Antimotility and antisecretory effect of Kutajarishtha: An ayurvedic antidiarrhoeal formulation

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ABSTRACT

Antidiarrhoeal effect of Kutajarishtha, an ayurvedic formulation was evaluated in castor oil and magnesium sulphate induced diarrhoea in mice. Effect of Kutajarishtha was also studied on intestinal propulsive movement and intestinal fluid accumulation in mice. Kutajarishtha showed antidiarrhoeal activity against castor oil and magnesium sulphate induced diarrhoea in mice. It has produced a significant decrease in the frequency of defecation and severity of diarrhoea. The % inhibition of diarrhoea in castor oil treated animals were 48.54 %, 71.27 %, 86.36 % and 92.45 % for Kutajarishtha 2.5, 5, 10 ml/kg dose (p.o.) and Loperamide (standard) 2 mg/kg dose (p.o.) respectively. The % inhibition of diarrhoea in magnesium sulphate treated animals were 50.98 %, 73.52 %, 85.78 % and 91.11% for Kutajarishtha 2.5, 5, 10 ml/kg dose (p.o.) and Loperamide (standard) 2 mg/kg dose (p.o.) respectively. Kutajarishtha produced significant reduction in the intestinal transit in mice. The mean peristaltic index (%) for Kutajarishtha 2.5, 5, 10 ml/kg dose (p.o.) and Atropine sulphate (standard) 5 mg/kg dose (i.p.) were 15.87 %, 27.33 %, 40.28 % and 55.94 % respectively. Kutajarishtha significantly reduced intraluminal fluid accumulation. The % inhibition of intestinal fluid accumulation for Kutajarishtha 2.5, 5, 10 ml/kg dose (p.o.) and Chlorpromazine (standard) 30 mg/kg dose (p.o.) were 45.54 %, 63.76 %, 76.23 % and 89.50 % respectively. The results obtained suggest that Kutajarishtha produces antidiarrhoeal effect through its antisecretory and antimotility effect. Preliminary phytochemical analysis revealed the presence of carbohydrates and alkaloids as major constituents.

Key words: Kutajarishtha, diarrhoea, intestinal transit, intestinal fluid accumulation.

INTRODUCTION

Diarrhoea is a condition of passage of loose, watery stools with increased frequency [1, 2]. Diarrhoea involves both an increase in the motility of the gastrointestinal tract, along with increased secretion, and a decrease in the absorption of fluid and thus a loss of electrolytes and water [3]. Diarrhoea is one of the major health threats to populations in tropical and subtropical poor countries, responsible for about 5 millions deaths annually [4].

Several antidiarrheals are available in both the modern and traditional medicines. Synthetic antidiarrheals used in modern medicines however show adverse effects like paralytic ileus, nausea, vomiting and abdominal cramps [5]. In recent years, there has been a surge of interest in herbal remedies for a number of ailments [6]. As the use of herbal formulations in diarrhoea is more safe and effective than allopathic drugs, Kutajarishtha an ayurvedic formulation is widely used in treating the diarrhoea and dysentery.

In view of these facts, this study was conducted to investigate the antidiarrhoeal activity of Kutajarishtha, an ayurvedic formulation in castor oil and magnesium sulphate induced diarrhoea, intestinal propulsive movement and intestinal fluid accumulation in mice. Phytochemical analysis of Kutajarishtha was done to find its active constituents which may be responsible for its antidiarrhoeal activity.
MATERIALS AND METHODS

Drugs

Composition of Kutajarishta
Each 10 ml of Kutajarishta contains i) Kutaja (3 gm.), ii) Draksa (1.5 gm), iii) Madhuka Puspa (300 mg), iv) Gambhari (300 mg), v) Dhataki (600 mg), vi) Guda (3 gm), vii) Asav Base Q.S.

Animals
“Swiss albino mice” of either sex, weighing; 20 – 25 gm obtained from VIPER, Pune (India), were used for the experiments. They were kept in standard environmental condition, fed standard food and water ad libitum. All experiments were performed after an overnight fast. The Institutional Animal Ethical Committee of Government College of Pharmacy, Aurangabad, Maharashtra, India (GCPA/IAEC/2011/235, 11/03/2011), approved the study.

Experimental procedure for antidiarrhoeal activity

Acute toxicity
Initially the Kutajarishta was studied for acute oral toxicity as per revised OECD guidelines number 423. Kutajarishta was devoid of any toxicity up to 20 ml/kg in albino mice by oral route. Hence for further studies 2.5 to 10 ml/kg doses of these formulations were used [7].

Castor oil induced diarrhea
The animals were divided in to control, positive and test groups containing six in each group. Each mouse was kept for observation under a glass funnel, the floor of which was lined with blotting paper and observed for 4 h. Diarrhea was induced by administering 0.2 ml. of castor oil orally to mice [8, 9]. The control group received only distilled water (10 ml/kg, po); the positive control group received loperamide (2 mg/kg, po ); test group received Kutajarishta at doses of 2.5, 5, 10 ml/kg, po, body weight 30 min before the administration of castor oil. During an observation period of 4 h, the parameters observed were: onset of diarrhoea, total weight of faecal output, total weight of wet faeces, total number of faecal output, and number of wet faeces [6].

Magnesium sulphate induced diarrhea
A similar protocol as for castor oil induced diarrhoea was followed [6, 10]. Magnesium sulphate was given in the dose of 2 g/kg, po, to the animals 30 min after pre-treatment with distilled water (10 ml/kg, po,) to the control group, loperamide (2 mg/kg, po) to the positive control group, Kutajarishta at doses of 2.5, 5, 10 ml/kg, po, to test group.

Gastrointestinal motility by charcoal meal
The animals were divided in to control, positive and test groups of six mice each. Each animal was given orally 0.2 ml of charcoal meal (3% charcoal in 5 % gum acacia). The test groups received the Kutajarishta at doses of 2.5, 5, 10 ml/kg, po, body weight immediately after charcoal meal administration. The positive control group received atropine sulfate (5 mg/kg, ip), while the control group received distilled water (10 ml/kg, po). After 30 min., the animals were sacrificed and the movement of charcoal from pylorus to caecum was measured. The peristaltic index, which is the distance travelled by charcoal meal to the total length of small intestine expressed in terms of percentage [1].

Small intestinal secretions
Effect of Kutajarishta on intestinal secretion was indirectly studied by enteropooling assay. The mice were divided in to different groups and treated with Kutajarishta (2.5, 5, 10 ml/kg, po), distilled water (10 ml/kg, po) and standard chlorpromazine (30 mg/kg, ip) before the oral administration of castor oil 0.2 ml per mouse. These mice were sacrificed 30 min later and entire small intestine from each animal was weighed and their group average was calculated. The difference in the weight of intestine in control and castor oil treated group was considered as the castor oil induced accumulation of intestinal fluid [11].

Preliminary phytochemical screening
Chemical tests were carried out on Kutajarishta using standard procedures, to identify its major groups of chemical constituents [12, 13, 14, 15].
Statistics
The results of all experiments were reported as mean ± S.E.M. Statistical analysis was carried out using Student’s ‘t’-test. A level of significance of \( P < 0.05 \) was regarded as statistically significant.

RESULTS

Effect of Kutajarishta on castor oil induced diarrhoea
In the course of observation for 4 h. after castor oil administration, all the mice in control group produced copious diarrhoea. Pretreatment of mice with the different doses of Kutajarishta caused a significant dose dependent decrease in the frequency of purging (reduction of number of wet stools and total no of stools) and, weight of wet stools. Kutajarishta showed 48.54 %, 71.27 %, 86.36 % inhibition of diarrhoea at doses of 2.5 ml/kg, 5 ml/kg and 10 ml/kg while loperamide at dose of 2 mg/kg showed 92.45 % inhibition of diarrhoea as shown in Table 1.

Effect of Kutajarishta on magnesium sulphate induced diarrhoea
All the mice in control group produced diarrhoea after magnesium sulphate administration during the observation period of 4 h. Pretreatment of mice with the different doses of Kutajarishta caused a significant dose dependent decrease in the frequency of purging (reduction of number of wet stools and total no of stools) and, weight of wet stools. Kutajarishta showed 50.98 %, 73.52 %, 85.78 % inhibition of diarrhoea at doses of 2.5 ml/kg, 5 ml/kg and 10 ml/kg while loperamide at dose of 2 mg/kg showed 91.11 % inhibition of diarrhoea as shown in Table 2.

Effect of Kutajarishta on small intestinal transit
The results revealed that Kutajarishta inhibited the gastrointestinal transit of charcoal in mice by 15.87 %, 27.33 % and 40.28 % at doses of 2.5 ml/kg, 5 ml/kg and 10 ml/kg respectively while atropine sulphate at dose of 5 mg/kg showed 55.94 % inhibition of gastrointestinal transit as shown in Table 3.

Effect of Kutajarishta on small intestinal secretion
Kutajarishta reduced the castor oil induced intraluminal accumulation of fluid by 45.54 %, 63.76 % and 76.23 % at doses of 2.5 ml/kg, 5 ml/kg and 10 ml/kg respectively while chlorpromazine hydrochloride at dose of 30 mg/kg showed 89.50 % inhibition of castor oil induced intraluminal accumulation of fluid as shown in Table 4.

Qualitative analysis of Kutajarishta
The phytochemical analysis of the Kutajarishta showed the presence of carbohydrates and alkaloids. Terpenoids, flavonoids, saponins and cardiac glycosides were absent.

DISCUSSION
The ricinoleic acid, the active ingredient of castor oil is liberated from the action of lipases on castor oil. The ricinoleic acid produces irritating and inflammatory actions on the intestinal mucosa leading to the release of prostaglandins. This condition induces an increase in the permeability of the mucosal cells and changes in electrolyte transport, which results in a hypersecretory response (decreasing Na⁺ and K⁺ absorption), stimulating peristaltic activity and diarrhoea [16]. Thus the castor oil induced diarrhoea demonstrates secretory diarrhea, since ricinolic acid induces diarrhoea by a hypersecretory response [17, 18]. Since the Kutajarishta successfully inhibited the castor oil induced diarrhoea, it can be assumed that the antidiarrhoeal action was exerted by antisecretory mechanism. This was also evident from the reduction of total number of wet faeces in the test groups in the experiment.

Magnesium sulphate produces the diarrhoea by osmotic properties, preventing reabsorption of water ions, leading to increase in the volume of the intestinal content. It promotes the liberation of cholecystokinin from the duodenal mucosa, which increases the secretion and motility of small intestine and thereby prevents the reabsorption of sodium chloride and water [19]. Kutajarishta found to reduce the diarrhoeic condition in this model. Kutajarishta may have increased the absorption of water and electrolyte from the gastrointestinal tract, since it delayed the gastrointestinal transit in mice as compared to the control.

Charcoal meal test in mice is a method used to study the effect of drugs on the motility of intestine [20, 21]. In present study Kutajarishta was found to be the inhibitor of intestinal motility. Castor oil produces permeability changes in the intestinal mucosa membranes to water and electrolytes resulting in fluid and watery luminal content that flows rapidly through small and large intestines [22, 23]. Kutajarishta inhibited the castor oil induced intestinal fluid accumulation. Preliminary phytochemical analysis revealed the presence of carbohydrates and alkaloids as major constituents.
### Table 1: Effect of Kutajarishta on castor oil (0.2 ml) induced diarrhoea in mice.

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (/kg)</th>
<th>Onset of diarrhoea (min)</th>
<th>Total weight of stool (g)</th>
<th>Weight of wet stools (g)</th>
<th>Total numbers of stools</th>
<th>Number of wet stools</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td>53±2.11</td>
<td>0.372±0.010</td>
<td>0.35±0.010</td>
<td>13.33±0.33</td>
<td>11.00±0.36</td>
<td></td>
</tr>
<tr>
<td>Kutajarishta 2.5 ml</td>
<td>74±2.18</td>
<td>0.205±0.005</td>
<td>0.181±0.007</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kutajarishta 5 ml</td>
<td>98±3.70</td>
<td>0.110±0.006</td>
<td>0.105±0.004</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kutajarishta 10 ml</td>
<td>157±4.03</td>
<td>0.053±0.002</td>
<td>0.049±0.003</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loperamide</td>
<td>2 mg</td>
<td>223±5.16</td>
<td>0.036±0.002</td>
<td>0.030±0.003</td>
<td>1.00±0.25</td>
<td>0.83±0.16</td>
<td>92.45</td>
</tr>
</tbody>
</table>

Values are mean ± standard error of mean.  
Each value represents average of six determinations.  
P < 0.05 vs. control, student’s ‘t’ test.

### Table 2: Effect of Kutajarishta on magnesium sulphate (2 g/kg) induced diarrhoea in mice.

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (/kg)</th>
<th>Onset of diarrhoea (min)</th>
<th>Total weight of stool (g)</th>
<th>Weight of wet stools (g)</th>
<th>Total numbers of stools</th>
<th>Number of wet stools</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td>41±2.06</td>
<td>0.32±0.01</td>
<td>2.91±0.009</td>
<td>11.50±0.42</td>
<td>8.16±0.30</td>
<td></td>
</tr>
<tr>
<td>Kutajarishta 2.5 ml</td>
<td>74±3.01</td>
<td>0.153±0.006</td>
<td>0.131±0.005</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kutajarishta 5 ml</td>
<td>109±2.19</td>
<td>0.084±0.004</td>
<td>0.077±0.004</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kutajarishta 10 ml</td>
<td>167±4.46</td>
<td>0.043±0.004</td>
<td>0.038±0.003</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loperamide</td>
<td>2 mg</td>
<td>207±6.58</td>
<td>0.030±0.004</td>
<td>0.027±0.006</td>
<td>0.83±0.16</td>
<td>0.66±0.21</td>
<td>91.11</td>
</tr>
</tbody>
</table>

Values are mean ± standard error of mean.  
Each value represents average of six determinations.  
P < 0.05 vs. control, student’s ‘t’ test.

### Table 3: Effect of Kutajarishta on castor oil (0.2 ml) induced intestinal transit in mice.

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (/kg)</th>
<th>Percent intestinal transit</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>73.3±1.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>81.33±2.13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kutajarishta 2.5 ml</td>
<td>61.66±2.30</td>
<td>15.87</td>
<td></td>
</tr>
<tr>
<td>Kutajarishta 5 ml</td>
<td>53.26±2.01</td>
<td>27.33</td>
<td></td>
</tr>
<tr>
<td>Kutajarishta 10 ml</td>
<td>43.76±1.77</td>
<td>40.28</td>
<td></td>
</tr>
<tr>
<td>Atropine sulphate 5 mg</td>
<td>32.29±1.02</td>
<td>55.94</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± standard error of mean.  
Each value represents average of six determinations.  
P < 0.05 vs. control, student’s ‘t’ test.

### Table 4: Effect of Kutajarishta on castor oil (0.2 ml) induced intraluminal fluid accumulation in mice.

<table>
<thead>
<tr>
<th>Experimental Group</th>
<th>Dose (/kg)</th>
<th>Weight of small intestine (mg)</th>
<th>Castor oil induced intraluminal fluid (mg)</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1123±25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1628±23</td>
<td>505±40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kutajarishta 2.5 ml</td>
<td>1398±38</td>
<td>275±22</td>
<td></td>
<td>45.45</td>
</tr>
<tr>
<td>Kutajarishta 5 ml</td>
<td>1306±17</td>
<td>183±19</td>
<td></td>
<td>63.76</td>
</tr>
<tr>
<td>Kutajarishta 10 ml</td>
<td>1243±26</td>
<td>120±8</td>
<td></td>
<td>76.23</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>30 mg</td>
<td>1176±24</td>
<td>53±8</td>
<td>89.50</td>
</tr>
</tbody>
</table>

Values are mean ± standard error of mean.  
Each value represents average of six determinations.  
P < 0.05 vs. control, student’s ‘t’ test.

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CONCLUSION

These results indicate that Kutajarishta produces antidiarrhoeal effect through its antisecretory and antimotility effect. The delay in the gastrointestinal transit prompted by the Kutajarishta might have contributed to their antidiarrhoeal activity by allowing a greater time for absorption. Preliminary phytochemical analysis showed the presence of carbohydrates and alkaloids as major constituents which may be responsible for the antisecretory and antimotility effect of Kutajarishta.

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REFERENCES