Anti-ulcer effect of Nigella sativa Linn. against gastric ulcers in rats

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The effect of alcoholic extract of Nigella sativa was investigated in rats to evaluate the anti-ulcer activity by using two models, i.e. pyloric ligation and aspirin-induced gastric ulcer. The parameters taken to assess anti-ulcer activity were volume of gastric secretion, free acidity, total acidity and ulcer index. The results indicate that the alcoholic extract significantly \((P < 0.001)\) decreases the volume of gastric acid secretion, free acidity, total acidity and ulcer index with respect to control.

NIGELLA sativa Linn., a plant belonging to the family Ranunculaceae, grows as a small herb and is cultivated throughout India and other tropical regions of the world\(^6\). It is active as an aromatic, respiratory stimulant, diuretic, hypoglycemic, anti-tumour and an analgesic\(^4\). The seed contains alkaloids nigellicin, nigellicin, quanzoline, tannin, steroid \(\alpha\)-spinasterol, campsterol, cholesterol, stigmas 7-en-3-beta-ol, stigmasterol and flavonoids of trigillin quercetin-3-glucoside\(^7\). The study assumes significance in the context that prolonged use of synthetic anti-ulcer drugs leads to adverse drug reactions and a search for new anti-ulcer agents that retain therapeutic efficacy and are devoid of adverse drug reaction is warranted. A study of the efficacy of an extract of \(N. sativa\) in gastric ulcer with pylorus ligation and aspirin-induced ulcers was undertaken in a rat model.

Seeds of \(N. sativa\) Linn. were purchased from the local market and their identification was confirmed. The seeds were dried and crushed into coarse powder which was used for extraction with alcohol (95% v/v) using Soxhlet apparatus. The extract was evaporated under vacuum. The extractive value (%w/w) of the alcoholic dry extract was 4.25%.

Male albino rats weighing between 140 and 175 g were selected for pyloric ligation ulcer model\(^12\). Rats were divided into three groups, each group consisting of six animals. Animals were fasted for 24 h. One group received normal saline 2 ml/kg (negative control), the second group received ranitidine 20 mg/kg by oral route (positive control) and the third group received alcoholic extract of \(N. sativa\) (150 mg/kg) by oral route, 30 min prior to pyloric ligation. Animals were sacrificed 4 h later and the stomach was opened to collect the gastric contents. The total volume of gastric content was measured. The gastric contents were centrifuged at 1000 rpm for 10 min. One ml of the supernatant liquid was pipetted out and diluted to 10 ml with distilled water. The solution was titrated against 0.01N NaOH using Topfer’s reagent as indicator, to the endpoint when the solution turned to orange colour. The volume of NaOH needed was taken as corresponding to the free acidity. Titration was further continued till the solution regained pink colour. The volume of NaOH required was noted and was taken as corresponding to the total acidity. Acidity was expressed as:

\[
\text{Acidity} = \frac{\text{Volume of NaOH} \times \text{normality} \times 100}{0.1} \text{ m Eq/l.}
\]

In the aspirin-induced ulcer experiments\(^13\), three groups of albino rats (150-175 g), with each group consisting of six animals were used. The first group served as a control group, the second group served as positive control and the third group served as the test group. The second and third groups were treated respectively with ranitidine (20 mg/kg) and alcoholic extract of seed of \(N. sativa\) (150 mg/kg), orally for 8 days. Control animals received normal saline (2 ml/kg) for 8 days. After 8 days of treatment, animals were fasted for 24 h. Ulcer was produced by administration of aqueous suspension of aspirin (a dose of 200 mg/kg orally) on the day of sacrifice. The animals were sacrificed 4 h later and stomach was opened to calculate the ulcer index by Kunchandy method\(^14\).

The effect of alcoholic extract of \(N. sativa\) on pylorus ligated rat and aspirin-induced ulcer models is presented in Tables 1 and 2, respectively. The results of the present study indicate that the alcoholic extract significantly reduces the total volume of gastric juice, free and total acidity of gastric secretion and also has activity against gastric ulcers in rats.

The control animals had ulcers and haemorrhagic streaks, whereas in animals administered with the extract of \(N. sativa\) there was significant reduction in ulcer index \((P < 0.001)\) (Figure 1).

It is generally accepted that gastric ulcers result from an imbalance between aggressive factors and the maintenance of the mucosal integrity through endogenous defence mechanisms\(^15\). The excess gastric acid formation by prostaglandin (PG) includes both increase in mucosal resistance as well as a decrease in aggressive factors, mainly acid and pepsin\(^16\). Inhibitions of PG synthesis by aspirin coincide with the earlier stages of damage to the cell membrane of mucosal, parietal and endothelial cells\(^17\). The preliminary phytochemical studies revealed the presence of flavonoids in alcoholic extract of \(N. sativa\); various flavonoids have been reported for its anti-ulcerogenic activity with good level of gastric protection\(^18,19\). So the possible mechanism of anti-
Table 1. Effect of alcoholic extract of *Nigella sativa* Linn. on gastric ulcer induced by pylorus ligation in rats

<table>
<thead>
<tr>
<th>Design of treatment</th>
<th>Dose</th>
<th>Volume of gastric secretion (ml/100 g)</th>
<th>Free acid (mEq/l)</th>
<th>Total acid (mEq/l)</th>
<th>Ulcer score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (normal saline)</td>
<td>2 ml/kg</td>
<td>8.5 ± 0.22</td>
<td>25.6 ± 0.04</td>
<td>60 ± 0.30</td>
<td>2.8 ± 0.07</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>20 mg/kg</td>
<td>4.1 ± 0.01</td>
<td>9.1 ± 0.02</td>
<td>20.3 ± 0.19</td>
<td>1.0 ± 0.08</td>
</tr>
<tr>
<td>Alcoholic extract of <em>Nigella sativa</em></td>
<td>150 mg/kg</td>
<td>5.1 ± 0.01*</td>
<td>10.4 ± 0.03*</td>
<td>30.6 ± 0.01*</td>
<td>1.4 ± 0.01*</td>
</tr>
</tbody>
</table>

*n = 6 animals in each group; Values are mean ± SEM; *P < 0.001 when compared with control; *P value was calculated using Student’s *t* test.

Table 2. Effect of alcoholic extract of *Nigella sativa* Linn. on aspirin-induced gastric ulcer in rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Design of treatment</th>
<th>Dose</th>
<th>Ulcer score</th>
<th>Percentage protection from ulcer</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control (normal saline)</td>
<td>2 ml/kg</td>
<td>3.2 ± 0.33</td>
<td>–</td>
</tr>
<tr>
<td>II</td>
<td>Ranitidine</td>
<td>20 mg/kg</td>
<td>1.0 ± 0.01</td>
<td>68.75</td>
</tr>
<tr>
<td>III</td>
<td>Alcoholic extract</td>
<td>150 mg/kg</td>
<td>1.6 ± 0.012*</td>
<td>50.00</td>
</tr>
</tbody>
</table>

*n = 6 animals in each group; Values are mean ± SEm.

*P < 0.001 when compared with control.

Figure 1. Stomach of *a*, control animal – pylorus ligated ulcer in rat; *b*, test drug treated animal – pylorus ligated ulcer in rat; *c*, control animal – aspirin-induced gastric ulcer in rat; *d*, test drug treated animal – aspirin-induced gastric ulcer in rat.

Ulcer action of *N. sativa* may be due to its flavonoid content. In this study we observed that *N. sativa* provides significant anti-ulcer activity against gastric ulcers in rats.

Folding and unfolding of chicken villin headpiece: Energy landscape of a single-domain model protein

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Folding and unfolding of a thermostable chicken villin headpiece subdomain, a 36-residue protein (HP-36), is studied by using Brownian dynamics simulations. The hydropathy scale of amino acids is used to obtain the varying interactions among the amino acids. A qualitative picture of the energy landscape funnel is obtained from simulations. Although there are several states near the minimum of the folding funnel, we could identify a stable native configuration. The energy of the folded protein scales with the hydrophobic contact parameter, as found in recent analyses. The model also allows for a description of cold denaturation by the salt-induced modification of the 'effective' interactions among the various amino acids. In this model, the kinetics of denaturation is found to be considerably different from that of folding–folding, seems to face more barriers and involves a more complex pathway.

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