CHAPTER - 5
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PHARMACOLOGICAL STUDIES

ANTI ULCEROGENIC ACTIVITY

5.1 Introduction

Gastro-intestinal tract is one of the major endocrine systems in the body. The hormones include endocrine secretion and paracrine secretion, or local hormones. These are regulatory peptides, the important one of which is histamine. The stomach secretes about 2.5 litres of gastric juice daily. The main exocrine secretions are pepsinogen from peptic cells, hydrochloric acid and an intrinsic factor from parietal or oxyntic cells. Mucus secreting cells found throughout the gastric mucosa secrete mucus. Bicarbonate is also secreted and trapped in the mucus and it creates a gradient of pH from 1 to 2 in the lumen and 6 to 7 in the mucosal surface. The mucus and the bicarbonate form an unstirred gel-like layer protecting the mucosa from the harmful effect of the gastric juice. Alcohol and bile are capable of disrupting this layer. Locally produced prostaglandins stimulate the secretion of both mucus and bicarbonate.

Disturbances in the above secretory functions are thought to be involved in the formation of peptic ulcer, and the treatment involves the use of drugs, which modify each of these factors.1

5.2 Aspirin - pylorus ligation - induced gastric ulcer in rats

Wistar albino rats weighing 100-200g of either sex were divided into nine groups, each group consisting of 6 animals. All groups of animals received treatments as shown below along with 200mg/kg of aspirin once daily for three days.
Group 1: received 1.0ml/kg, p.o 1% CMC as vehicle control

Group 2: received 50mg/kg, p.o ranitidine as standard control

Group 3: received 300mg/kg, p.o ethanolic extract of *S.acuta*

Group 4: received 300mg/kg, p.o ethanolic extract of *S.fruticosa*

Group 5: received 300mg/kg, p.o ethanolic extract of *T.ciliata*

Group 6: received 300mg/kg, p.o ethanolic extract of *B.spectabilis*

Group 7: received 300mg/kg, p.o ethanolic extract of *F.glomerata (bark)*

Group 8: received 300mg/kg, p.o ethanolic extract of *P.longifolia*

Group 9: received 300mg/kg, p.o ethanolic extract of *F.glomerata (leaves)*

Ulceration in rats was induced as described by Goel *et al*. On the fourth day pylorus was ligated following 36 h fasting as per the method of Shay *et al*. The rats were anaesthetized using light ether anaesthesia. Abdomen was opened by midline incision below the xiphoid (sternum). Pylorus was lifted lightly and ligated carefully without damaging its blood vessels. The stomach was replaced carefully and closed by interrupted sutures and collodion applied.

Four hours after the pyloric ligation the animals were sacrificed by decapitation. The abdomen was opened and the esophageal end (cardiac end) of the stomach was lightly secured by bulldog clip. The entire stomach from the body of the animal was removed. A small cut was made at the pyloric region just above the knot and the contents of the stomach were collected in a graduated centrifuge tube.
The stomach was opened along the greater curvature and washed it slowly under the running tap water. It was then placed on a glass slide and observed under 10x magnification for ulcers. A score for the ulcer was made as follows.

\[
\begin{align*}
0 & = \text{Normal coloured stomach} \\
0.5 & = \text{Red colouration} \\
1 & = \text{Spot ulcers} \\
1.5 & = \text{Haemorrhagic streak} \\
2 & = \text{ulcers} \\
3 & = \text{Perforation}
\end{align*}
\]

Ulcer index was determined by the method of Ganguly and Bhatnagar. Mean Ulcer score for each animal was expressed as ulcer index. The percentage of ulcer inhibition was determined as follows:

\[
\text{Control mean ulcer index} - \text{test mean ulcer index} \\
\% \text{ Inhibition} = \frac{\text{Control mean ulcer index}}{\text{of ulcer}} \times 100 \\
\]

The gastric content was centrifuged at 1000 rpm for 10 minutes and the volume of the gastric juice was measured. 1ml of supernatant liquid pipetted out and was diluted to 10ml with distilled water. The pH of this solution was recorded. The solution was then titrated against 0.01N sodium hydroxide using Topfer’s reagent as indicator. Titration was carried out to the end point when the solution turns to orange
colour. The volume of NaOH, used was noted, which corresponds to the free acidity. In order to estimate the total acidity the solution was titrated further till the color changes to pink $^{6-8}$. Acidity (mEq/l/100g) can be expressed as:

$$\text{Acidity} = \frac{\text{Titre value of NaOH} \times \text{actual molarity of NaOH} \times 100}{\text{Assumed molarity}}$$

The typical profile of the stomach is shown in Fig.5.1-5.2. The results are furnished in Table 5.1 and Fig 5.3 - 5.7
Table 5.1

Effect of various plant extracts on gastric secretion, acidity, pH and ulcer score in aspirin plus pylorus ligated rats

<table>
<thead>
<tr>
<th>Treatment mg/kg</th>
<th>Volume of gastric secretion ml/100g</th>
<th>Free acidity mEq/l/100g</th>
<th>Total acidity mEq/l/100g</th>
<th>pH</th>
<th>Ulcer score</th>
<th>%Ulcer inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle control</td>
<td>2.633±0.042</td>
<td>225.00±6.124</td>
<td>555.00±7.500</td>
<td>2.200±0.163</td>
<td>3.600±0.200</td>
<td></td>
</tr>
<tr>
<td>Ranitidine 50mg</td>
<td>1.317±0.172</td>
<td>148.75±13.475**</td>
<td>492.50±20.736*</td>
<td>3.167±0.166*</td>
<td>0.166±0.166**</td>
<td>95.37</td>
</tr>
<tr>
<td>S.acuta 300mg</td>
<td>0.950±0.017**</td>
<td>150.00±11.292**</td>
<td>507.50±21.448</td>
<td>2.500±0.223</td>
<td>1.667±0.333**</td>
<td>53.69</td>
</tr>
<tr>
<td>S.fruticosa 300mg</td>
<td>1.567±0.288**</td>
<td>168.75±14.459**</td>
<td>325.00±5.701**</td>
<td>2.500±0.223</td>
<td>0.500±0.223**</td>
<td>86.11</td>
</tr>
<tr>
<td>T.ciliata 300mg</td>
<td>1.583±0.144**</td>
<td>111.25±3.579**</td>
<td>310.00±18.131**</td>
<td>3.000±0.258</td>
<td>0.00±0.00**</td>
<td>100</td>
</tr>
<tr>
<td>B.spectabilis 300mg</td>
<td>0.966±0.185**</td>
<td>55.00±6.021**</td>
<td>263.75±11.361**</td>
<td>3.000±0.258</td>
<td>0.00±0.00**</td>
<td>100</td>
</tr>
<tr>
<td>F.glomerata (bark) 300mg</td>
<td>1.667±0.108**</td>
<td>132.50±7.906**</td>
<td>295.00±4.61**</td>
<td>3.167±0.166*</td>
<td>0.00±0.00**</td>
<td>100</td>
</tr>
<tr>
<td>P.longifolia 300mg</td>
<td>0.983±0.083**</td>
<td>135.00±10.782**</td>
<td>552.50±10.724</td>
<td>2.333±0.210</td>
<td>1.667±0.307**</td>
<td>53.69</td>
</tr>
<tr>
<td>F.glomerata (leaves) 300mg</td>
<td>0.916±0.162**</td>
<td>31.25±3.579**</td>
<td>243.75±11.415**</td>
<td>3.333±0.210**</td>
<td>0.00±0.00**</td>
<td>100</td>
</tr>
</tbody>
</table>

Each value is the mean± S.E.M of six determinations
P*<0.05,P**<0.01 Dunnet test as compared to control
Fig. 5.1 Aspirin Plus pylorus ligation induced ulcer in rats and its prevention of formation of ulcer by control, ranitidine and various plants at 300mg / kg. In addition all groups of animals received aspirin 200mg / kg once daily for 3 days. On 4th day pylorus was ligated. Animals were sacrificed using anaesthetic ether.
Fig. 5.2 Photomicrograph of glandular portion of the stomach of control, standard and test rat showed protective action against gastric ulcer induced by aspirin plus pylorus ligation.
Effects of various plant extracts on gastric volume (ml/100g in aspirin pylorous-induced gastric ulcer in rats)

Fig. 5.3
Effects of various plant extracts on free acidity (mEq/L/100g) in aspirin-pylorus ligation-induced gastric ulcer in rats

![Graph showing the effects of various plant extracts on free acidity.](image1)

Fig. 5.4

Effects of various plant extracts on total acidity (mEq/L/100g) in aspirin-pylorus ligation-induced ulcer in rats

![Graph showing the effects of various plant extracts on total acidity.](image2)

Fig. 5.5
Treatment Effect of various plant extracts on pH in aspirin-pylorus ligation-induced gastric ulcer in rats

Control Ranitidine S.acuta S.fruticosa T.ciliata B.spectabilis F.glomerata-bark P.longifolia F.glomerata-leaves

Fig.5.6

Treatment Effects of various plant extracts on %inhibition of ulcer

Ranitidine S.acuta S.fruticosa T.ciliata B.spectabilis F.glomerata - bark P.longifolia F.glomerata -leaves

Fig.5.7
Fig. 5.9 HCl/ethanol induced ulcer in mice and its prevention of formation of ulcer lesion by ethanolic extract of various plant at 300mg / kg. The extracts were given to the animals 1h before the administration of HCl/ethanol mixture. Animals were killed 1 h after ethanol ingestion.
5.3 Ulcer lesion Index method: Hcl/Ethanol induced ulcer

Fifty-four swiss albino mice of either sex deprived of food (water *ad libitum*) for 24 h were randomly grouped into nine groups, each consisting of 6 animals. All groups of animals received treatments as shown below,

Group 1: received 1.0ml/kg, p.o 1% CMC as vehicle control
Group 2: received 100mg/kg, p.o sucralfate as standard control
Group 3: received 300mg/kg, p.o ethanolic extract of *S.acuta*
Group 4: received 300mg/kg, p.o ethanolic extract of *S.fruticosa*
Group 5: received 300mg/kg, p.o ethanolic extract of *T.ciliata*
Group 6: received 300mg/kg, p.o ethanolic extract of *B.spectabilis*
Group 7: received 300mg/kg, p.o ethanolic extract of *F.glomerata (bark)*
Group 8: received 300mg/kg, p.o ethanolic extract of *P.longifolia*
Group 9: received 300mg/kg, p.o ethanolic extract of *F.glomerata (leaves)*

The experiment was performed as described by Yesilada *et al.* After one hour all animals were treated with 0.2 ml of HCl / ethanol mixture p.o (0.3M hydrochloric acid and ethanol 60%) to induce gastric ulcer. Animals were killed by cervical dislocation one hour after administration of HCl ethanol mixture and the stomach was excised and inflated by injection of normal saline (2ml). The stomach was fixed in 5% formalin solution for 30 min. and was cut open along the greater curvature and pinned on a flat wooden board. The presence of elongated black streak along the gastric mucosa provided evidence of gastric damage. Lesion index of the stomach was determined by measuring each lesion along its greater length measured in mm. In case of petachial, five such lesions were taken as equivalent of 1mm length ulcer.
Cytoprotection percentage was calculated for each group and compared with vehicle control group.

Percentage inhibition of ulcer was determined as follows

\[
\% \text{ Inhibition} = \frac{\text{Control mean lesion index} - \text{test mean lesion index}}{\text{Control mean lesion index}} \times 100
\]

The results are furnished in Table 5.2 and Fig.5.8 & 5.9

**Table 5.2**

**Effect of various plant extracts against HCl/ethanol Induced gastric lesion in mice**

<table>
<thead>
<tr>
<th>S.No</th>
<th>Treatment</th>
<th>Dose in mg/kg</th>
<th>Mean ± S.E.M</th>
<th>% Ulcer Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
<td>1% CMC</td>
<td>22.667±3.509</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Sucralfate</td>
<td>1mg</td>
<td>1.167±0.5426**</td>
<td>94.85</td>
</tr>
<tr>
<td>3</td>
<td><em>S</em>.acuta</td>
<td>300mg</td>
<td>10.167±0.945**</td>
<td>55.14</td>
</tr>
<tr>
<td>4</td>
<td><em>S</em>.fruticosa</td>
<td>300mg</td>
<td>14.167±2.750**</td>
<td>37.40</td>
</tr>
<tr>
<td>5</td>
<td><em>T</em>.ciliata</td>
<td>300mg</td>
<td>10.667±1.054**</td>
<td>52.94</td>
</tr>
<tr>
<td>6</td>
<td><em>B</em>.spectabilis</td>
<td>300mg</td>
<td>2.333±0.494**</td>
<td>89.71</td>
</tr>
<tr>
<td>7</td>
<td><em>F</em>.glomerata (bark)</td>
<td>300mg</td>
<td>2.667±0.333**</td>
<td>88.23</td>
</tr>
<tr>
<td>8</td>
<td><em>P</em>.longifolia</td>
<td>300mg</td>
<td>2.333±0.557**</td>
<td>89.71</td>
</tr>
<tr>
<td>9</td>
<td><em>F</em>.glomerata (leaves)</td>
<td>300mg</td>
<td>2.000±0.258**</td>
<td>91.18</td>
</tr>
</tbody>
</table>

Each value is the mean ± S.E.M of 6 determinations

**P <0.01 Dunnet test as compared to control value**
Effect of various plant extracts against HCl/ethanol induced gastric lesion in mice

Treatment

Sucralfate  S.acuta  S.fruticosa  T.ciliata  B.spectabilis  F.glomerata - bark  F.glomerata -leaves

% ulcer

Fig. 5.8
5.4 Water immersion stress induced ulcer in rats

Stress is a condition, which is known to alter the physiological homeostasis of the organisms and elicits various endocrinal and visceral changes in plasma cortisone and gastric mucosal integrity. Stress also increases brain serotonin (5-HT) level.

The effect of ethanolic extract of some of the Indian medicinal plants was tested with water immersion stress induced ulcer in rats.

Method

Male Wistar albino rats weighing 100-200g were divided into nine groups, each group consisting of 6 animals. All groups of animals received treatments as shown below,

Group 1: received 1.0ml/kg, p.o 1% CMC as vehicle control
Group 2: received 20mg/kg, p.o omeprazole as standard control
Group 3: received 300mg/kg, p.o ethanolic extract of *S.acuta*
Group 4: received 300mg/kg, p.o ethanolic extract of *S.fruticosa*
Group 5: received 300mg/kg, p.o ethanolic extract of *T.ciliata*
Group 6: received 300mg/kg, p.o ethanolic extract of *B.spectabilis*
Group 7: received 300mg/kg, p.o ethanolic extract of *F.glomerata* (bark)
Group 8: received 300mg/kg, p.o ethanolic extract of *P.longifolia*
Group 9: received 300mg/kg, p.o ethanolic extract of *F.glomerata* (leaves)

Stress ulcers were induced by forcing them to swim in the glass cylinder (height 45cm, diameter, 25cm) containing water to the height of 35cm maintained at 25°C for 3 h. Animals were fasted for 24 h prior to the experiment. Ethanolic extract of the above plants 300 mg/kg suspended in 1% CMC, vehicle control, standard drug treatment
omeprazole 20 mg/kg were given orally using oral cavage tube. After 30 min., animals were allowed to swim in water (temperature 25°C) for 3 h. Then they were removed from the cylinders and sacrificed by a blow on the head. The stomach of each animal was removed and cut longitudinally along the greater curvature and the severity of gastric ulcer was assessed in terms of mean ulcer index using the following scoring system as described by Alphine and Word 15-17.

Denuded epithelium = 10
Petachial and frank haemorrhage = 20
One or 2 ulcers = 30
Multiple ulcers = 40
Perforated ulcers = 50

The percentage of ulcer inhibition was determined as follows

\[
\% \text{ Inhibition} = \frac{\text{Control mean ulcer index} - \text{test mean ulcer index}}{\text{Control mean ulcer index}} \times 100
\]

The results are furnished in Table 5.3 and Fig. 5.10
Table 5.3
Effect of ethanolic extract of the plant on water immersion stress induced ulcer in rats

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose in mg/kg</th>
<th>Mean ulcer score ± standard error mean</th>
<th>% ulcer inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle control</td>
<td>1% CMC</td>
<td>143.3 ± 12.01</td>
<td></td>
</tr>
<tr>
<td>Omeprazole</td>
<td>20 mg/kg</td>
<td>0.0 ± 0.0***</td>
<td>100</td>
</tr>
<tr>
<td><em>S. acuta</em></td>
<td>300 mg/kg</td>
<td>108.3 ± 10.775</td>
<td>24.4</td>
</tr>
<tr>
<td><em>S. fruticosa</em></td>
<td>300 mg/kg</td>
<td>101.66 ± 16.00</td>
<td>29.0</td>
</tr>
<tr>
<td><em>T. ciliata</em></td>
<td>300 mg/kg</td>
<td>81.66 ± 4.73</td>
<td>43.0</td>
</tr>
<tr>
<td><em>B. spectabilis</em></td>
<td>300 mg/kg</td>
<td>40.0 ± 8.94*</td>
<td>72.0</td>
</tr>
<tr>
<td><em>F. glomerata</em> (bark)</td>
<td>300 mg/kg</td>
<td>33.33 ± 4.21*</td>
<td>76.7</td>
</tr>
<tr>
<td><em>P. longifolia</em></td>
<td>300 mg/kg</td>
<td>6.66 ± 2.10***</td>
<td>95.3</td>
</tr>
<tr>
<td><em>F. glomerata</em> (leaves)</td>
<td>300 mg/kg</td>
<td>26.66 ± 4.216**</td>
<td>81.3</td>
</tr>
</tbody>
</table>

Each value is the mean ± S.E.M of 6 determinations

*P<0.05, **P < 0.01, ***P<0.001 dunnet test as compared to control value
Effect of ethanolic extract of the various plant on the water immersion stress induced ulcer

Fig. 5.10
Statistical analysis

The statistical analysis of all the results was carried out using one-way ANOVA followed by Dunnett's multiple comparisons using graph pad in stat 3 and all the results obtained in the study were compared with the vehicle control group. P values <0.05 were considered statistically significant.

5.5 Results

Aspirin plus pylorus ligation induced gastric ulcer: All the plant extracts (300mg/kg; p.o) showed significant reduction in gastric volume, free acidity and ulcer score as compared to vehicle treated group (P<0.01) (Table 5.1 and Fig 5.1 - 5.7). With S.fruticosa, T.ciliata, B.spectabilis, P.longifolia and F.glomerata the total acidity was reduced significantly as compared with vehicle control group. In the case of S.acuta and P. longifolia there was no significant reduction in total acidity. F.glomerata (bark) and F.glomerata (leaves) both increased the pH significantly as compared to control group (P<0.05 and P<0.01). In contrast, the other plant extracts S.acuta, S.fruticosa, T.ciliata, B.spectabilis and P.longifolia did not increase the pH significantly.

The anti-ulcerogenic effect of standard drug, ranitidine was also examined in the present study. Ranitidine significantly reduced gastric volume, free acidity, total acidity, and ulcer score but increased the pH as compared with the control group.

In terms of percentage of ulcer inhibition the ethanolic extracts of T.ciliata, B.spectabilis, F.glomerata (bark) and F.glomerata (leaves) showed 100% ulcer inhibition as compared to vehicle control group and the activity was very well comparable to standard drug ranitidine. In case of S.fruticosa ethanolic extract, ulcer inhibition was found to be 86.11% while both S.acuta and P.longifolia extract exhibited 53.69% activity.
Oral administration of HCl/ethanol mixture (0.3m hydrochloric acid and ethanol 60%) at a dose of 2ml/animal was sufficient to induce ulcer (Table 5.2 and Fig 5.8 & 5.9). The ulcer lesion index of the stomach was determined by measuring each lesion along its greater length in mm. All the extracts at a dose of 300mg/kg, p.o. showed significant reduction in ulcer lesion as compared with vehicle control group (P<0.01).

On a comparison of percentage reduction of ulcer lesion among various extracts, the cytoprotective activity recorded was found to be in the descending order as *F.glomerata* (leaves)(91.18%) > *B.spectabilis* (89.71%) > *P.longifolia* (89.71%) > *F.glomerata* (bark)(88.23%) and the effect was comparable to sucralfate used as the reference drug (94.85%). While the percentage activity of other plant extracts observed were *S.acuta* (55.14%), *T.ciliata* (52.94%) and *S.fruticosa* (37.4%).

Effect of the ethanolic extract on water immersion induced stress in rats: The plant extracts *B.spectabilis*, *F.glomerata* (bark) (P<0.05) *P.longifolia* (P<0.001) and *F.glomerata* (leaves) (P<0.01) exhibited significant reduction in ulcer score as compared with vehicle treated group. With *S.acuta*, *S.fruticosa* and *T.ciliata* the reduction in ulcer score was found to be not significant with vehicle control group.(Table 5.3 and Fig 5.10)

In terms of percentage ulcer inhibition the order of activity was found to be *P.longifolia* 95.3%> *F.glomerata* (leaves) 81.3%, *F.glomerata* (bark) 76.7% and *B.spectabilis* 72.0%. The other plant extracts *S.acuta*, *S.fruticosa* and *T.ciliata* showed 24.4%, 29.0%, 43.0% activity respectively.

5.6 Discussion

Drugs in peptic ulcer such as H₂ blocker (ranitidine, famotidine, etc.,), M₁ blockers (pinenzipine, telonzipine, etc), Proton pump inhibitors (omeprazole, lansoprazole etc.,) decrease the acid secretion while drugs like sucralfate,
carbinoxolone promote mucosal defences. Although these drugs have a long history in treating ulcers, the clinical evaluation shows adverse effect and drug interaction during the course of treatment. Therefore it is necessary to look for an ideal anti-ulcer drug, especially from herbal preparations, which may afford better protection and decrease the incidence of relapse. Hence the afore-mentioned plant extracts, which are being extensively used in folk medicine in the treatment of gastric ulcer, were examined for their efficacy and for determination of their possible mechanism of action.

The method used here was (1) Aspirin – pylorous ligation induced gastric ulcer model in rats, (2) HCl/ethanol induced gastric ulcer in mice, (3) Water immersion stress induced ulcer in rats, each approach defining its own mechanism of antiulceration.

The plants extracts were safe and free from toxicity since LD 50 cut off for the extracts was found to be greater than 2000mg/kg, p.o (OECD guidelines).

In aspirin-pylorus ligation induced gastric ulcer model the ethanolic extracts attenuated the gastric volume, free acidity, total acidity and ulcer index thus showing the antisecretary mechanism involved in these extracts for their antiulcerogenic activity. The order of potency of the plant extract was found to be *F.glomerata* (leaves) > *B.spectabilis* > *T.ciliata* > *F.glomerata* (bark) > *S.fruticosa*. Ulcer index parameter was used for the evaluation of anti-ulcer activity since ulcer formation is directly related to factors such as reduction in gastric volume, decrease in free acidity and total acidity. However the plant extracts of *S.acuta* and *P.longifolia* showed moderate activity and the total acidity was not reduced significantly. It is significant to note when the pH reached 3, the ulcer score appeared less. This is born out by the decrease in free acid, which might have contributed to the antiulcer property of the plant extract. In case of vehicle control, aspirin plus pylorus ligation aggravated the acid
secretion, which in turn caused increase in gastric volume, increased free acidity, total acidity, low pH and increased ulcer index. This could possibly be attributed to the inhibition of COX1 and COX2 enzyme, which are responsible for prostaglandin synthesis\textsuperscript{18,19}.

It is a known fact that reduction in prostaglandin level leads to the formation of more ulcer\textsuperscript{20}; further the acidic nature of aspirin may aggravate the situation.

Hence the drug, which is capable of controlling COX1 and COX2 pathways, may be useful in combating the ulcer formation. So a further detailed study may be required to confirm the inhibition of COX1 and COX2 enzyme with regard to the effective plant extracts \textit{F.glomerata} (leaves), \textit{F.glomerata} (bark), \textit{B.spectabilis} and \textit{T.ciliata}. Ulcers were thought to be due to increase in offensive factors like gastric acid, pepsin, \textit{Helicofactor pylori} and bile salts but it has been observed that gastric ulcer patients have either normal or below normal acid level in the stomach\textsuperscript{21}. This indicates that other mechanisms are also involved in ulcer formation. Moreover the disturbance of defensive factors like mucus secretion, bicarbonate secretion and mucosal blood flow has been reported to cause ulcers\textsuperscript{22}. It is a known fact that ethanol-induced gastric lesions are not inhibited by antisecretary agents like ranitidine but are inhibited by agents, which enhance mucosal defensive.

Ethanol induces severe gastric damage in mice possibly through leukotriences production and also involvement of 5-lipoxygenase in the formation of ulcer lesion. Prostaglandins also play a role in ethanol-induced ulcer. So the protective actions of all the plant extracts against the gastric damage might be due to protection against 5-lipoxygenase or leukotriene pathway. The cytoprotective action possibly stimulates the prostaglandin synthesis, which in turn is involved in cytoprotection of the gastric mucosa.
Water immersion stress is one of the best models of stress in rats to induce ulcer. The model provides both emotional stress as well as physiological stress to the animal. It is a significant finding that of all the extracts *P. longifolia* exhibited to afford a distinctively high protection against water immersion stress induced ulcer.

In aspirin plus pylorus ligation model the extracts of *F. glomerata* (leaves), *F. glomerata* (bark), *B. spectabilis* and *T. ciliata* were found to be effective. The results indicate that the plant extracts decreased the total gastric volume, free acidity, total acidity and favorably raising the pH and therefore found to be effective in inhibition of ulcer formation. In HCl/ethanol induced ulcer the plant extracts of *F. glomerata* (leaves), *B. spectabilis*, *P. longifolia*, *F. glomerata* (bark) were found to be effective choice in protecting the gastric mucosa. It was found that the plant *P. longifolia*, and *F. glomerata* (leaves) were particularly useful for preventing stress-induced ulcer.
Structure of compounds possessing anti ulcerogenic activity

β-Carotene

Kaempferol

Quercetin
5.7 References


