



## 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 ethylextract 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 Daruhardralocal to the Himalayas in India and in Nepal. It is also found in Nilgiri slopes in South India<sup>1,2,3</sup>. The plant is utilized customarily in irritation, wound mending, skin ailment, menorrhagia, looseness of the bowels, jaundice and fondness of eyes. Alcoholic extract of bark yielded berberine chloride, palmatine chloride and a mixture of both<sup>4</sup>. The chief constituent of the roots and stem bark of *B. aristata* is an alkaloid, berberine are responsible for hepatoprotective activity<sup>5</sup>. The crude extract of *B. aristata* fruits exhibit preventive and curative effects on paracetamol and chloroform induced hepatotoxicity<sup>6</sup>. *Berberis aristata* also exhibits anti-diarrhoeal, anti-fungal, anti-histaminic and anticholinergic activities<sup>4</sup>.

## 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 <sup>7,8</sup>.

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.

<b>Group I</b>	: Normal Control
<b>Group II</b>	: Ulcer control
<b>Group III</b>	: EEBAL (100 mg/kg <i>b.w. p.o.</i> )
<b>Group IV</b>	: EEBAL (200 mg/kg <i>b.w. p.o.</i> )
<b>Group V</b>	: EEBAL (400 mg/kg <i>b.w. p.o.</i> )
<b>Group VI</b>	: Ranitidine (50 mg/kg <i>b.w. p.o.</i> )

### 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 <sup>9</sup>.

$$\% \text{ Ulcer protection} = \frac{\text{Control Ulcer Index} - \text{Test Ulcer index}}{\text{Control Ulcer Index}} \times 100$$

$$\text{Ulcer Index (UI)} = \frac{U_N + U_S + U_P}{10}$$

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<sup>10</sup>. The stomach was etched

alongside the more prominent ebb and flow and analyzed for ulcers score.

### 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<sup>11</sup>.

## Results

### Extractive values of *Berberis aristata*

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

**Table 1 : %Yield of different parts of *Berberis aristata***

S. No	Part used of <i>B. aristata</i>	50% EtOH	% Yield (Extract)
1.	Leaf	EtOH : H <sub>2</sub> O (1:1)	14.10
2.	Flower	EtOH : H <sub>2</sub> O (1:1)	7.5
3.	Bark	EtOH : H <sub>2</sub> 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<sub>50</sub> of the extractives was completed to exceed 2000 mg/kg *b.w*, the highest dose tested in the study (Table 2).

**Table 2: Mortality observation in each tested groups**

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

**Table 3: Effect of EEBAL (twice daily for five days) on Ethanol induced gastric ulcers**

Group	Treatment	Dose(mg/kg)	Ulcer index(mm <sup>2</sup> /rat)	Percent protection
I	Normal Control	--	2.10 1.41 <sup>#</sup>	--
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 <sup>a</sup>	55.4
V	EEBAL	400	4.7 0.71 <sup>b</sup>	71.6
VI	Ranitidine	50	3.4 1.7 <sup>b</sup>	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(mm <sup>2</sup> /rat)	Percent Protection
I	Normal Control	-	2.10 1.41 <sup>#</sup>	--
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 <sup>a</sup>	47.4
V	EEBAL extract	400	8.4 0.9 <sup>b</sup>	60.9
VI	Ranitidine	50	4.4 1.8 <sup>b</sup>	78.43

Values are mean ± SEM for 6 rats;

<sup>#</sup> P < 0.001 as compared to their respective normal control group.

<sup>a</sup> P < 0.01, compared to respective disease control group.

<sup>b</sup>P < 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 (mm <sup>2</sup> /rat)	Percent protection
I	Normal Control	--	2.10 1.41 <sup>#</sup>	--
II	Disease Control	--	18.3 1.7	--
III	EEBAL	100	15.2 1.2	16.4
IV	EEBAL	200	10.5 0.72 <sup>a</sup>	42.6
V	EEBAL	400	4.2 0.59 <sup>a</sup>	77.04
VI	Ranitidine	50	3.5 1.2 <sup>a</sup>	84.66

Values are mean ± SEM for 6 rats;

<sup>#</sup> P < 0.001 as compared to their respective normal control group <sup>a</sup> P < 0.001 compared to respective disease control group

## Discussion

There are numerous studies identified with the antiulcerogenic properties of flavonoids<sup>12,13</sup>. Flavonoids are optional metabolite with a wide scope of organic action<sup>14</sup>. 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<sup>10</sup>. EEBAL would in general diminishing the acid and pepsin discharge in the stomach. Decline in gastric juice shows increment in life expectancy of mucosal cells<sup>15</sup>. 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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