

# Evaluation of Anti-diarrheal and Anti-nociceptive Activity of Methanolic Unripe Fruit Peels Extract of *Mesua ferrea* Linn. on Mice Models

Kishor Mazumder<sup>1,3,\*</sup>, Ziku Chandra Dey<sup>2</sup>, Suparna Dey<sup>4</sup>, Md. Fazlul Kabir<sup>2</sup>, Minhazur Rahman<sup>2</sup>, Sadiur Rahman Sajon<sup>1</sup>

Kishor Mazumder<sup>1,3,\*</sup>, Ziku Chandra Dey<sup>2</sup>, Suparna Dey<sup>4</sup>, Md. Fazlul Kabir<sup>2</sup>, Minhazur Rahman<sup>2</sup>, Sadiur Rahman Sajon<sup>1</sup>

<sup>1</sup>Department of Pharmacy, Jessore University of Science and Technology, Jessore-7408, Jessore, BANGLADESH.

<sup>2</sup>University of Science & Technology Chittagong (USTC), Chittagong, BANGLADESH.

<sup>3</sup>School of Biomedical Sciences and Graham Centre for Agricultural Innovation, Charles Sturt University, Boorooma St, Wagga Wagga, NSW, AUSTRALIA.

<sup>4</sup>Center for Specialized Care and Research, Chittagong-4000, BANGLADESH.

## Correspondence

Dr. Kishor Mazumder

Associate Professor, Department of Pharmacy, Jessore University of Science and Technology, Jessore-7408, Jessore, BANGLADESH.

Adjunct Lecturer, School of Biomedical Sciences and Graham Centre for Agricultural Innovation, Charles Sturt University, Boorooma St, Wagga Wagga, NSW, AUSTRALIA.

Phone no: +88-0224142034; ext. 213; +88-01817754648

E-mail: kmazumder@csu.edu.au, mazumderkis2002@yahoo.com

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## ABSTRACT

**Background:** Though traditionally the plant *Mesua ferrea* has been used by south east Asian people in inflammation and septic conditions, the present study was designed to investigate the anti-diarrheal and anti-nociceptive activities of unripe fruit peel of *Mesua ferrea* on animal models. **Methods:** Various methods were employed for investigating these activities such as castor-oil induced diarrhea, castor-oil induced enteropooling and gastrointestinal motility test, acetic acid induced writhing test, tail immersion and hot plate methods. **Results:** From the experimental data it was found that the diarrheal episode was inhibited by 39.68% and 49.21% for methanol extract at the doses of 100 and 200 mg/kg respectively. The extract significantly lessened the intestinal volume for methanolic extract at 200 mg/Kg dose  $0.54 \pm 0.01$  ml ( $p < 0.05$ ) and at 200 mg/Kg dose  $0.47 \pm 0.02$  ml ( $p < 0.01$ ) compared to control  $0.65 \pm 0.03$  ml in castor-oil induced enteropooling and also decreased intestinal transit  $29.07 - 48.54\%$  for methanolic extract comparable with standard (loperamide 5 mg/kg). *Mesua ferrea* peels significantly ( $P < 0.05$ ,  $P < 0.01$  and  $P < 0.001$ ) reduced the number of writhing, increased latency to flick tail in tail immersion method and elevated the mean basal reaction time in hot plate method respectively. Besides, no delayed toxicity was observed in given doses. **Conclusion:** The methanolic extract exhibited highly significant anti-diarrheal and anti-nociceptive activity in a dose-dependent manner, which supports its use in traditional herbal medicine.

**Key words:** *Mesua ferrea*, Anti-diarrheal, Anti-nociceptive, Castor oil, Intestinal transit, Tail immersion method.

## INTRODUCTION

In many developing countries, the individuals and communities of the country consider medicinal plants as a great source of primary health care. As herbal products are obtained from nature, they are considered safer. Now-a-days, herbal medicine are a great component of traditional medicinal system and an inseparable part of Ayurvedic, Siddha, Homeopathic, Naturopathic, Native American medicine and Traditional Chinese medicine. A lot of attention is being concentrated on developing natural products obtained from plant sources<sup>1</sup>. Moreover, as it has spiritual and traditional value, it is also used by 80% of the population of developing country and thus acts as a great alternative to costly Western medicine.<sup>2</sup> In third world countries diarrhea is a major health problem and causes the death of over one million per year. Diarrhea is caused by an alteration in normal intestinal movement and generally is characterized by increased water content, volume or frequency of stools.<sup>3</sup> Local herbal practitioners use medicinal plants effectively in the treatment of diarrhea. For these reasons, exploration in the search of medicinal plants that possess antidiarrheal activity is very popular, so that it could be of benefit to find an effective option for treating diarrhea in third

world countries.<sup>4</sup> Diarrhea causes one third of the child death in Bangladesh.<sup>5</sup> In this scenario, WHO proposed the use of traditional plant in its Diarrhea Control Program.<sup>6</sup> On the other hand, pain acts as a major indicator of many diseases. Analgesics act on the central nervous system or peripheral nervous system without changing the consciousness.<sup>7</sup> Response towards pain is ameliorated by analgesics by reducing the sensitivity of the painful organ towards external factors.<sup>8</sup>

*Mesua ferrea* is a medium to large sized ornamental tree which is evergreen in nature and distributed throughout Burma, Cambodia, Indochina region, Malaysia, Myanmar, Nepal (southern), Philippines, Sri Lanka, Sumatra and Thailand. Mature leaves (7-15 cm long) of *Mesua ferra* are blue grey to dark green in color, whereas, young leaves appear as reddish yellow. In flowering season, it produces large fragrant flowers with four petals with numerous yellowish stamens at the centre, whereas, fruits are sometimes beaked with slight woody appearance and contains 1-4 seeds. Bark appears as reddish brown and flower, fruit, seeds and leaves of this plant are edible.<sup>9</sup> Traditionally, different parts of this plant is used as antipyretic, antimicrobial, anticancer, cardiotoxic, diuretic, expectorant, poultice, aroma, wound healer, bleeding piles, excessive thirst, itching, sweating,

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immunity boosters, sorethroat and many more.<sup>10</sup> By phytochemical screening, it has been revealed that, *Mesua ferrea* contains molecules such as- mesuaxanthone-A, mesuaxanthone-B, 1,5-dihydroxyxanthone (II), euxanthone 7-methyl ether (IV) and  $\beta$ -sitosterol, Ferrol-A, eight different types of xanthenes, 1,3-dimethoxy-5,6-dihydroxyxanthone (E)- $\alpha$ -bisabolene,  $\alpha$ -selinene,  $\alpha$ -copaen,  $\beta$ -caryophyllen,  $\alpha$ -copaene, germacrene D etc.<sup>11-18</sup>

However, there was no study on the green peels of unripe fruit, hence an effort has been made to investigate the potential uses of unripe peels of this plant to evaluate anti-diarrheal and anti-nociceptive potentials.

## MATERIALS AND METHODS

### Plant material

Fruit samples of this plant were collected from the forests of Chittagong and Chittagong Hill Tracts in May 2010 when fruits were in their maximum productivity. The plant was identified by the Department of Botany, University of Chittagong, Bangladesh. A voucher specimen SBU 1121. Dt.06.03.2009. CTGUH, has been deposited. The fruits peels were thoroughly washed with water and dried in a shade at room temperature for 7 days; afterwards, they were dried in an oven at 40°C to facilitate grinding for the next 2 days.

### Preparation of extract

The dried fruit peels were powdered coarsely and about 500 g of powdered material was soaked in methanol (2 L) at room temperature for seven days while shaking and stirring occasionally. The whole mixture was then filtered and the filtrate thus obtained was concentrated by using a rotary evaporator (Bibby RE200, Sterlin Ltd, UK) to get a viscous mass which was air dried afterwards.

### Animals

Swiss Albino mice of either sex, weighting 25 to 30 gm was obtained from animal house of Department of Pharmacy, Jahangirnagar University, Dhaka, Bangladesh and housed in polypropylene cages under controlled conditions. The animals were exposed to alternative 12h light/12h dark cycle at an ambient temperature of  $27 \pm 1^\circ\text{C}$  with a relative humidity of 55% - 65%. Animals were allowed free access to drinking water ad libitum and pellet diet (obtained from International Centre for Diarrheal Disease and Research, Bangladesh). All the animals were acclimatized for 10 days in the laboratory environment prior to the study. For conducting all experiments with animals, we followed the guidelines of Institutional Animals Ethics Committee (IAEC) and before the experiments, study protocols were approved by the University of Science and Technology Medical Ethics, Biosafety and Biosecurity Committee (USTMEBBC) at the Life Science Faculty, University of Science and Technology Chittagong, Bangladesh. The test animals were divided into several groups for different dose such as 100 mg/kg, 200 mg/kg of 400 mg/kg etc. The animals were acclimatized to laboratory condition for one week prior to experimentation.

### Chemicals

Following chemicals were used in conducting the experiment- Diclofenac sodium (Beximco Pharmaceuticals Ltd., Dhaka, Bangladesh), nalbuphine (Incepta Pharmaceuticals Ltd., Dhaka, Bangladesh), acetic acid (MERCK, Mumbai, India), Loperamide hydrochloride 99.71% (Square Pharmaceuticals Ltd., Bangladesh), castor oil (WELL's Health Care, Spain), normal saline solution, 0.9% NaCl (Popular Pharmaceuticals Ltd., Bangladesh) and charcoal preparation (10% activated charcoal in 5% gum acacia) were used.

## Anti-diarrheal activity

### Castor oil induced diarrhea

We followed the method of Awouters, *et al.* for conducting the experiment.<sup>19</sup> The experimenting mice were fasted 14 hours prior to experiment with water ad libitum. Four groups of mice were taken for this experiment. Group I was treated as control (saline 2 ml/kg body weight, i.p.), Group II received standard drug (loperamide 5 mg/kg b. wt. i. p.) and Group III-IV received methanolic extract (100 and 200 mg/kg b. wt. i. p.). After 1-hour interval, each animal was given castor oil orally in the purpose of inducing diarrhea. Then the mice were caged with white blotting paper placed at the bottom of the cage and the papers were changed every 1 hour for the purpose of ease in stool count. The total number of both dry and wet feces were counted every hour and the process continued up to 4 hours. Then the total number of excreted feces were compared with control group whereas total number of diarrheal feces of the control group was considered 100%.

### Castor oil induced enteropooling

Intra-luminal fluid accumulation was determined by the method of Robert, *et al.*<sup>20</sup> 14h fasted mice were divided into four groups (Group I-IV) of five animals each and treated as previously described method. Then 1 h later, all the animals were administered with castor oil in oral route. And with one-hour interval of administering castor oil, the mice were sacrificed by overdose of chloroform anesthesia. Then we dissected out the small intestine at pyloric sphincter and ileocecal junction. The small intestine was weighed, and intestinal contents were milked into a graduated tube and the volume was measured. The intestines were reweighed the empty intestine and the differences between full and empty intestines were calculated.

### Gastrointestinal motility test

The experiment employed according to the method described by Mascolo, *et al.*<sup>21</sup> The animals were fasted for 18 hours prior to experiment with water ad libitum and the fasted mice were grouped as- Group I (Control group: treated with saline 2 ml/kg body weight orally), Group II (Standard group: treated with loperamide 5 mg/kg b. wt. i.p), Group III-IV (treated with 100 and 200 mg/kg b. wt. dose of *Mesua ferrea* aqueous extract i.p.) with five animals in each group. Before 1 hour of treating the groups with respective materials, the animals were given castor oil orally to induce diarrhea. After 1 hour of treating the animals with respective material, the animals were given charcoal preparation (10% charcoal suspension in 5% gum acacia) orally for tracking the movement of the contents afterwards. With one-hour interval, the animals were sacrificed by overdose of chloroform anesthesia and the distance traveled by the charcoal preparation from pylorus to caecum was measured and expressed as a percentage of the total distance of the intestine.

## Anti-nociceptive activity

### Acetic acid induced writhing test

The experimental animals were partitioned into four groups, each group containing five mice each. The groups are- control group (saline: 2 ml/kg b.w.), standard group (diclofenac sodium: 10 mg/kg b.w.), group III and IV (methanolic extract: 200 and 400 mg/kg b.w. respectively). With 30 minutes interval, the treated animals were injected with 0.7% acetic acid.<sup>22</sup> With 15 minutes intervals after administering acetic acid, mouse were observed and the number of writhing or stretches were counted for 5 min. Mean abdominal writhes and stretches for each group was calculated and reduction in writhes compared to control group was considered as evidence of analgesic activity. The percent inhibition (% analgesic activity) was calculated by;

$$\% \text{ inhibition} = \{(A-B)/A\} \times 100$$

Where, A= Average number of writhing of the control group;

B= Average number of writhing of the test group.

#### Tail immersion method

The experimental animals were divided into four groups, each group containing five mice each. The groups are- control group (saline: 2 ml/kg b.w.), standard group (diclofenac sodium: 10 mg/kg b.w.), group III and IV (methanolic extract: 200 and 400 mg/kg b.w. respectively). The latency of mice tail flick from hot water was noted as the basal reaction time. The lower 3 cm portion of the tail of mice was dipped in a water bath maintaining at temperature of  $55 \pm 0.5^\circ\text{C}$ . The reaction time was noted at 0, +30, +60 and +90 min and a cut off time of 15 sec was maintained to prevent thermal organ damage to the animals.<sup>23</sup>

#### Hot plate method

In hot plate method of anti-nociceptive activity evaluation was conducted according to Eddy and Liembach.<sup>24</sup> The experimental animals were divided into four groups, each group containing five mice each. The groups are- control group (saline: 2 ml/kg b.w.), standard group (diclofenac sodium: 10 mg/kg b.w.), group III and IV (methanolic extract: 200 and 400 mg/kg b.w. respectively). The mice were placed in a one-liter glass beaker on a heated surface maintained at  $55 \pm 0.5^\circ\text{C}$ . The reaction time was counted when the experimental animals were placed on the hot surface until the moment animal licked its feet or jumped out and the time in between was taken as latency time. A cut off time of 20s

was followed to avoid any thermal injury to the paws. The reaction time were recorded before and after 0, +15, +30, +45 and +60 min following administration of test or standard drug.

#### Statistical analysis

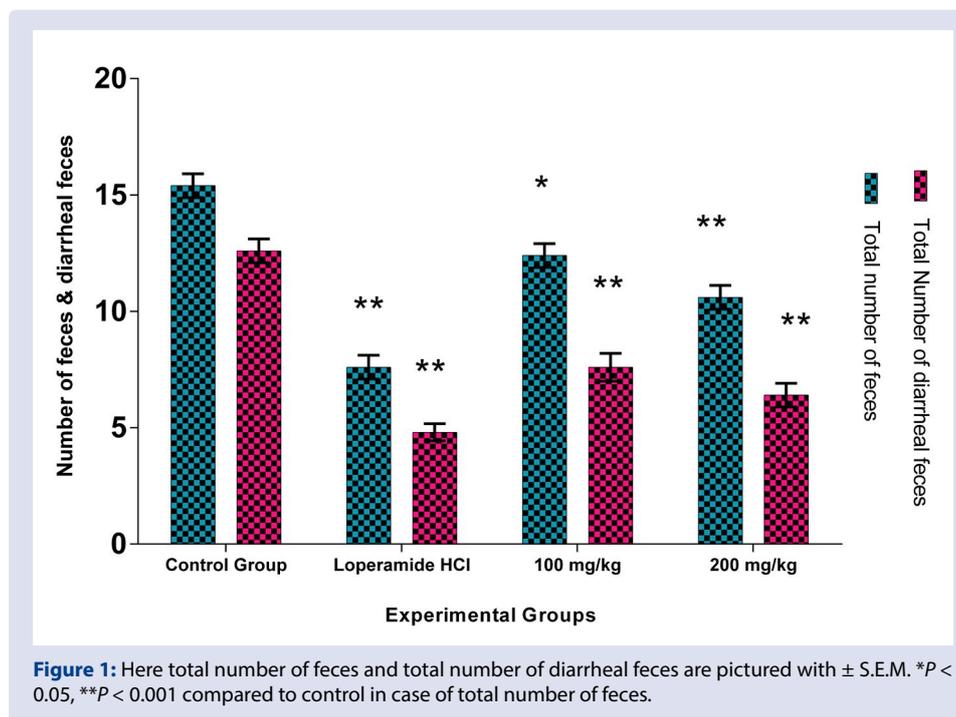
All results are expressed as (mean  $\pm$  standard error) and to represent the significance we used one-way ANOVA (Analysis of Variance) followed by Bonferroni test. P value less than 0.05 or 0.001 was considered statistically significant. All data were calculated with SPSS software (version: 16; IBM corporation, New York, USA). All the graph in the study were drawn with GraphPad Prism (version: 6) for windows operating system.

## RESULTS

### Anti-diarrheal activity

#### Castor oil induced diarrhea

In the castor oil-induced diarrhea, at doses of 100 and 200 mg/kg, the methanolic extracts produced very significant inhibition of ( $p < 0.001$ ) defecation when compared to control. The total number of wet feces produced upon administration of castor oil decreased ( $7.60 \pm 0.60^{**}$  at 100 mg/kg and  $6.40 \pm 0.51^{**}$  at 200 mg/kg) in dose dependent fashion compared to control ( $12.60 \pm 0.51$ ) group while in case of loperamide, the decreased value is  $4.80 \pm 0.37^{**}$  at the dose of 5 mg/kg. Total number of feces and total number of diarrheal feces with  $\pm$ SEM are displayed in Figure 1 while percent inhibition in both total feces and diarrheal feces are shown in Table 1.



**Table 1:** Effect of methanolic extract of *M. ferrea* fruit peel on castor oil induced diarrhea in mice.

Group	Treatment	% Inhibition of defecation	% Inhibition of diarrheal feces
I	Castor oil + Saline (2 ml/kg p. o.)	---	--
II	Castor oil + Loperamide (5 mg/kg i. p.)	50.65	61.90
III	Castor oil + Extract (100 mg/kg i. p.)	19.48	39.68
IV	Castor oil + Extract (200 mg/kg i. p.)	31.16	49.21

### Castor oil induced enteropooling

Castor oil caused aggregation of water and electrolytes in intestinal loop. Treatment with the *M. ferrea* extract (100 and 200 mg/kg) produced moderately significant ( $p < 0.05$ ,  $p < 0.01$ ) and dose-dependent reduction in intestinal weight and volume (Table 2). We can see that, in case of control, the weight of intestinal content is ( $1.78 \pm 0.08$ ) g and volume is ( $0.65 \pm 0.03$ ) ml. For standard group, the value is ( $1.50 \pm 0.03$ )\*\* g and ( $0.41 \pm 0.01$ )\* ml respectively. In case of 100 mg/kg b.w. extract of methanolic extract of *M. ferrea*, weight of intestinal content is ( $1.60 \pm 0.01$ )\* g and volume is ( $0.54 \pm 0.01$ ) ml. And, for 200 mg/kg b.w. methanolic extract of the plant, the values are ( $1.57 \pm 0.03$ )\*\* g and ( $0.47 \pm 0.02$ ) ml respectively. The intestinal volume was decreased by 16.92% and 27.69% for methanolic extracts at doses 100 and 200 mg/kg respectively. On the other hand, the standard drug, loperamide (5 mg/kg), also significantly inhibited ( $p < 0.05$ ) intestinal fluid accumulation (36.92%). These values are represented in Figure 2 and Table 2.

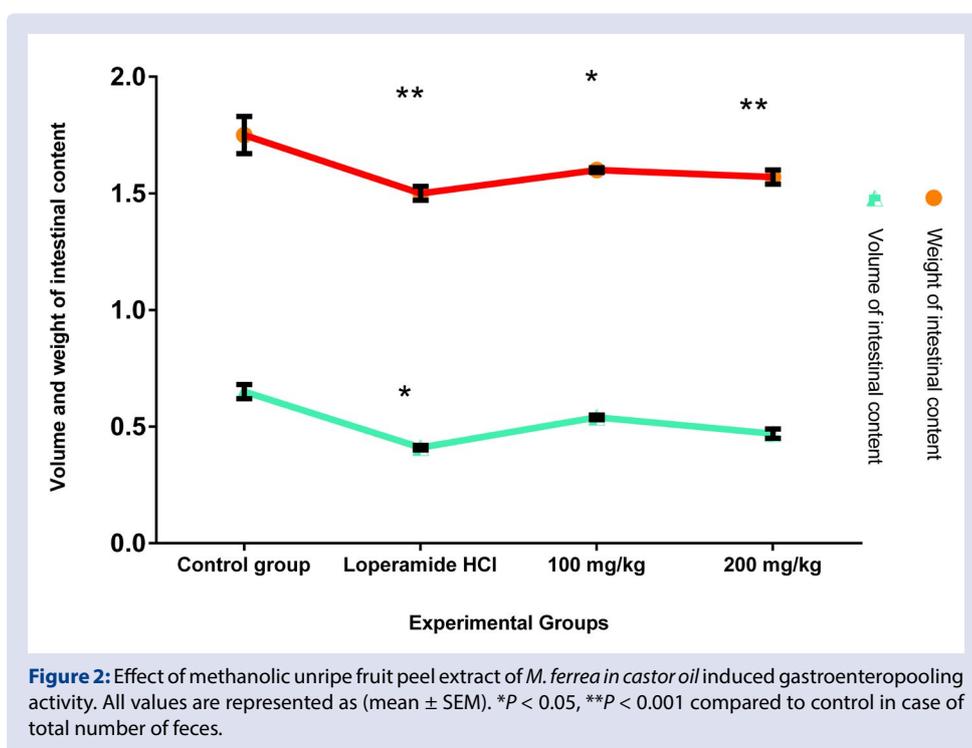
### Gastrointestinal motility test

In this method, the methanolic extract of *M. ferrea* was also significantly lessened the gastrointestinal distance ( $36.67 \pm 2.70$  cm for 100 mg/kg and  $29.33 \pm 2.08$  cm for 200 mg/kg for methanolic extract) traveled by the charcoal meal in the mice gastrointestinal tract compared with the control ( $40.67 \pm 3.48$  cm) group (Table 3). Loperamide (5 mg/kg) produced a marked (72.18%) decrease in the propulsion of charcoal meal through gastrointestinal tract.

### Analgesic Activity

#### Acetic acid induced writhing test

Table 4 shows the effects of the methanolic extract of *M. ferrea* on acetic acid induced mice. Oral administration of the extract moderately ( $p < 0.01$ ) inhibited writhing response induced by acetic acid which was comparable to the reference drug. Inhibition of writhing by methanolic extract was dose dependent (such as 16.67% and 25.56% inhibition



**Table 2:** Effect of methanolic extract of *M. ferrea* fruit peel on castor oil induced enteropooling in mice.

Group	Treatment	Inhibition (%)
I	Castor oil + Saline (2 ml/kg p. o.)	--
II	Castor oil + Loperamide (5 mg/kg i. p.)	36.92
III	Castor oil + Extract (100 mg/kg i. p.)	16.92
IV	Castor oil + Extract (200 mg/kg i. p.)	27.69

Values are expressed as mean ± SEM. (n = 5). \* $P < 0.05$ , \*\* $P < 0.001$  when compared with control group.

**Table 3:** Effect of methanolic extract of *M. ferrea* fruit peel on Gut transit test in mice.

Group	Treatment	Total length of intestine (cm)	Distance traveled by marker (cm)	Inhibition (%)
I	Castor oil + Saline (2 ml/kg p. o.)	54.0 ± 0.58	40.67 ± 3.48	--
II	Castor oil + Loperamide (5 mg/kg i. p.)	52.7 ± 0.88	14.66 ± 1.45**	72.18
III	Castor oil + Extract (100 mg/kg i. p.)	51.7 ± 0.88	36.67 ± 2.70	29.07
IV	Castor oil + Extract (200 mg/kg i. p.)	57.0 ± 3.05	29.33 ± 2.08	48.54

Values are expressed as mean ± SEM. (n = 5). \* $P < 0.05$ , \*\* $P < 0.001$  when compared with control group.

for the dose of 200 mg/kg and 400 mg/kg respectively) and significant effect was found at a dose of 400 mg/kg.

#### Tail immersion test

There was a significant increase in latency time following administration of the extract at dose of 200 mg/kg ( $8.34 \pm 1.20$  sec) and 400 mg/kg ( $9.33 \pm 1.20$  sec). The result was statistically significant ( $P < 0.05$ ,  $P < 0.01$ ) and was comparable to the reference drug Nalbuphine ( $10.67 \pm 0.41$ ) (Table 5). The highest nociceptive inhibition was exhibited by *M. ferrea* (200 mg/kg and 400 mg/kg) at 90 min.

#### Hot plate method

*Mesua ferrea* (200 and 400 mg/kg) significantly ( $P < 0.05$ ,  $P < 0.01$ ) elevated the mean basal reaction time as compared to control group.

The highest nociceptive inhibition was exhibited by *M. ferrea* (400 mg/kg) at 60 min ( $14.30 \pm 1.06$  sec). The maximum nociception inhibition by Diclofenac was observed at 45 min ( $14.90 \pm 1.02$  sec) and 60 min ( $16.23 \pm 1.66$  sec). *M. ferrea* (200 mg/kg) also produce significant inhibition of nociception and it was observed at 60 min ( $12.22 \pm 2.02$  sec) when compared to control group. All the values are graphically represented in Figure 3.

## DISCUSSION

In different regions of the world, medicinal plants are widely used as part of their primary health care. As medicinal plants are natural products it causes less side effect in people than other synthetic drug. For this, we investigated the presence of anti-diarrheal activity of *M. ferrea* unripe fruits peel and discovered that it reduced diarrhea in all three tests- castor oil induced diarrhea test, castor oil induced enteropooling

**Table 4: Effect of methanolic extract of *M. ferrea* fruit peel on Acetic acid induced writhing test.**

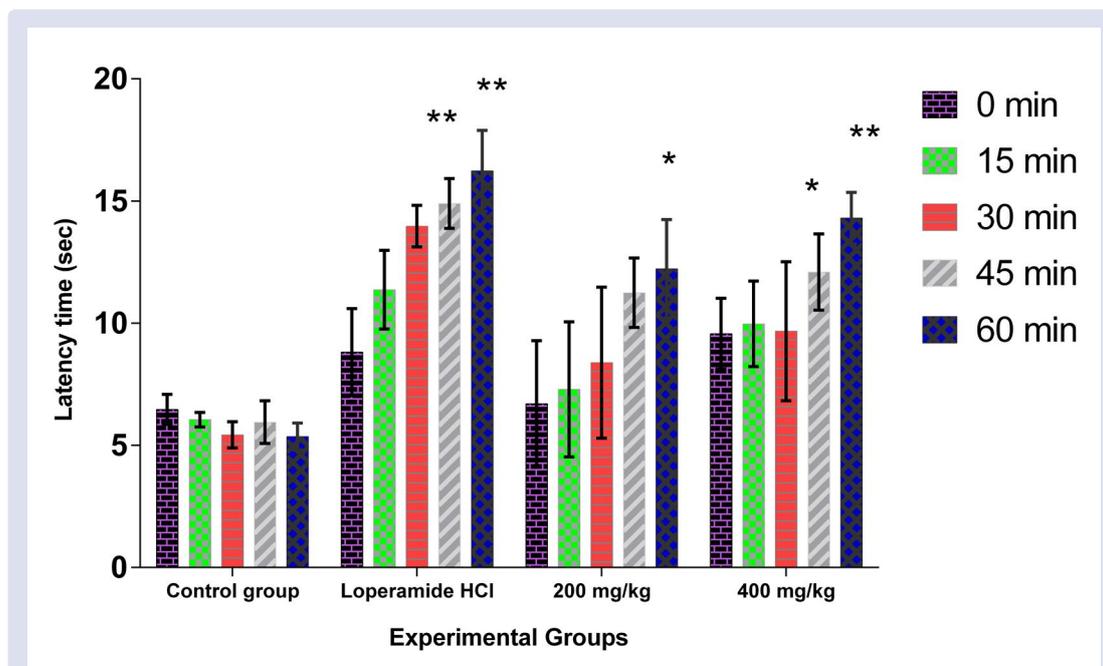
Group	Treatment	Dose, Route	No. of Writhing	Percent of inhibition
Control	Saline water (0.9% Nacl solution)	10 mg/kg, p. o.	$60 \pm 2.89$	---
Positive	Diclofenac-sodium	10 mg/kg, i. p.	$31.67 \pm 2.03^{***}$	47.23
<i>M. ferrea</i>	Methanolic extract	200 mg/kg p. o.	$50 \pm 1.53$	16.67
<i>M. ferrea</i>	Methanolic extract	400 mg/kg p. o.	$44.67 \pm 2.03^{**}$	25.56

Values are expressed as mean  $\pm$  SEM. (n = 5). \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$  when compared with control group.

**Table 5: Effect of methanolic extract of *M. ferrea* fruit peel in tail immersion test of mice.**

Group	Treatment	Dose, Route	0 min.	+30min.	+60min.	+90min.
Control	Saline water (0.9% Nacl solution)	10 mg/kg, p. o.	$3.36 \pm 0.52$	$3.86 \pm 0.17$	$3.64 \pm 0.30$	$3.97 \pm 0.22$
Positive	Nalbuphine	10 mg/kg, i. p.	$3.94 \pm 0.42$	$5.15 \pm 0.57$	$7.62 \pm 0.82^*$	$10.67 \pm 0.41^{**}$
<i>M. ferrea</i>	Methanolic extract	200 mg/kg p. o.	$3.24 \pm 0.61$	$4.29 \pm 0.43$	$5.67 \pm 1.20$	$8.34 \pm 1.20^*$
<i>M. ferrea</i>	Methanolic extract	400 mg/kg p. o.	$2.46 \pm 0.55$	$4.42 \pm 0.59$	$6.27 \pm 0.45$	$9.33 \pm 1.20^{**}$

Values are expressed as mean  $\pm$  SEM. (n = 5). \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$  when compared with control group. Here, 0 min indicates 30 min before administration of plant extract, standard drug or saline water and +30, +60, +90 indicates 30 min, 60 min and 90 min after administration of plant extract, standard drug or saline water.



**Figure 3: Effect of methanolic unripe fruit peel extract of *M. ferrea* on hot plate method. All values are represented as (mean  $\pm$  SEM). \* $P < 0.05$ , \*\* $P < 0.001$  compared to control in case of total number of feces. Here, 0 min indicates 15 min before administration of plant extract, standard drug or saline water and 15, 30, 45, 60 min indicates 15 min, 30 min, 45 min and 60 min after administration of plant extract, standard drug or saline water.**

test and gastrointestinal motility test. Castor oil contains a chemical compound named ricinolic acid which is mainly responsible for inducing diarrhea. Ricinolic acid causes irritation and inflammation of intestinal mucosa and as a result the peristaltic movement of the intestine is stimulated and for this the electrolyte permeation of the stomach is varied. In consequence, absorption of sodium and potassium ions are decreased.<sup>25</sup> On the other hand, in enteropooling method, the extract depicted significant ( $P < 0.001$ ) effect at the dose of 200 mg/kg and also reduced the volume of intra-luminal contents respectively (Table 2). These effects, which have direct consequences to reduced water and electrolytes secretion into the small intestine,<sup>26</sup> suggest that the extract may enhance electrolyte absorption from the intestinal lumen consistent with inhibition of hyper-secretion. Hyper-motility characterizes diarrhea where the secretory component is not the causal factor.<sup>27</sup> Pre-treatment with the this extract suppressed the propulsive movement or transit of charcoal preparation through the gastrointestinal tract which significantly indicates that the fruits peel extract may be able to reduce the frequency of stooling in diarrheal conditions such as 29.07% and 48.54% inhibited by methanolic extract at the dose of 100 mg/kg and 200 mg/kg respectively (Table 3). All these findings strongly suggested that the methanolic crude peels extract might have anti-diarrheal activity and as per our best of knowledge which was never been explored before.

On the other hand, in acetic acid induced writhing test the methanolic unripe fruit peel extract of *M. ferrea* L. showed significant ( $P < 0.01$ ) inhibition such as 16.67% and 25.56% at the dose of 200 mg/kg and 400 mg/kg respectively, (Table 4). Whereas, Hassan, et al<sup>28</sup> reported that n-Hexane, ethyl acetate and methanol extracts of *M. ferrea* leaves also exhibited significant analgesic activity in acetic acid induced writhing response in mouse. The response is thought to be mediated by the prostaglandin pathways, peritoneal mast cells and acid sensing ion channels.<sup>29-31</sup> In hot plate method, the methanolic unripe fruit peels extract of *M. ferrea* L. at a dose of 200 mg/kg and 400 mg/kg body weight showed significant anti-nociceptive activity. The results were found to be statistically significant ( $P < 0.05$ ,  $P < 0.01$ ) at 45 min and 60 min. In tail immersion method, latency time shown by the crude extracts are less than that of the standard drug nalbuphine but many folds more than that of the control group, which justifies its activity. The results were found to be statistically significant ( $P < 0.05$ ,  $P < 0.01$ ) at 90 min. This tail immersion method was used to evaluate the central mechanism of analgesic activity. Narcotic analgesics inhibit both peripheral and central mechanism of pain, while non-steroidal anti-inflammatory drugs inhibit only peripheral pain.<sup>32,33</sup> This peels extract acted as both analgesics; peripherally and centrally.

## CONCLUSION

Above observations suggest that the extract reduces diarrhea by inhibiting peristalsis, gastrointestinal motility and castor oil induced enteropooling and inhibit both peripheral and central mechanism of pain in a dose dependent manner. Earlier studies suggests that anti-dysenteric and anti-diarrheal properties of medicinal plants were due to tannins, alkaloids, flavonoids, sterol and/or triterpenes and anti-nociceptive properties of medicinal plants due to alkaloid, flavonoid, steroids, glycoside etc. Hence, tannins, alkaloids, steroids, saponin and glycoside may be responsible for the mechanism of action of unripe fruit peels extract of *M. ferrea* against diarrheal and nociception.

## ACKNOWLEDGMENT

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## CONFLICTS OF INTEREST

The authors declare that they have no conflict of interests.

## ABBREVIATIONS

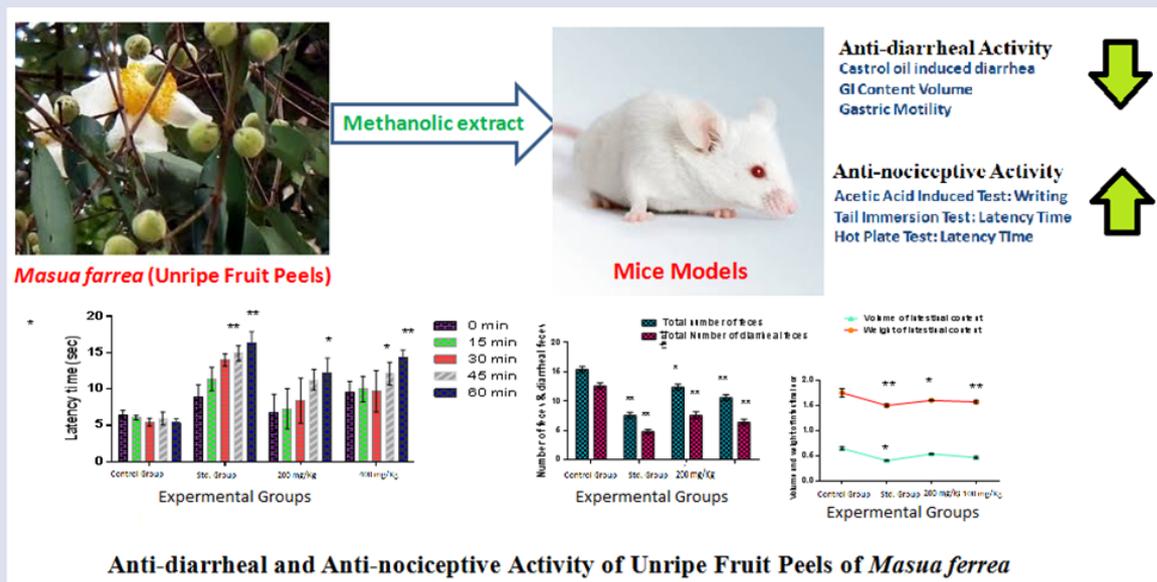
i.p.: intra-peritoneal; b.w.: body weight; ANOVA: Analysis of Variance; SPSS: Statistical Package for the Social Sciences.

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## GRAPHICAL ABSTRACT



## SUMMARY

*Mesua ferra* is widely used as a source of anti-diarrheal and analgesic action in traditional herbal medicine. So, we aimed at evaluating the medicinal property of the plant and at the end of the study we came to the conclusion that *M. ferra* shows significant anti-diarrheal and anti-nociceptive activity and the effect is delivered in a dose dependent manner as we found that in case of anti-diarrheal activity the 200 mg/kg b.w. dose of methanolic extract of *M. ferra* exerts better effect than 100 mg/kg b.w. dose and in case of anti-nociceptive activity 400 mg/kg b.w. dose induced nociception in a significant manner than 200 mg/kg b.w. dose.

## ABOUT AUTHORS



**Dr. Kishor Mazumder** has completed his PhD at the age of 34 years from Osaka University, Japan and postdoctoral studies from Charles Sturt University School of Biomedical Sciences, Australia. He is the Chairman and Associate professor as well as advisor, Research Cell of Jessore University of Science and Technology, Jessore Bangladesh, Bangladesh. In addition, he is also an Adjunct Sr. Lecturer, School of Biomedical Sciences, CSU, NSW, Australia. He has published more than 40 papers in reputed journals and has been serving as reviewer of many reputed journals. His research interest is on antidiabetic and anticancer drug development and discovery from natural sources.



**Ziku Chandra Dey**, received bachelor's degree in pharmacy from IIUC, in 2011, and master's in pharmacy from the USTC, in 2013. He has finished project on in-vivo evaluation of Neuro Pharmacological and anti-diabetic activities of different Plant extracts on mice model. Further, in 2013, have performed different in-vivo tests on Mice with different plant extracts. In 2014, after that he joined the product management department, Kemiko Pharmaceuticals, as an Executive. In 2015, he joined in Beximco Pharmaceuticals as a Sr. Asst. Officer. He published more than 10 articles in different international journals.



**Suparna Dey**, received MBBS degree from University of Chittagong in 2011 and joined as WHO fellow in Breast Cancer Screening center, Chittagong. She took her postdoctoral training in Japan and awarded NIPS fellowship. Recently she has joined as MOMCH in Ministry of Family Planning and Welfare, GoB. Her research interest is on child and women health and natural products for disease irradiation. She published more than 5 research articles.



**Md. Fazlul Kabir**, received bachelor's degree in pharmacy from USTC, in 2013, and master's in pharmacy from the USTC, in 2018. He finished project on in-vivo evaluation of anti-diabetic and antidiarrhoeal activities of different plant extracts on mice models. He joined the Production department in Eskayef Pharmaceuticals Ltd and now working as assistant manager.



**Minhazur Rahman**, received bachelor's degree in pharmacy from USTC, in 2013, and master's in pharmacy from the USTC, in 2015 from the same institute. He finished project on in-vivo evaluation of neuropharmacological and antidiarrhoeal activities of different plant extracts on mice models. He joined in the quality control department in Eskayef Pharmaceuticals Ltd and now working as Sr. Executive.



**Sadiur Rahman Sajon**, completed Bachelor of Pharmacy (Professional) 5-year integrated course in the year 2017 from Jashore University of Science and Technology and currently pursuing M. Pharm student (Medicinal Chemistry). His research interest is on bioinformatics, analytical chemistry and ethnopharmacology. He has published more than 22 articles in different journals.

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