ANTIULCER ACTIVITY OF PIPAL EXTRACT

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ABSTRACT: An ethanol extract of Pipal has been studied for its ability to inhibit gastric acidity and to protect gastric mucosa against the injuries caused by pyloric ligation, acetyl salicylic acid and cytodestructing agents (80% ethanol, 0.6M Hcl and 0.2 M Hcl) in rats. The results of this study demonstrate that ethanol extract of papal has significant effects on various experimentally induced ulcers. It reduced significantly the intensity of gastric lesions induced by pylorus ligation, acetyl salicylic cid (ASA) and mucosal damaging agents. Also the total acidity was found to be decreased Acutic toxicity test is shoed no toxic symptoms or mortality over a period of 7 days with doses 0.25-1.5 gm/kg. These findings suggests that ethanol extract of papal exerts anticiulcer effects by increasing gastric mucosal resistance and cyto-protective activities.

INTRODUCTION:

Pipla consists of the dried fruits of Piper longum Linn of family Piperaceae. It is still used in the traditional medicines of many countries including India. (C.K.Kokate, 1990) it is used for abdominal discomfort, as a carminative and for stomach ache. It is a tonic and is used in making irritant snuffs. As a liniment it reduces rheumatic pains and paralysis. It is useful in chronic bronchitis (S.K. Jain, 1968) A survey of the literature showed that no experimental data are available to justify the medicinal use of the fruits of this plant alone. As it is used in folkgone medicine for the treatment of ulcer, the present study was carried out to investigate the antiulcer activity of pipal fruits in rats.

MATERIALS AND METHODS

Fruits of Piper longum were purchased from the local market and air dried. The powdered fruits were subjected to successive solvent extraction using petroleum ether (40-60) hexane, chloroform, acetone and ethanol in a soxhlet apparatus. The solvents were then removed at low temperature under reduced pressure and the extracts were stored in a refrigerator for pharmacological studies.

Wistar albino rats of either sex, approximately of the same age weighing 150-200 gm and fed standard chow diet were used. They were divided into groups of 6 animals each. The distribution of animals in groups, the sequence of trials, and the treatments were randomized. The solutions for the experiments were freshly prepared. The animals were killed by ether euthanasia. The stomachs were removed, opened along the greater curvature, washed with saline and examined with a magnifying lens. Lesions were assessed and scored according to their dimensions and severity and scored between 0, no visible ulcer, and 3 deep lesions with diameter greater than 5mm in each stomach. The scored for each single
lesion were then totaled (Valcavi et al, 1982). The results refer to average lesion 
score ± SEM. Statistical analysis of the 
severity of gastric ulcers was done by 
student’s t-test.

**CUTE-TOXICITY STUDIES**

Acute toxicity was performed on six groups 
consisting 10 mice per group. They were 
intubated orally with graded doses (50, 100, 
200, 40, 800, 1500 mg/kg) of the ethanol 
extract and were observed for any 
behavioural or toxic symptoms. They were 
observed or a period of 14 days to record 
any morality.

**ANTICUCERSTUDIES**

1. **PYLORUSLIGATED (SHAY) RATS**

The animals were made to fast for 48 hours 
but allowing free access to water upto 18 
hours prior to operation procedure, the 
pylorus was ligated under light ether 
anesthesia, car being taken mot to cause 
bleeding or to occlude blood vessels (Shey 
et al, 1945) Ethanol extract and ranitidine 
(25mg and 50 mg/kg) were administered 
intraperionetally (i.Q) soon after pylorus 
ligation. The animals were maintained in 
cages without food and water for 6 hours 
and then sacrificed by an overdose of ether. 
Stomachs were removed and contents 
collected, measured, centrifuged and 
subjected to analysis for titrable acidity 
against 0.01 N NaOH. Each stomach was 
examined for lesions as described above.

2. **ACETYLSALICYCLICACID**

**INDUCED (ASA) GASTRICLESIONS**

ASA induced ulcers were produced in albino 
rats deprived off food for 36 hours. ASA in 
1% carboxymethyl cellulose (CHC) in water 
was administered P.O in a dose of 200mg/kg 
body wt. To these rats, ethanol extract was 
administered 1 hours before administration 
of ASA. The control and standard groups 
received 1% CMC and ranitidine (50mg/kg 
body wt) respectively. This was repeated on 
the following day also. Four hours after the 
second dose, all animals were killed and 
examined for lesions (Okabe et al, 1974).

3. **Gastric lesion induced necrotizing**

**agents (Cytoprotection studies)**

The experiments were done on Wistar male 
rats, fasted of 36 hours with access to 
drinking water ad libitum. The following 
necrotizing agents were administered in the 
volume 1ml: 80% ethanol, 0.6 M HCL, 
0.2M NaoH (Robert et al, 1983).

4. **Ulcer healing tests**

Male albino rats weighing between 250-275 
gm were used after an overnight fasting. 
Under ether, anaesthesia laparatomy was 
performed and after exposing the stomach, 
0.05ml 30% acetic acid was injected into the 
gastric wall at the junction of the body of the 
glandular stomach and the antrum of the 
anterior wall (Takagi et al, 1969). The rats 
were then maintained; in cages with normal 
food and water ad libitum and were 
sacrificed on the 12th day after operation. 
Ethanol extract of pipla in doses 25 and 50 
mg/kg body wt. Were given orally, daily 
from one day after operation for 10 
consecutive days. Ulcer index and healing 
rate were then calculated as described by 
Okabe et al (1976).
**TABLE I**

Effect of Ethanol Extract of Pipal on the Gastric Secretion, Acidity and Lesions in Pylorus – ligated (Shay) rats

| Group   | Dose (mg.Kg) | Gastric secretions at 6 hr (Mean±SEM) | Titrable acidity | Ulcer index |
|---------|--------------|---------------------------------------|------------------|-------------|
|         |              | Vol. of Gastric Secretion              |                  |             |
| Control | 1% CMC (1ml/kg) | 13.13 ± 0.478                  | 18.94 ± 0.361    | 0.196 ± 0.021 |
| Ethanol Exl | 25mg       | 10.56 ± 0.33                        | 12.728 ± 0.478   | 0.124 ± 0.033* |
| Ethanol Ext | 50mg       | 2.08 ± 0.238                         | 2.146 ± 0.729*   | 0.072 ± 0.006*** |
| Ranitidine | 50mg       | 1.33 ± 0.247                         | 1.295 ± 0.519    | 0.056 ± 0.014*** |

*P<0.05, **P<0.01, ***P<0.001

**TABLE II**

Effect of Ethanol Extract of ASA induced Gastric Lesion

| Group   | Dose (mg.Kg) | Intraluminal bleeding | Gastric lesion |
|---------|--------------|-----------------------|---------------|
|         |              | Scare (mean ± SEM)    | Ulcer under (Mean ± SEM) |
| Control | 1% CMC (1ml/kg) | 1.83 ± 0.40           | 19.66 ± 2.02 |
| Ethanol Exl | 25mg       | 1.12 ± 0.33           | 12.16 ± 0.23** |
| Ethanol Ext | 50mg       | 0.5 ± 0.22            | 8.16 ± 0.83*** |
| Ranitidine | 50mg       | 0.33 ± 0.21**         | 6.66 ± 2.10*** |

*P<0.05, **P<0.01, ***P<0.001

**TABLE III**

Effect of Ethanol Extract of ASA induced Gastric Lesion induced by various necrotizing agents

| Group   | Dose (mg.Kg) | Various index (mean ± SEM) |
|---------|--------------|----------------------------|
|         |              | 80% EtOH | 0.6 M HCL | 0.2 MnaOH |
| Control | 1% CMC (1ml/kg) | 6.16 ± 0.41 | 7.5 ± 0.32 | 6.0 ± 0.87 |
| Ethanol Exl | 25mg       | 3.16 ± 0.79* | 3.33 ± 0.21** | 2.80 ± 1.20** |
| Ethanol Ext | 50mg       | 0.66 ± 0.21** | 1.66 ± 0.16** | 0.66 ± 0.21** |
| Ranitidine | 50mg       | 4.16 ± 0.70 | 3.97 ± 0.61 | 1.91 ± 1.2** |

*P<0.05, **P<0.01, ***P<0.001
TABLE IV
Effect of Ethanol Extract of papal on Rats (Ulcer healing test)

| Group      | Dose (mg.Kg)       | Ulcer index       | % age of healing |
|------------|--------------------|-------------------|------------------|
| Control    | 1% CMC (1ml/kg)    | 28.9 ± 0.477      | -                |
| Ethanol Exl| 25                 | 12.66 ± 0.33*     | 56.19**          |
| Ethanol Ext| 50                 | 6.33 ± 0.243 ***  | 78.09%***        |

*P<0.05, **P<0.01, ***P<0.001

RESULTS AND DISCUSSIONS

This study reveals the capacity of ethanol extract of papal to inhibit significantly the formation of gastric ulcers in rats by various ulcerogenic procedures and necrotizing agents compared to ranitidine. It produced a dose dependent reduction in gastric acidity and a decrease in the gastric ulceration in shay rats as observed from reduced ulcer index. The cytoprotective activity is very significant and it is found to be more than that of ranitidine. From the ulcer healing test it is evident that papal extract in 50 mg.kg exerts very significant curative effect. From all these results it is proved that papal extract has prophylactic, cytoprotective as well as curative effects on various experimentally induced gastric lesions. Further studies are deemed necessary to elucidate the exact mode of action and therapeutic value in prophylactic and/or treatment of peptic ulcer disease in traditional medicine.

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