Anti-ulcer activity on siddha herbo-mineral formulation against aspirin induced gastric ulcer in rats

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ABSTRACT

The present study was to analyse the siddha drug arputha mathirai for anti ulcer activity in aspirin induced in rats. Arputha mathirai was used to treat eri gunmam (peptic ulcer). Arputha mathirai at the dose level 200mg/kg and 400mg/kg were administered orally. Anti-ulcer effects were compared with standard drug omeprazole 20mg/kg b.w.,p.o.). The effect was assessed by parameters like pH, free acidity, total acidity and ulcer index. These observations helped us to conclude that Arputha mathirai 200mg/kg and 400mg/kg is endowed with antiulcer property.

Keywords: Arputha mathirai, Aspirin, Peptic ulcer, Omeprazole.

1. INTRODUCTION

Ancient siddha literatures notified the diseases as 4448. Among them, the diseases pertaining to gunnam are 8. Eri gunnam is one of the 8 types of gunnam mentioned in yugi vaithiya cinthamani 800.[2] Gunnam is a clinical entity which depresses both body and mind since it is called as gunnam. The signs and symptoms of Eri Gunnam in siddha literature may be correlated with peptic ulcer disease in modern disease of classification. So it is considered to evaluate a classical siddha herbo mineral formulation “Arputha mathirai” mentioned in kosayee anuboga vaithiya brahma ragasiyam, part-II, [1] for the treatment of Eri Gunnam (Peptic ulcer).

Peptic ulceration is one of the common disease affecting millions of people. It is now considered to be one of the modern age epidemics affecting nearly 10% of world population [3]. There is a rich abundance of plants reputed in traditional medicine to possess anti-ulcer properties [4]. Peptic ulcer, also known as ‘ulcus pepticum’ are ulcers which occur in that part of the gastrointestinal which is exposed to gastric acid and pepsin, i.e., the stomach and duodenum. However, the etiology of peptic ulcer is not clearly known. It results probably due to an imbalance between the aggressive (acid, pepsin and H-pylori) and the defensive (gastric mucus and bicarbonate secretion, prostaglandin, nitric oxide and innate resistance of mucosal cell factors [5]. Complications such as obstruction, haemorrhage and perforations may occur.[ 6]

In a gastric ulcer, generally, the acid secretion is normal or low. In a duodenal ulcer, acid secretion is high in half of the patients but normal in the rest. Gastric and duodenal ulcers are common pathologies that may be induced by a variety of factors such as stress, smoking, nutritional deficiencies and noxious
agents including non-steroidal anti-inflammatory drugs (NSAID)[7].

2. MATERIALS AND METHODS

2.1. Ingredients of Aruptha Mathirai

*Cuminum cyminum* – 70 grams  
*Piper nigrum* - 70 grams  
*Zingiber officinale* – 70 grams  
*Piper longum* – 70 grams  
*Allium sativum* – 70 grams  
*Ferula asafoetida* – 70 grams  
*Purified rock salt* – 70 grams  
*Purified sulphur* – 70 grams  
*Citrus limon* – sufficient quantity.

2.2. Preparation

All the drugs are powdered and grounded with lemon juice for 12 hours and rolled into pills of 500mg and dried. It is stored in an air tight container.

2.3. Experimental animals

Albino rats (wistar rats) of either sex, weighing (160-250 g) were procured from animal housing facility, K.K College of pharmacy, Gerugambakkam, Chennai. All animals were placed in a polypropylene cages in a controlled room temperature 24°C±1°C and relative humidity of 60-70 % in animal house. The animals were maintained in standard pellet diet and water ad libitum. They were acclimatized to laboratory condition for seven days before commencement of the experiment. All the protocols and the experiments conducted in strict compliance according to ethical principles and guidelines provided by committee for the purpose of control and Supervision of Experiments on Animals (KKCP / 2013 / 008 / CPCSEA). Animal experimentation protocols are approved by Institutional Animal Ethical Committee.

2.4. Acute toxicity studies

The Acute toxicity studies were performed in accordance with the OECD 423 guidelines (Table 1). Female Wistar rats weighing 100-150g were selected and divided into groups containing three animals in a group. The single dose of the Arupuda mathirai starting from 50mg/kg up to 2000mg/kg (5, 50,300,2000mg/kg) was administered orally. The drug treated animals were carefully observed individually for the toxicity signs and mortality. The parameters such as changes in skin and fur, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous system, behavioural pattern, convulsions, tremors, salvation, lethargy, diarrhoea, sleep and coma were observed. From the maximum dose 1/5th or 1/10th of the dose was considered as therapeutic dose for further study. Based on these findings, no toxic effect was observed upto 400 mg/kg of Arputha mathirai treated via oral route over a period of 28 days. So, it can be concluded that the Arputha mathirai can be prescribed for therapeutic use in human with the dosage recommendations of upto 400mg/kg. Body weight p.o.

<table>
<thead>
<tr>
<th>S.No</th>
<th>Parameters</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Motor activity</td>
<td>No effect</td>
</tr>
<tr>
<td>2</td>
<td>Tremors</td>
<td>No effect</td>
</tr>
<tr>
<td>3</td>
<td>Convulsion</td>
<td>No effect</td>
</tr>
<tr>
<td>4</td>
<td>Piloerection</td>
<td>No effect</td>
</tr>
<tr>
<td>5</td>
<td>Straub reaction</td>
<td>No effect</td>
</tr>
<tr>
<td>6</td>
<td>Loss of lighting effects</td>
<td>No effect</td>
</tr>
<tr>
<td>7</td>
<td>Sedation</td>
<td>No effect</td>
</tr>
<tr>
<td>8</td>
<td>Muscle relaxation</td>
<td>No effect</td>
</tr>
<tr>
<td>9</td>
<td>Hypnosis</td>
<td>No effect</td>
</tr>
<tr>
<td>10</td>
<td>Analgesia</td>
<td>No effect</td>
</tr>
<tr>
<td>11</td>
<td>Ptosis</td>
<td>No effect</td>
</tr>
<tr>
<td>12</td>
<td>Lacrimination</td>
<td>No effect</td>
</tr>
<tr>
<td>13</td>
<td>Change in skin colour</td>
<td>No effect</td>
</tr>
</tbody>
</table>

2.5. Anti-ulcer activity

2.5.1. Aspirin Induced Gastric Ulcers

Aspirin is a NSAID which inhibit the synthesis of prostaglandins. Prostaglandins protect the gastric mucosa by producing leukotrienes and bicarbonate ions.Aspirin also inhibit the gastric peroxidase and may increase mucosal hydrogen peroxide and hydroxyl ions level to cause oxidative mucosal damage.

2.5.1.1. Procedure

Albino rats of either sex weighing between 150-250 gms were divided into five groups and each consisting of six rats.Group I receives vehicle control (2ml/kg p.o.) Group II receives Standard drug omeprazole, Group III: Received Arupuda Mathirai 200mg/kg and Group IV: Received Arupuda Mathirai
Table 2. Effect of Arpudha Mathirai on Free Acidity and Total Acid

<table>
<thead>
<tr>
<th>Group No.</th>
<th>Body wt. gms</th>
<th>Treatment</th>
<th>Free acidity</th>
<th>Total acidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>155.67±0.56</td>
<td>Control (distilled water 2ml/kg)</td>
<td>21.83 ± 0.833</td>
<td>41.66 ± 0.760</td>
</tr>
<tr>
<td>II</td>
<td>164.23±1.23</td>
<td>Standard drug Omeprazole (20 mg/kg)</td>
<td>16.0 ± 0.61**</td>
<td>26.33± 1.05**</td>
</tr>
<tr>
<td>III</td>
<td>172.09±2.67</td>
<td>Arputha Mathirai(200mg/kg)</td>
<td>16.66±1.89*</td>
<td>27.50±1.62</td>
</tr>
<tr>
<td>IV</td>
<td>164.23±1.46</td>
<td>Arputha Mathirai(400mg/kg)</td>
<td>16.1±1.90**</td>
<td>27.16±1.08*</td>
</tr>
</tbody>
</table>

Values are expressed in terms of mean ± SEM of 6 rats (ANOVA)
Effects are statistically significant *P<0.05;**p<0.01 (in comparison with Standard)

Table 3. Effect of Arputha Mathirai on Ulcer index and Percentage of ulcer protection

<table>
<thead>
<tr>
<th>Group No.</th>
<th>Body wt. gms</th>
<th>Treatment</th>
<th>Ulcer Index</th>
<th>Percentage of ulcer protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>182.12±0.67</td>
<td>Control (distilled water 2ml/kg)</td>
<td>5.666 ±0.19</td>
<td>-</td>
</tr>
<tr>
<td>II</td>
<td>188.34±1.46</td>
<td>Standard drug Omeprazole (20 mg/kg)</td>
<td>1.083 ±0.24</td>
<td>77.5**</td>
</tr>
<tr>
<td>III</td>
<td>178.18±2.87</td>
<td>Arputha Mathirai(200mg/kg)</td>
<td>2.41 ±0.35</td>
<td>57.42</td>
</tr>
<tr>
<td>IV</td>
<td>169.67±1.23</td>
<td>Arputha Mathirai(400mg/kg)</td>
<td>1.5±0.22</td>
<td>73.49*</td>
</tr>
</tbody>
</table>

Values are expressed in terms of mean ± SEM of 6 rats (ANOVA)
Percentage protection = (Control mean ulcer index – Test mean ulcer index)/Control mean ulcer index ×100
Effects are statistically significant *P<0.05;**p<0.01 (in comparison with Standard)

400mg/kg The animals are fasted for 24 hours. The test drug in varying concentrations based on the design of the experiment is administered orally 30 minute prior to aspirin at dose of 500 mg/kg. 4 hours later the rats are sacrificed by using anaesthetic ether and their stomachs dissected and they were opened along greater curvature for the determination of gastric lesions. Ulcer index calculated by noting the number of ulcers per animal and severity scored by observing the ulcers microscopically with the help of 10 X lens.

2.5.1.2. Ulcer assessment [16]

The stomachs were harvested, opened along the greater curvature and the mucosa was exposed for macroscopic evaluation. The ulcerated area was assessed and the ulcer index (UI, mm²) was calculated as the arithmetic mean for each treatment. Following the analysis, the mucosal layer was blotted dry and scraped off the underlying muscularis externa and serosa.

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2.5.1.3. Ulcer Scoring [16]

After sacrificing the rat, stomach was removed and opened along the greater curvature, and washed it slowly under running tap water. Put it on the glass slide and observe under 10X magnification for ulcer.

Score the ulcers as below.

0= Normal coloured stomach
0.5= Red colouration
1= Spot ulcers
1.5= Haemorrhagic streaks
2 = Ulcers ≥ 3mm but ≤ 5mm
3 = Ulcers >5 perforation

Mean ulcer score for each animal is expressed as Ulcer Index.

2.5.1.4. Ulcer index [17]

Ulcer index was calculated as

\[ \text{Ulcer index} = \frac{10}{x} \]

Where \( x \) = Total mucosal area/Total ulcerated area.

3. RESULTS

3.1. Effect of Free Acidity and Total Acidity

The free acidity and total acidity was determined based on the titre values (Table 2). The free acidity and total acidity of Test drug on albino rats decreased significantly in comparison with the standard group treated with omeprazole.

3.2. Ulcer index

The ulcer index was calculated by taking the mean ulcer score of each group (Table 3). Then the mean ulcer score graph was plotted with groups on x-axis and ulcer index on y-axis. The histograms of different groups were then interpolated by comparing the ulcer index of group I with group II, III and IV. It was noticed that the ulcer index of Dose group (Dose-I & II) was significantly less when compared to the standard group (Group-II) treated with Omeprazole significantly (Figure 3).

3.3. Statistical Analysis

Since the p value is significant in all symptoms except diarrhoea. So there is significant reducing of symptoms among the patients for the treatment of Eri Gunmam (Peptic Ulcer). Hence it is concluded that the treatment was effective and significant. McNemat test, C.I: 95%, *P<0.05; **P<0.01

4. DISCUSSION

The gastro protective effects of Arputha mathirai were investigated against aspirin-induced ulcer model in rats. It has shown significant gastro protective effects against these models. Arputha mathirai has shown significant reduction in ulcer index as compared to control group in aspirin induced gastric ulcer model in both doses. Arputha mathirai 200mg/kg and 400mg/kg b.wt were also significantly decreased ulcer index as compared to control group. Further the acid secretory parameters like total acidity, volume of gastric acid secretion and total acid output were also studied in aspirin-induced gastric ulcer model. Significant reduction was observed in total acid output and volume of gastric acid secretion although total acidity was observed to be reduced insignificantly against aspirin-induced gastric ulcer model as compared to control group.

5. CONCLUSION

Administration of the Arputha mathirai significantly decreased the gastric volume in comparison with rats treated with Omeprazole. Comparing the gastric volume and acidity, the gastric volume gets decreased, simultaneously the gastric acidity also
decreased significantly. This study demonstrates that the Arputha mathirai has a potent ulcer healing effect.

Conflict of Interest

The authors declare that they have no conflicts of interest.

References