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Research Article

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Pharmacological evaluation of Anti-ulcer activity of *Embelia ribes burm.*

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Abstract In this study the operation of was administered studying the antiulcer results orally. Toxicity experiments on albino rats over a period indicate no morality at a dose of 2000mg/kg Duration: 14 days. In the rats no significant was seen during the study. This assist in predicting this It contains no toxicity whatsoever, and is completely healthy. So, 250 & 500 mg / kg t dose was chosen for further analysis. The comments suggested the long- term The extract administration had no negative impacts on the pets' general health. No Important variations in body weights or in animal food intake were observed. Thus, this formulation can be medically used. The animals had ethanol-induced ulcer Aspirin and the ulcerated pets were handled with fresh juice at a dosage of 250 & 500 mg / kg Standard oral omeprazole prescription.

Keywords Anti-ulcer activity, *Embelia ribes* burm

Introduction

Ulcer is a significant gastrointestinal disease with various aetiologies affecting 10 per cent of the global population. Repeated consumption of alcohol, smoking, excessive stress, repeated overuse – anti-steroidal anti-inflammatory drugs and *H. pylori* outbreak are primary factors of chronic ulcerative colitis, mucous membrane bleeding & stomach pain in sufferers [1-2]. Such ulcers may grow whenever the gastroprotective (mucus, bicarbonate and prostaglandins) & inflammatory (acid, pepsin, bile salts and Helicobacter pylori bacteria) imbalances occur [3]. The rapid emergence to ulcers is controlled for successful cure by inhibiting gastric acid secretion, fostering gastro-protection, blocking apoptosis and stimulating epithelial cell proliferation. The traditional medications utilized in the diagnosis of ulcer involve receptor of histamine prostaglandin equivalents, antagonists, proton pump blocker, cytoprotective agents, antacids and anticholinergics, but most of these medicines cause adverse side effects or drug interactions, and may even change the body's biochemical processes upon prolonged usage. Therefore, herbal medicinal products are typically used for such chronic cases where drugs are needed for extended periods of use [4]. *Embelia Ribes Burm* (Myrisiancae) commonly known as Vidanga, Bavding (Gujrati) and False Black Pepper in English is a large woody climbing shrub and is widely distributed throughout in India. It is esteemed in Ayurveda as a powerful anthelmintic. Ayurveda also describes vidanga as a pungent and cures flatulence and colic. whole plant

is used as anti- inflammatory drug to relieve Rheumatism and Fever. One Ayurvedic formulation, vidangadya churna (powder of vidanga), containing vidanga as main ingredient is taken with honey to alleviate obesity [5-27].

Methodology

In jan 2022, the *in-vivo* antiulcer study was conducted and ethical approval from Accuprec research lab Ahmedabad.

Selection & Plant Authentication

Embelia Ribes Burm

Identification of the Fruits of *Embelia Ribes Burm* Deputy conservator of Forest sikar (Reference no: DCF/2022/17).

Plant is authenticated by Bhima ram choudhary. Material was shade dried at room temperature and powdered mechanically and passed through a sieve #40.

Phyto chemical screening

The plant might be including the accompanying synthetic compounds like protein, starch, and lipids. That is utilized as food by individuals. It additionally incorporates the synthetic concoctions, for example, Tannins, glycosides, alkaloids, Volatiles oils. The exacerbate that assume pivotal job for bunches of therapeutic properties.

Carbohydrates test

Molish test: The powdered of model was consolidated with 1 ml of alpha napthol game plan close by conc Sulphuric destructive course of action in the test tube blushing concealing was made at the crossing point between 2 liquids this is shows the closeness of sugar.

Fehling test: The specimen powder was given both the Fehling A and Fehling B plan and put for a satisfactory time in the water shower. It shows the concealing square red. This shows the Carbohydrateproximity.

Benedicts test: Include 8 drops of benedict reagents to the example powder, and overwhelmingly heat up the example for 5 min, indicating the red ppt. This demonstrates starch presents

Alkaloids test: For the small amount of stored powder (sample) were taken and a few drops of hydrochloric acid were applied and filtered. The filtered one was checked with various alkaloid agents.

Mayer's reagents: Apply modest quantities of Mayer 's reagent to a modest quantity of above channel to shape cream accelerate. This demonstrates alkaloids are available.

Dragendorff sreagents: A modest quantity of Dragendorffs reagents is applied from the above channel and it frames an orange earthy colored accelerate. This shows alkaloids present.

Flavonoids test: Apply 5 ml of depleted alkali solution to extract tank from the plant and start by adding concentrated corrosive sulphuric. It forms yellow, a shading. It indicates removal demonstrated association with flavonoid.

Steroids test

Salkowaski test: Few plant extracts have been combined with chloroform, and the same amount of sulphuric acid has been added. The chloroform layer got cherry red color. It means the sample containshormones.

Libbbermann burchatd test: The extract is dissolved in 10 drops of acetic acid and conc, 2 ml of chloroform. Added sulphuric acid. Now the solution turns to reddish colour, then turns to bluish green. This shows the presents of steroids indicated by plant extraction.

Tannins: With vanillin hydrochloric acid reagent is prepared from only a few amounts of plant extract. Because of the formation of phloroglucinol it produces, pink or red colour, suggesting the presence of tannins**.**
Ninhydrin test: From the specimen arrangement involve 2 drops applied to the concentrate andheating a freshly arranged 0.2 percentninhydrine reagent. Advancing the blue shading that display the peptide, amino acid (PROTEIN) closeness.

Test glycosides:
Test of Keller- killani: From the little amount of little powder acidic corrosive was broken up and includes hardly any drops of ferric chloride and moved to the outside of conc Sulphuric corrosive. At the intersection, ruddy earthy colored shading was framed, which slowly becomes blue shows the presents of heart glycosides.

Saponins Test
Test of Foam: From the sample arrangement involve 2 drops applied to the concentrate and heating a freshly arranged 0.2 percent in hydrine reagent. Advancement of blue shading that display the proximity of peptide 1 ml of extract solution is diluted separately with distilled water to 20 ml and shaken for 15 minutes in a graduated cylinder. The presence of Saponins, amino corrosive (Protein) suggests a 1 cm layer of foam.

Pharmacological Screening Animals
The pale skinned person rodent (normal body weight 200-300g), used from in house research center. The creatures were kept up under normalized natural conditions (22-28 °C, 60-70 %relative moistness, 12hr dull/light cycle) in creature house, Biological Signature Analtytical laboratory, Ghaziabad. The creatures were given standard mouse chow and water not obligatory.

Fixation of Dose
Methods

Table 1: Details of Animals uder

Guideline	OECD – 420-fixed dose method
Test	Limit test
Species	*Rattus norvegicus*
Strain	Albino Wistar rats
Number of animals	05
Sex	Male/female
Initia ldose	2ml/kg

Table 2: Investigational architecture for toxicity practical research

Groups	Conc. ($mgkg^{-1}$)
First	10
Second	60
Third	400
Fourth	3000

Research Design

Test animal – 6- 9 weeks retract Wistar rats of females and males, nulliparous and non-pregnant species were picked from College of Pharmaceutical Sciences, and modified for multi-week earlier dose. Conditions of residency.

Temperature – OECD rule 425, 2001 maintained room temperature of the test creature at 22 °C ± 3 °C. Such ranges are meant to allow homeotherms to maintain the metabolic rate or to be within their impartial thermo zones. Since temperature below the prescribed range prompts expanded food consumption, increased vitality utilization has yet decreased productivity. In contrast, temperature above the recommended range induces reduced food intake, reduced weight and decreased vitality use. With temperature the toxicity can change. Will increase with temperature linearity.

Humidity: The relative mugginess kept up at 40 percent - 60 percent doesn't ideally surpass 70 percent (OECD-425, 2001). The relative mugginess underneath the suggested range may create sores, for example, ring tail and may build food utilization.

Light: 11-12 hours, dark / light period. Good lighting and light cycle play a significant role in maintaining the physiology and actions of rats. Neuroendocrine offered adequate vision and regulation of the diurnal and circadian cycles (CPCSEA guidelines for laboratory animal facilities, 2003).

Light intensity: The light level was maintained at 325 lux, about 1m above ground. Consideration of differences in light intensity is critical to place animals on cage rack for toxicology analysis.

Caging: Cages of polypropylene, with sturdy foundation and walls. Lids made from steel grill which can accommodate both water and food.

Feeding condition: Sterile laboratory feed (*ad libitum*) and RO water bottles daily.

Feed: Brown colored chow diet

Drug administration: Animals were fed on day 0 for 12 hours before dosing. Control rats were givenorally using a curved and ball tipped stainless feeding needle with an acacia solution of 20 per cent.

Clinical observations: All rodents in the wake of dosing were persistently checked for poisonous indications for 4 hours. Creatures and any extra social or clinical indications of harmfulness were observed for the remainder of the 14-day study period. The body weight of the creature was measured before dosing and on days 7 and 14. All creatures were killed and LD_{50} morale was built up towards the end of the investigation. It was achieved with clinical understanding and gross neurotic examination. Ethanol triggers stomach ulcer.

Both sex (150-200 g) Albino Wistar rats are divided into 5 classes of 6 animals each. They are kept insingle cages and fasted for 24 hours allowing free access to drinks hot. Beware of maintaining a strategic distance from coprophagy. Ulceration was introduced by the organization of 80 per cent ethanol orally in a portion of 1ml for each rodent in 36 hours without taking care of the rodents. Test and Standard is given for each rodent stage, one hour before ethanol organization. After two hours of ethanol organisation, harming CO_2 can yield to animals. The stomach is measured, opened along the more prominent bend and in an axis tube the material is depleted and has been centrifuged for 10 minutes at 1000rpm and the volume is noted. Using a pH meter, the pH of the gastric juice is recorded. At that point the material is revealed for nothing and utter causticity to be tested. The glandular part of the stomach is then washed with running water to search for ulcers. The quantity of ulcers per stomach is noted, and the severity of the ulcers is scored minutely with 10x focal point support.

Table 3: Effect of *Embelia Ribes* fruits extracts on ethanol induced ulcer

S. No.	Body weight	Treatment	Ulcer Index						Total score	Mean Ulcer Index ± SEM	% Protection
			Normal coloured stomach	Red Coloured	Spot ulcer	Haemo rrhagic	Ulcers >3 but < 5	Ulcers >5			
			(0)	(0.5)	(1.0)	(1.5)	(2.0)	(3.0)			
1	150	Normal	0	-	-	-	-	-	0	0±0	-
	155	Control	0	-	-	-	-	-	0		
	160		0	-	-	-	-	-	0		
	158		0	-	-	-	-	-	0		
	165		0	-	-	-	-	-	0		
	160		0	-	-	-	-	-	0		
2	160	Control	0	0.5	1.0	1.5	2.0	-	5.0	4.5±	0
	165	(Ulcerated)	0	0.5	1.0	1.5	2.0	-	5.0	0.341	
	150	ethanol	0	0.5	1.0	1.5	-	-	3.0		
	157	1ml/200gm	0	0.5	1.0	1.5	2.0	-	5.0		
	160		0	0.5	-	1.5	2.0	-	4.0		
	170		0	0.5	1.0	1.5	2.0	-	5.0		
3	165	Omeprazole	0	0.5	-	-	-	-	0.5	0.58±	87.11
	162	(20mg/kg)	0	0.5	-	-	-	-	0.5	0.08**	
	158		0	0.5	-	-	-	-	0.5		
	167		0	0.5	-	-	-	-	0.5		
	160		0	0.5	1	-	-	-	1.5		
	170		0	0.5	-	-	-	-	0.5		
4	175	Ethanolic	0	0.5	1.0	-	-	-	1.5	2.25±	50.0
	150	Fruits	0	0.5	1.0	1.5	-	-	3.0	0.33**	
	165	Extract	0	0.5	1.0	1.5	-	-	3.0		
	165	(250mg/kg)	0	0.5	1.0	1.5	-	-	3.0		
	155		0	0.5	1.0	-	-	-	1.5		
	160		0	0.5	1.0	-	-	-	1.5		
5	155	Ethanolic	0	0.5	1.0	-	-	-	1.5	1.16±	74.22
	160	Fruits	0	0.5	1.0	-	-	-	1.5	0.21**	
	158	Extract	0	0.5	-	-	-	-	0.5		
	165	(500mg/kg)	0	0.5	1.0	-	-	-	1.5		
	165		0	0.5	-	-	-	-	0.5		
	155		0	0.5	1.0	-	-	-	1.5		

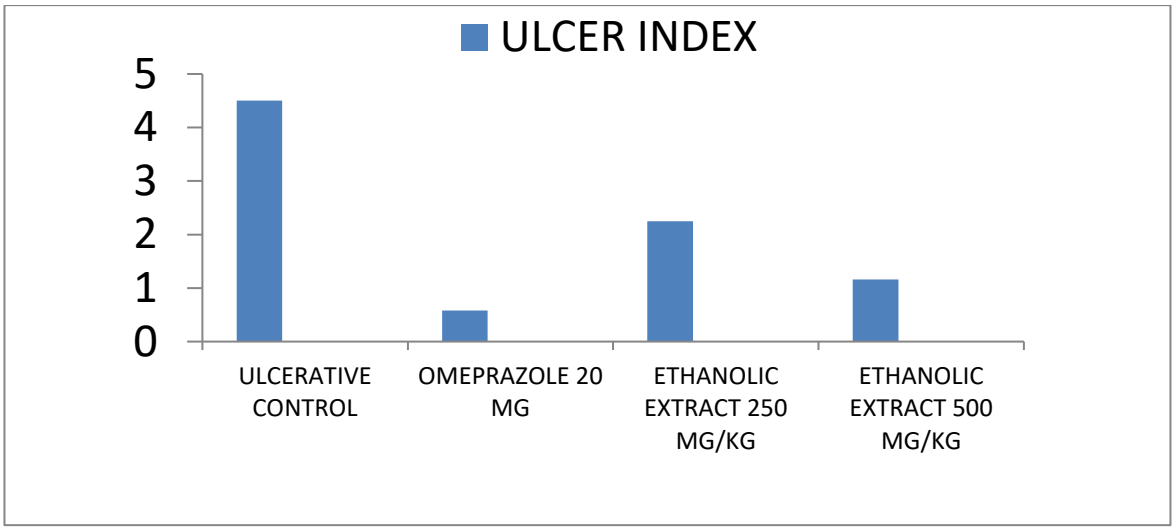


Figure 1: Ulcer Index

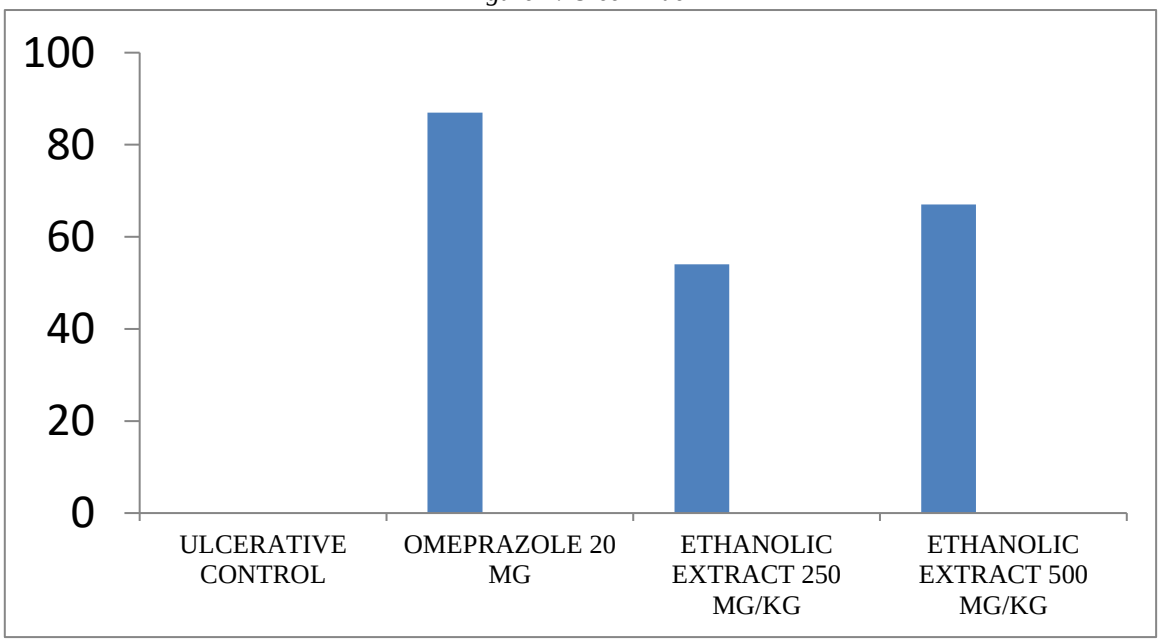


Figure 2: % Protection of Ulcer

Index of Ulcer

Animal in the ethanol-triggered ulcer community had exposure to drinking water ad libitum for 36 hours starving to death. Oral administration was be 1 ml of 80 per cent ethanol. One group was given meprazole, and the other groups are given fruit 250 & 500 mg until ethanol administration. Animals will be killed by excess dose of ether after 2 hours of ethanol administration. The abdomen was separated and fitted to a cork board, and the numbers and extent of ulcers was reported using the following scores with a stereo-microscope.

Score on seriousness:

0 = Standard stomach color.
0.6 = Red Colouring
1.0 = Ulcers spot
1.6 = Hemorrhagic streaks
2.0 = Ulcers ≥ 3.0 but ≤5.0
3.0 = ulcers > 5.0

Calculation

The index of ulcer is calculated using the appropriate formula;

$$BI = BN+BS+ BP \times 10^{-1}$$

Where,
BI = index of ulcer
BN = A usual number of ulcers per petBS
= Mean intensity score
BP = animal bothered ulcer (%)

Total Acidity

The gastric acid sample was moved to an evaporating porcelain platter. 1-2 drops of Topfer's reagent is added. A color shift has been observed; where free hydrochloric acid is present, a bright red color appears. 1-2 drops of phenolphthalein and the Topfer reagent were applied to the gastric juice. Titrated from a desk with 0.1 NaOH, mixing was done after each addition until the last trace of red color disappeared and a canary yellow color was replaced. The numbers of millilitres of NaOH used was read from the burette. This represents the amount of free hydrochloric acid. The titration was continued until the red colour of phenolphthalein appeared (deep pink), titrated to the point at which the further addition of alkali did not deepen the colour. Reading was taken (ml NaOH) for total acidity.

Calculation

Y = ml of 0.1 N NaOH x 10
Where,
Y= Total acidity (mEq/L)

Acid volume

Animals in the ethanol-induced ulcer community had exposure to drinking water ad libitum for 36 hours starving to death [2]. Oral administration will be 1 ml of 80 per cent ethanol. One group is given pantoprazole, and the other groups are given fresh juice 1 hour before ethanol administration. After 2 hours of ethanol treatment, animals will be killed by overdose of ether.

Result & Discussion

Preliminary Screening of Phyto Chemical

Fruts of Embelia ribes was oppressed different substance tried according to the standard strategies for the ID of the different constituents. The outcome if this phyto compound investigation is recorded underneath.

Table 4: Screening of Phyto chemical of *Embelia ribes*

S. No.	Phytoconstituents	Chemical tests	Hexane Extract	Dichloro methane	Ethyl acetate	EtOH	Water
1	**Alkaloids**	Dragendorff's test	-	+	+	+	+
		Mayer's test	-	+	+	+	+
		Hager's test	-	-	-	+	+
		Wagner's test	-	-	-	+	+
2	**Glycoside**	Legal's test	-	-	-	-	-
		Baljet's test	-	-	-	-	-
		Keller-Killani test	-	-	-	-	-
		Borntrager's test	-	-	-	-	-
		Modified Borntrager's	-	+	+	-	-
		Shinoda's Test	-	-	-	+	+
3	**Flavonoid**	Sulfuric acid test	-	-	-	+	+
		Alkaline Reagent	-	-	-	+	+
		Lead Acetate Test	-	-	-	+	+
4	**Tannins & phenolic compounds**	With $FeCl_3$	-	-	-	+	+
		With lead acetate	-	-	-	+	+
		With $KMnO_4$	-	-	-	+	+
		Gelatin Test	-	-	-	+	+
5	**Steroids**	With dilute HNO_3	-	-	-	+	+
		Liebermann-Burchard reaction	+	-	-	+	+
6	**Terpenoids**	With H_2SO_4	+	-	-	+	+
		Biuret test	-	-	+	+	+
7	**Proteins**	Ninhydrin test	-	-	+	+	+
		Millon's test	-	-	-	+	+
		Xanthoproteic test	-	-	-	+	+
		Sulpher Test	-	-	-	+	+
		Precipitation test	-	-	-	+	+
8	**Carbohydr ates**	Molisch's test	-	+	-	+	+
		Fehling's test	-	+	+	+	+
		Benedict's test	-	-	-	+	+
		Barfoed's test	-	-	-	+	+
9	**Saponins**	Foam test	+	+	+	+	+
		With lead acetate	+	+	+	+	+
10	**Fixed Oils and Fats**	Spot Test	+	+	+	-	-
		Saponification test	+	+	+	-	-
11	**Gums and Mucilage**	With alcohol	-	-	-	+	+

Study of Pharmacology

Pylorus Ligated Ulcer in Rats

The anti-ulcer activity of methanol of *Embelia Ribes* was studied at two dose levels (250 & 500 mg/kg) in pylorus ligated ulcerogenesis in rats.

Effect on Ulcer Index

The results indicated that *Embelia Ribes* at dose levels of 250 mg/kg and 500mg/kg significantly decreased the ulcer index ($p<0.01$) which was also evidenced by significant increase in percentage ulcer protection at both the dose levels. The percentage protection of ulcers in the treated groups at 250 and 500 mg/kg of ethanol extract of Fruits was found to be 47.86% and 77.78% respectively and aqueous extracts showed 41.12% and 61.20% respectively. Omeprazole at 20 mg/kg showed a protection index of 88.89% (Table 5).

Effect on Gastric Volume

Gastric volume in *Embelia Ribes* treated groups indicated that there was no significant decrease in the volume of the gastric juice at 250 mg/kg. But at 500 mg/kg there was a significant decrease in gastric volume in comparison to the control group ($p<0.01$) (Table 5).

Effect on pH of Gastric Juice

The ethanolic s extracts of Fruits of *Embelia Ribes* (Linn.) at 250 mg/kg and 500 mg/kg significantly increased the pH of gastric juice ($p<0.01$) and was comparable to the control and standard, Omeprazole at 20mg/kg (Table 5),

Table 5: Effect of *Embelia Ribes* Fruits extracts on pylorus ligated rats

S. No.	Body weight	Treatment	Ulcer Index						Total score	Mean Ulcer Index ± SEM	% Protection
			Normal coloured stomach	Red Coloured	Spot ulcer	Haemo rrhagic	Ulcers >3 but < 5	Ulcers >5			
			(0)	(0.5)	(1.0)	(1.5)	(2.0)	(3.0)			
1	150	Normal	0	-	-	-	-	-	0	0±0	-
	155	Control	0	-	-	-	-	-	0		
	160		0	-	-	-	-	-	0		
	158		0	-	-	-	-	-	0		
	165		0	-	-	-	-	-	0		
	160		0	-	-	-	-	-	0		
2	160	Control	0	0.5	1.0	1.5	2.0	-	5.0	4.5±	0
	165	(Ulcerated)	0	0.5	1.0	1.5	2.0	-	5.0	0.341	
	150	ethanol	0	0.5	1.0	1.5	-	-	3.0		
	157	1ml/200gm	0	0.5	1.0	1.5	2.0	-	5.0		
	160		0	0.5	-	1.5	2.0	-	4.0		
	170		0	0.5	1.0	1.5	2.0	-	5.0		
3	165	Omeprazole	0	0.5	-	-	-	-	0.5	0.58±	87.11
	162	(20mg/kg)	0	0.5	-	-	-	-	0.5	0.08**	
	158		0	0.5	-	-	-	-	0.5		
	167		0	0.5	-	-	-	-	0.5		
	160		0	0.5	1	-	-	-	1.5		
	170		0	0.5	-	-	-	-	0.5		
4	175	Ethanolic	0	0.5	1.0	-	-	-	1.5	2.25±	50.0

	150	Fruits	0	0.5	1.0	1.5	-	-	3.0	0.33**	
	165	Extract	0	0.5	1.0	1.5	-	-	3.0		
	165	(250mg/kg)	0	0.5	1.0	1.5	-	-	3.0		
	155		0	0.5	1.0	-	-	-	1.5		
	160		0	0.5	1.0	-	-	-	1.5		
5	155	Ethanolic	0	0.5	1.0	-	-	-	1.5	1.16±	74.22
	160	Fruits	0	0.5	1.0	-	-	-	1.5	0.21**	
	158	Extract	0	0.5	-	-	-	-	0.5		
	165	(500mg/kg)	0	0.5	1.0	-	-	-	1.5		
	165		0	0.5	-	-	-	-	0.5		
	155		0	0.5	1.0	-	-	-	1.5		

Values are expressed as mean ± SEM (n=6) in each group.
*P < 0.05, **P<0.01 compared with the control (ANOVA test)

Determination of Free Acidity and Total Acidity

Effect on free acidity and total acidity

Estimation of gastric juice indicated that there was a significant (p<0.01) decrease in the free acidity and total acidity of the gastric juice in animals treated with 250 mg/kg and 500 mg/kg of *Embelia Ribes* and was comparable to that of Omeprazole (20 mg/kg) treated group (p<0.01) (Table 6).

Table 6: Effect of Fruits and stems extracts of *Embelia Ribes* on antisecretory parameters of pylorus ligated rats

S. No.	Treatment	Does (mg/kg b.w.)	Gastric Volume (ml/100g)	pH	Free Acidity (mEq/l/100g)	Total Acidity (mEq/l/100g)
1	Normal Control	-	-	-	-	-
2	Control (Ulcerated)	-	4.86± 0.11	1.7 ± 0.096	73.88± 1.257	155.98± 2.344
3	Omeprazole	20 mg/kg	2.18± 0.079**	5.3 ± 0.141**	26.15± 0.761**	65.11± 0.326**
4	Ethanolic Fruits Extracts	250 mg/kg	4.18± 0.079	2.71± 0.101**	63.58± 0.866**	131.80± 0.435**
5	Ethanolic Fruits Extracts	500 mg/kg	3.08± 0.047**	4.05± 0.084**	46.71± 0.819**	91.30± 0.447**

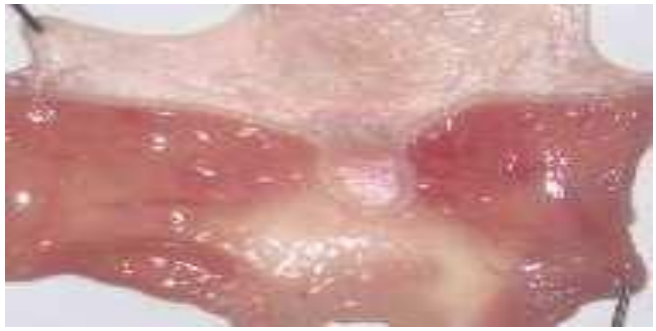
Values are expressed as mean ± SEM (n=6) in each group.
*P < 0.05, **P< 0.01 compared with the control (ANOVA test)

Histopathological Studies

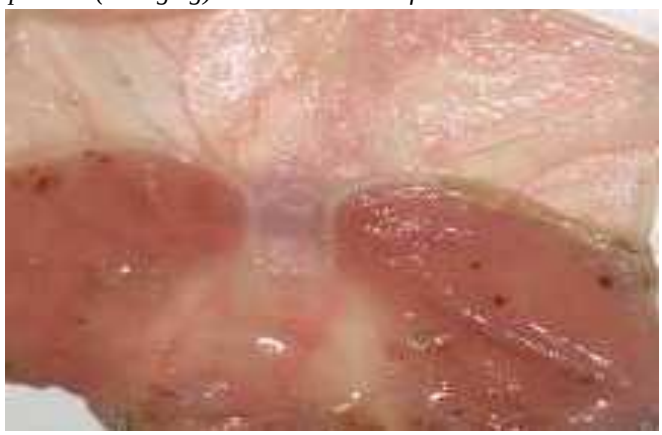
The control group of rats treated with absolute alcohol showed histopathological changes of the gastric mucosa characterized by loss of glandular architecture, oedema and erosions of the epithelial layer, evident oedema, congestion and infiltration by inflammatory cells. The rats treated with the ethanol and aqueous extracts at 250 and 500 mg/kg, b.w showed minimum ulceration and oedema but gastric epithelium was not intact. However, at a dose

of 500 mg/kg ethanol and aqueous extracts of Fruits and stems of *Embelai ribes*, the rats showed significant regenerative changes indicating healing (Plate 1).

(a) Ulcerated control stomach of ethanol induced ulcers in rats



(b) Omeprazole (20 mg/kg) treated stomach of ethanol induced ulcers in rats



(c) Methanol Fruits extract (500mg/kg) treated stomach of ethanol induced ulcers in rats

Plates 1: Morphological appearance of gastric ulcers in ethanol induced ulcers in rats

Summary

From the above results it can be inferred that the ethanol extracts of *Embelia Ribes* leaves displayed significant anti-ulcer activity. The extracts impart anti-ulcer activity due to presence of polyphenol and flavonoids component.

These phytoconstituents scavenge the free radical produce by pylorus ligation and NSAID drug, and reduced the gastric mucosal damage. Moreover, it also protects the stomach from mucosal injury by inhibiting the succession of gastric ulcers. Accordingly, the anti-ulcer activity of the extracts is referred to the impressive antioxidant properties of the extracts.

Additionally, it is also documented that terpenoids heal the ulcer present in stomach, due to the activation of cellular protection, reduction of mucosal prostaglandins metabolism, cytoprotective action and reduction of gastric vascular permeability. On the basis of phytochemical investigation, we also referred that extract contributes antiulcer activity due to terpenoids present in extracts.

The outcomes of the existing investigation affirm that the *Embelia Ribes* can used for the healing of necrosis of hepatic cell and hemorrhagic ulcers of stomach.

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