of the methanol extract of *B. thomsonii* on hind paw licking in the formalin test in mice.

DISCUSSIONS

It was observed from the study that in both analgesic activity assay models the leaves extract demonstrated antinociceptive effects. This means that the extract may possess both peripheral and central analgesic effects. The leaves extract of *B. thomsonii* exhibited significant dose dependent inhibition of acetic acid–induced writhing in mice in comparison to that of the control. Acetic acid induced writhing test, which is the visceral pain model, was employed to evaluate the peripheral analgesic activity of the plant material. The abdominal constriction response induced by acetic acid is a sensitive procedure to determine analgesia at peripheral level. This response is thought to involve local peritoneal receptors [12]. Acetic acid is known to trigger the production of noxious substances such as prostaglandins specifically PGE2 and PGF2 as well as lipoxygenase products [13]. These prostaglandins and lipoxygenase products cause inflammation and pain by increasing capillary permeability [14]. Acetic acid may also cause release of other algesic mediators such as bradykinin, histamine and 5-hydroxytryptamine [15]. The substance inhibiting the writhings will have analgesic effect preferably by inhibition of prostaglandin synthesis, a peripheral mechanism of pain inhibition [16].

It was observed from the study that in both analgesic activity assay models the plant extract demonstrated analgesic effects. This means that the extract may possess both peripheral and central analgesic effects. The leaves extract of *B. thomsonii* exhibited significant dose dependent inhibition of acetic acid–induced writhing in mice in comparison to that of the control (saline). Acetic acid induces inflammatory pain by impelling capillary permeability [17], and releasing substances that excite pain nerve endings [18]. The peripheral analgesic effect is generally mediated by the NSAIDs through inhibition of cyclooxygenase and/or lipoxygenase (and other inflammatory mediators) or inhibition of pain responses mediated by noiceptors peripherally [19]. Therefore, it is possible that methanol extract of *B. thomsonii* may be showing analgesic effect through these mechanisms although the exact mechanism of action is yet to be discovered. Again in hot plate test the extract also showed prominent antinociceptive effect against the standard drug Diclofenac Na. Moreover, activation of μ2 opioid subtype receptor leads to spinal analgesia [20]. Therefore, by considering the test report, it may be assumed that the antinociceptive activity of *B. thomsonii* extract is likely to be mediated centrally although the exact mechanism is yet to be discovered.

CONCLUSION

The study showed that methanol extract of *Begonia thomsonii* possesses significant analgesic activity which was validated by various pain models in this study. The results substantiate the ethnomedicinal use of *B. thomsonii* to palliate pain disorder. The findings of present studies warrant further studies for isolation and identification of the responsible bioactive component(s) and to elucidate the mechanism(s) lying with these effects.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

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