Phytopharmacological Evaluation of Alcoholic Extract of *Berberis aristata* Leaf in the Treatment of Gastric Ulcer

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**Abstract**: For over a century, peptic ulcer has been one of the most common gastrointestinal tract (GIT) disorder. There are number of drugs are now available for treatment. Drugs of herbal origin reduce the offensive factors and have proved to be safe, clinically effective, relatively less expensive, globally competitive, and with better patient tolerance. This study was performed to assess the anti-ulcer activity on different parts of *B.aristata*. Apart from that, acute toxicity, qualitative chemical analysis, total phenolic content (TPC), total flavonoid content (TFC) and *in vitro* antioxidant activities were evaluated. The potentially active plant part was selected for screening as gastro protective, *in vivo* antioxidant and antisecretory activities in ulcerated rats. The 50% ethanolic extract of *B. aristata* were subjected to preliminary phytochemical screening, estimation of TFC and TPC. The crude extract from the leaves of *B. aristata* gave best antiulcer activity among flower and stem. In acute toxicity studies, the administration of the crude extract of *B. aristata* leaves did not reveal any adverse effects or toxicity in rats at fourteen days observations. The results of these studies have shown that ethylexract of *B.aristata* leaf (EEBAL) produced a significant dose dependent ulcerprotective, antioxidant and antisecretory activity by blocking the activity of proton pump, protecting from antioxidants produced during stress induced ulcer and by enhancing glycoprotein levels.

**Abbreviation**: TPC, total phenolic content; TFC, total flavonoid content; EEBAL, ethanolic extract of *Berberis aristata* leaf.

**Introduction**: Peptic ulcer represents a major health problem, both in terms of morbidity and mortality. The aggressive acid-pepsin factors are responsible for the induction of ulcers. *Berberis aristata* DC var. *aristata* (Berberidaceae), are commonly known as Daruharidralocal to the Himalayas in India and in Nepal. It is also found in Nilgiri slopes in South India.¹²³ The plant is utilized customarily in irritation, wound mending, skin ailment, menstruation, looseness of the bowels, jaundice and fondness of eyes. Alcoholic extract of bark yielded berberine chloride, palmatine chloride and a mixture of both.⁴ The chief constituent of the roots and stem bark of *B. aristata* is an alkaloid, berberine are responsible for hepatoprotective activity⁵. The crude extract of *B.aristata* fruits exhibit preventive and curative effects on paracetamol and chloroform induced hepatotoxicity⁶. *Berberisaristata* also exhibits anti-diarrhoeal, anti-fungal, anti-histaminic an anticholinergic activities⁴.

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Material and Methods

Plant materials

The plant part of *Berberis aristata* Linn. (Family: Berberidaceae) was collected from Botanical Garden of National Botanical Research Institute (NBRI), Lucknow, India in month of Sep 2017. The plant materials authenticated by Dr. A.K.S. Rawat and the voucher specimens (NBRI-SOP-204) were deposited in the departmental herbarium (Pharmacognosy and Ethnopharmacology Division, NBRI, Lucknow) for future reference.

Animals

The adult Sprague Dawley albino rats of either sex weighing 130-180 g were taken. Pharmacological studies were carried out at National Botanical Research Institute, Lucknow.

Acute Toxicity Study

It is performed by OECD rule no. 425 following the process of Up and Down 7,8.

The hydroalcoholic extract of different plant parts at doses of 400, 800 and 2000 mg/kg b.w by oral gavage were given to different groups. All the animals were deprived of food for 2 h before and 4 h after dosing. The animals were continuously monitored during first 4 h and every one hour during the first 12 h for any adverse effects. Later they were monitored (daily, twice) for any abnormal changes throughout the study period (14 days).

Antiulcer studies

The EEBAL was subjected to gastroprotective studies using ethanol, aspirin, and pylorus ligation induced ulcers models. The adult Sprague Dawley albino rats of either sex weighing 140-180 g were on fasting for 48h with free access to water and divided into six groups.

| Group | Description                  |
|-------|------------------------------|
| I     | Normal Control               |
| II    | Ulcer control                |
| III   | EEBAL (100 mg/kg b.w. p.o.)  |
| IV    | EEBAL (200 mg/kg b.w. p.o.)  |
| V     | EEBAL (400 mg/kg b.w. p.o.)  |
| VI    | Ranitidine (50 mg/kg b.w. p.o.) |

Ethanol (EtOH)-Induced Ulcer

After 5 days of treatment, EtOH, (100%, 1mL/200 g, 1h) was administered orally on the day of the experiment and the animals were slaughtered by cervical dislocation and stomach was incised along with greater curvature and investigated for ulcers. The ulcer index was measured, based upon the product of length and width of ulcer present in stomach 9.

\[
\text{Control Ulcer Index – Test Ulcer index}
\]

\[
\text{% Ulcer protection} = \frac{x100}{\text{Control Ulcer Index}}
\]

\[
\text{Ulcer Index (UI)} = U_N + U_S + U_P / 10
\]

Where, \( U_N \) = Average no of ulcer per rat; \( U_S \) = Average no of severity of ulcer per rat; \( U_P \) = percent of rat with ulcer.

Aspirin (ASP) Induced Ulcer

Following 5 days of treatment, aspirin at a portion of 200 mg/kg b.w. (20 mg/mL) was directed orally on day 6 of the investigation with the help of an orogastric tube as a suspension 10. The stomach was etched
Pylorus Ligated (PL) Induced Ulcers

Following 5 days of treatment rats were kept for 18 h fasting before pylorus ligation, after that the rodents were anesthetized by Pentobarbitone (35 mg/kg b.w, IP). The abdomen was opened and the pyloric piece of the stomach was ligated. Abdomen was then sutured in two layers and rodents were left in a pan. Promptly a short time later, midriff was again opened, ligated the cardiovascular piece of the stomach and expel the stomach. The stomach was cut, opens along the more prominent ebb and flow and analyzed the ulcers on the mucosal end of the stomach$^{11}$.

Results

Extractive values of *Berberis aristata*

The % yield of freshly collected plant parts of *Berberis aristata* were shown in table1:

| S. No | Part used of *B. aristata* | 50% EtOH (EtOH : H$_2$O (1:1)) | % Yield (Extract) |
|-------|-----------------------------|---------------------------------|-------------------|
| 1. Leaf | EtOH : H$_2$O (1:1) | 14.10 |
| 2. Flower | EtOH : H$_2$O (1:1) | 7.5 |
| 3. Bark | EtOH : H$_2$O (1:1) | 10.9 |

Acute Toxicity Studies

The result indicates that there were no deformity found in all groups. The given test drug at the doses of 400, 800 and 2000 mg/kg b.w was found to be safe. Accordingly, the acute oral LD$_{50}$ of the extractives was completed to exceed 2000 mg/kg b.w, the highest dose tested in the study (Table 2).

| Plant parts | Leaf | Flower | Bark |
|-------------|------|--------|------|
| Group       | 1    | 2      | 3    | 1    | 2      | 3    |
| Dose (mg/Kg b.w) | 400  | 800    | 2000 | 400  | 800    | 2000 |
| Number of animal dead | Nil  | Nil    | Nil  | Nil  | Nil    | Nil  |

Ethanol (EtOH)-Induced Ulcer

The oral intake of EEBAL decreased the index of gastric abrasions by 13.2 1.9 -4.7 1.7, respectively (21.08 – 71.6 % protection) in comparison to control 16.6 3.9 (Table 3).

| Group | Treatment | Dose(mg/kg) | Ulcer index(mm$^2$/rat) | Percent protection |
|-------|-----------|-------------|-------------------------|-------------------|
| I     | Normal Control | -- | 2.10 1.41$^a$ | -- |
| II    | Disease Control | 1ml/0.2kg | 16.6 3.9 | -- |
| III   | EEBAL      | 100 | 13.2 1.9 | 21.8 |
| IV    | EEBAL      | 200 | 7.4 0.94$^b$ | 55.4 |
| V     | EEBAL      | 400 | 4.7 0.71$^b$ | 71.6 |
| VI    | Ranitidine | 50  | 3.4 1.7$^b$ | 79.51 |
Aspirin (ASP) induced ulcers

Administration of EEBAL 1 h before the induction of gastric abrasions by ASP, decreased the total ulcer index of by 16.2 1.6 –8.4 0.9, respectively. Ranitidine lowers the total ulcer index of by 4.4 1.8 (78.43% protection) (Table 4).

Table 4: Effect of EEBAL extract (twice daily for five days) on Aspirin induced gastric ulcers

| Group   | Treatment     | Dose(mg/kg) | Ulcer index(mm²/rat) | Percent Protection |
|---------|---------------|-------------|----------------------|--------------------|
| I       | Normal Control| -           | 2.10 1.41           | --                 |
| II      | Disease Control| 200         | 21.5 3.4            | --                 |
| III     | EEBAL extract | 100         | 16.2 1.6            | 24.6               |
| IV      | EEBAL extract | 200         | 11.3 0.75           | 47.4               |
| V       | EEBAL extract | 400         | 8.4 0.9             | 60.9               |
| VI      | Ranitidine    | 50          | 4.4 1.8             | 78.43              |

Values are mean ± SEM for 6 rats;

*P <0.001 as compared to their respective normal control group.

aP < 0.01, compared to respective disease control group.

bP < 0.001 compared to respective disease control group.

Pylorus ligation induced gastric ulcers

The oral intake of EEBAL in P.L induced ulcer model decreased the ulcer index by 15.2 1.2- 4.2 0.59, respectively (16.4 – 77.04% protection) in comparison to control 18.3 1.7 (Table 5).

Table 5: Effect of EEBAL extract (twice daily for five days) on Pylorus ligation induced gastric ulcers

| Group   | Treatment | Dose(mg/kg) | Ulcer index (mm²/rat) | Percent protection |
|---------|-----------|-------------|-----------------------|--------------------|
| I       | Normal Control | -           | 2.10 1.41           | --                 |
| II      | Disease Control | --         | 18.3 1.7            | --                 |
| III     | EEBAL     | 100         | 15.2 1.2            | 16.4               |
| IV      | EEBAL     | 200         | 10.5 0.72           | 42.6               |
| V       | EEBAL     | 400         | 4.2 0.59            | 77.04              |
| VI      | Ranitidine | 50          | 3.5 1.2             | 84.66              |

Values are mean ± SEM for 6 rats;

*P <0.001 as compared to their respective normal control group  aP < 0.001 compared to respective disease control group

Discussion

There are numerous studies identified with the antiulcerogenic properties of flavonoids12,13. Flavonoids are optional metabolite with a wide scope of organic action14. An attempt was made on the necessity of nontoxic, antioxidant and antiulcer compounds preferably from traditional medicinal plants such as B. aristata for their protection against various experimental gastric ulcer models. Pylorus ligation-prompted ulcers are believed to be brought about by expanded emission of acid and pepsin in the stomach 10. EEBAL would in general diminishing the acid and pepsin discharge in the stomach. Decline in gastric juice shows increment in life expectancy of mucosal cells15. Increment in mucosal defensive elements might be the central point in charge of the defensive impact of EEBAL.

Conclusion

The present examination inferred that concentrate of B. aristata leaf had the capacity to shield the
gastric mucosa from synthetic (headache medicines), physical (pylorus ligation) and stress initiated ulcers by restraining gastric acid discharge, upgrading glycoprotein levels and offering cancer prevention agent insurance against oxidative pressure incited gastric harm. This finding affirms the conventional utilization of *B. aristata* leaves in the treatment of gastric ulcer.

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