Anti-Ulcer Activity Of Methanolic Bark Extract Of Nerium Indicum Mill

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ABSTRACT

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Antiulcer activity of bark extract of Nerium indicum Mill plant was studies in rat in which induce by oral administration of Indomethacine. Anti ulcer activity was determine and assessed by comparing gastric volume and total acidity, ph and ulcer inhibition and perform indomethacine modal. The ulcer index comparing test group and control group. The methanolic bark extract showed 67.51 % ulcer protection in indomethacine induce ulcer. It is used ranitidine in reference drug. it is present study perform that Nerium indicum bark extract have potant anti ulcer activity have indomethacine modal tested.
INTRODUCTION:
A peptic ulcer is a kind of disease that is hurting a cross or ulcer in the lining of the stomach. the present in part of the small intestine is also called a duodenal ulcer. Gastric ulcer is defined as present in the stomach region also know as stomach ulcer [1,2]. Gastric ulcer is a familiar disease that is a kind of multiple etiologies. The gastric mucosa is perforation through the muscular arms mucosa. The imbalance is a gastric mucosal barrier and Aggressive factor. The antagonistic factor cause mucosal injury append gastric acid and hydrochloric acid 3,4] the gastric mucosa is unchanging reveal the aggressive factor in which the mucosa injury include gastric hydrochloric acid [3,4]. The gastric mucosa is regularly exposed injured such as acids like bile acid, food ingredients, and helicobacter pylori bacteria and drug. They are implicated in the pathogenesis of gastric ulcers including increase gastric acid and pepsin secretion inhibit of prostaglandin synthesis and cell spread growth decrease gastric blood flow and gastric mucosa [5,6].

ULCER TYPE
The most common types of ulcer are –
1. Peptic ulcer- peptic ulcer is defined as related to pepsin and can cause in different regions.
2. Gastric ulcer- Gastric ulcer is defined as present in the stomach region also known as a stomach ulcer.
3. Duodenal ulcer – this type of ulcer is present in the duodenal region of the GIT tract or Gastrointestinal tract.
The less common types of ulcer are-
1. Esophageal ulcer- Esophageal ulcer is defined as a come about in the lower end of a patient's esophagus .esophagus ulcer is caused by harmful bacteria.
2. Bleeding ulcer –someday internal Bleeding ulcer is caused by internal bleeding because a peptic ulcer, now days referred to as a bleeding ulcer and is the most dangerous type of ulcer.
3. Refractory ulcer- Simple peptic ulcer is not healed but after 4 months of treatment know as called a refractory ulcer.
4. Chronic leg ulcer: chronic leg ulcer is regarded as a disease of old people. It is a severe chronic disorder the age distribution is heavy bodyweight and an aging population trend is likely to continue. The patients were under age 60 at the time of the survey [7].
5. Pressure ulcer- Pressure ulcers are present in the dermal region of the body. It is known as pressure ulcer thepresent on the skin which gives rise to obstruction of blood flow to the skin. A pressure ulcer can cause all areas of the body[8].
6. Genital ulcer. Genital ulcers are present in the genital area called scrotal ulcer .it is present in male or female as called sexually transmitted diseases such as genital herpes syphilis, Granuloma inguinale, lymph granuloma venereum. This causes many types of suffering from chronic skin diseases or skin cancer. They are cause genital ulcer approx. 65 to 75 % infected patient from HSV-1(Herpes simplex virus) or HSV-2[9].
7. Stress ulcer - stress ulcers are present in the group of the lesion and found in the stomach or duodenum. Stress ulcer is commonly present in the people which added other illness or critically problems [10].
CAUSES OF PEPTIC ULCER:-

1. **Helicobacter pylori (H.pylori)** - H. pylori a bacterial is responsible for cause ulcer which most ulcer this organism indicated the protective coating of the stomach layer and duodenum and damaging the digestive juice to irritating the sensitive stomach lining under.

2. **Non – steroidal anti-inflammatory drug (NSAIDs)** - Non – the steroidal anti-inflammatory drug is long time use which causes an ulcer. These drugs are like aspirin, ibuprofen, and naproxen diclofenac indomethacin are the higher acidic drug.

SYMPTOMS

Some people observe suffering peptic ulcer disease do not have some symptoms. They are cause not symptoms are known as sometimes called “silent ulcers. People who do have symptoms may experience are different type-

- It is feeling full quickly when eating
- It is Stomach pain and belching or feeling bloated after some time eating
- It is produced heartburn or acid reflux
- Nausea
- Vomiting
- Blood in the stools.
- It is postprandial abdominal bloating, distension, and nausea.
- It is swollen state retention of fluid or gas called bloating.
- Mild gastric mucosa pain [16,17].

NERIUM INDICUM BARK

Nerium Indicum mill plants are belonging to family Apocynaceae which plant know Kaner in Hindi. It is an evergreen plant as a long history of traditional medicinal used in different countries in the world [18]. The plant has been used as anti-inflammatory and anti-nociceptive, immune-stimulating and anti-bacterial, cardiotonic, diuretic[19’22]. The plant leaves prepare decoction process used has been applied externally in the treatment of scabies and Reduce swelling [23]. The root bark oil is used to treat skin diseases and leprosy [24]. All parts of the plant having anti-cancer properties[25’26]. The plant part of the bark is used in insecticide[27]. This plant was studied the anti-ulcer potential on different models on gastric ulceration. The methanolic bark extract of Nerium Indicum plant present undertaken to study the effect indomethacin by inducing ulcers in rats.

MATERIALS AND METHODS

**Plant material**
The bark of Nerium Indicum Mill was collected from botanical garden Prayagraj Uttar Pradesh India. The sample was identified ( G.P Sinha) Scientist and plant taxonomist Department of Botanical Survey of India office of the scientist Chatham lines Allahabad.

**Preparation of extract**
The bark was shade dried and powdered prepare by mechanical method. The bark powder of plant material (120 gm) was extracted in a 500 ml round-bottomed flask with 350 ml of methanol. It is increasing polarity solvent with petroleum ether. The reflux time for each solvent was 35 cycles. The bark extract was cooled at room temperature than a filter and evaporated to dryness under reduced pressure in a rotary evaporator.

**Experiment animal**
The Wister rat (140-190g) of either sex, obtained from Saha enterprise west Bengal India Registration No. 1828/PO/Br/S/15/CPCSEA(CPCSEA register under the ministry of environment welfare division, Govt of India) IAEC No.SIP-IAEC/007/10/19.The department animal house at 27±1˚C and humidity 42-54. the animal was standard solid and visible Diet and water ad libitum. The animal was the previous experiment prepare for the laboratory condition.

**Acute toxicity study**
The acute toxicity for a methanolic extract of Nerium Indicum bark was decided in Wistar albino rats provide under standard conditions. According (OECD guideline No. 423 ) follows the fasted overnight previous to the experiment fixed dose method of CPCSEA ) was adopted for toxicity studies.

**Indomethacin induced ulcer[28-30]**
The Wistar rat weighing 140-190 g were used for the experiment. They are randomized divided into five groups of six animals each. The food was withdrawal 20 h and water 1 h before the experiment.

- **Group, I (Control)** received only indomethacin (20 mg/kg⁻¹).
- **Group II (standard or reference)** receive ranitidine (50mg/kg⁻¹).
- **Group III** was pretreated with Nerium Indicum bark extract (250mg/kg⁻¹) and **Group IV** was pretreated with Nerium Indicum bark extract (500mg/kg⁻¹). After about 30 minutes Group III and IV were administration indomethacin the administration of 5 h
after indomethacin were animal killed by decapitation method. The stomach was separate and open along the greater curvature. The help of microscopic was carried out with a hand lens examination and the presence of lesion was scored. 

**It is scoring off the ulcer will be made as following [31]**

**Table 1: Result of microscopic examination of ulcer:**

<table>
<thead>
<tr>
<th>Observation</th>
<th>scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal stomach</td>
<td>0.0</td>
</tr>
<tr>
<td>Red coloration</td>
<td>0.4</td>
</tr>
<tr>
<td>Hemorrhagic streak</td>
<td>1.2</td>
</tr>
<tr>
<td>Spot ulcer</td>
<td>0.8</td>
</tr>
<tr>
<td>Ulcer</td>
<td>1.5</td>
</tr>
<tr>
<td>Perforation</td>
<td>2.5</td>
</tr>
</tbody>
</table>

The animal will be expressed as a mean ulcer score for ulcer index. The ulcer protection was a percentage and determine as follows [32].

Control means ulcer Index – Test means ulcer index

\[
\% \text{Protection} = \frac{\text{Control means ulcer index} - \text{Test means ulcer index}}{\text{Control means ulcer index}} \times 100
\]

**Pylorus ligation induced ulcer:-[33, 36]**

The animal has fasted for overnight before the pylorus ligation method with water ad libitum. under light ether anesthesia the stomach was opened by midline incision process .the pyloric portion was slightly lifted out and in the stomach, damage to its blood supply. Nerium Indicum bark extract was administration before pylorus ligation the stomach was placed back carefully and the abdominal wall was closed with sutures. the animal was sacrificed 5 h after pylorus ligation. The stomach was isolated and collected the content of centrifuge. The gastric juice was measured of volume and used for estimation of free acidity.1 ml of centrifuged and filtered gastric secretion was titrated against 0.1N sodium hydroxide using Topper's reagent as an indicator which determination of free acidity and 1% phenolphthalein as an indicator for combine with acidity. Some of the two titrations were total acidity. The stomach was open along with the greater curvature and observes for ulcers. The ulcer index was determined as mentioned above.

\[
\text{Acidity} = \frac{\text{The volume of NaOH} \times \text{Normality of NaOH}}{0.1N} \times 100 \text{mEq}/1/100g
\]

**Statistical analysis:**

The experiment is presented as mean± SEM and one way ANOVA using a Statistical significance between treated and control group followed by Dunnett's test where P<0.001, P<.01 was considered statistically significant.

**RESULT AND DISCUSSION**

In indomethacin-induced model pretreatment of the rat with Nerium Indicum bark extract dose-dependent protection from indomethacin-induced ulceration, when compared to the ulcer control animal. The result showed in Table2. In pyloric ligation induced ulcer effect of Nerium Indicum bark extract on gastric volume, free acidity, total acidity and ulcer in pylorus ligated result was shown in Table 3.

**Table2: The effect of methanolic bark extract of Nerium Indicum in indomethacin-induced ulcer**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Treatment</th>
<th>Ulcer index</th>
<th>Protection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control (Indomethacine 20mg/kg⁻¹)</td>
<td>14.95±0.511</td>
<td>-</td>
</tr>
<tr>
<td>II</td>
<td>Ranitidine (50mg/kg⁻¹)</td>
<td>5.246±0.350*</td>
<td>70.59%</td>
</tr>
<tr>
<td>III</td>
<td>N. indicum bark extract(250mg/kg⁻¹)</td>
<td>5.016±0.200 *</td>
<td>63.81%</td>
</tr>
<tr>
<td>IV</td>
<td>N. Indicum bark extract(500mg/kg⁻¹)</td>
<td>4.232±0.420*</td>
<td>67.51%</td>
</tr>
</tbody>
</table>
Value is represented as mean±SEM of 6 observation, statistical comparisons as follow: significant at ***P<0.001 compare to control group

Table 3. Effect of Nerium Indicum bark extract in pylorus ligation induced ulcer

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Standard</th>
<th>T1 (250mg/kg)</th>
<th>T2 (500mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcer index</td>
<td>13.042±0.443</td>
<td>5.242±0.628</td>
<td>6.282±0.422</td>
<td>5.442±0.750</td>
</tr>
<tr>
<td>% protection</td>
<td>_</td>
<td>68.12%</td>
<td>58.42%</td>
<td>66.22%</td>
</tr>
<tr>
<td>Ph of gastric juice</td>
<td>2.6±0.042</td>
<td>4.2±0.110</td>
<td>2.5±0.118</td>
<td>3.6±0.880</td>
</tr>
<tr>
<td>Gastric vol(ML/100gm)</td>
<td>8.4±0.242</td>
<td>2.2±0.122</td>
<td>3.2±0.262</td>
<td>2.4±0.042</td>
</tr>
<tr>
<td>Free acidity (meq/11/100g)</td>
<td>72.24±0.244</td>
<td>32.72±0.122</td>
<td>52.6±0.211</td>
<td>32.11±0.121</td>
</tr>
<tr>
<td>Total acidity (Meq/1/100g)</td>
<td>98.42±0.120</td>
<td>44.42±0.155</td>
<td>74.15±0.158</td>
<td>44.12±0.144</td>
</tr>
</tbody>
</table>

Value is are express as mean±SEM of 6 Observation statistical comparison as following significant at P>0.001, P>0.05 Compare to control group

CONCLUSION
The result suggests that the flower extract of Nerium Indicum Mill produces an antiulcer effect. Nerium Indicum bark extract and ranitidine significantly decrease the total acidity and free acidity that prevented the development of gastric ulcers induced by indomethacin. The percentage of ulcer protection 63.81% and 67.51% which was observed at the dose of 250 and 500 mg/kg. The pylorus ligation of the stomach produces an accumulation of gastric acid in the stomach. The ulcer index is determined 5hours after pylorus ligation. The Nerium Indicum bark extract and ranitidine significantly decrease the total acidity and free acidity.

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