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Research Article

GASTROPROTECTIVE EFFECT OF 50% ETHANOLIC EXTRACT OF BAEL { *AEGLE MARMELOS (L)CORR.}* FRUIT ON EXPERIMENTAL GASTRIC ULCERS IN RATS

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ABSTRACT

World is endowed with a rich wealth of medicinal plants. Herbs have always been the principle from of medicine in India and to treat illness with medicines that work in count with the body's won defense. Preliminary Phytochemical screening of *A.marmelos* fruits shows the positive test for alkaloids, flavonoids, glycosides,t annins, saponins, steroids and triterpenoides. In the present study the antiulcer potential of *A. marmelos* was assessed which has prominent gastro protective effect. Pre treatment of rats with 50% alcoholic extract of unripe A. marmelos fruit at the dose level of 50-200 mg/kg was administered orally twice daily for 5 days in five groups of animals. After five days ulcer was induced in the animals and histopathological studies shows that A. marmelos fruit extract produced a significant inhibition of ASP induced, CRS induced, EtOH induced and PL induced gastric lesions and provide significant gastro protective effect in comparison to control drug ranitidine 50 mg/wt. The result indicated that 50% ethanolic *Aegle marmelos* fruits extract possess antiulcer activity.

Keywords: ASP (Aspirin), CRS (Cold restraint stress), EtOH (Ethyl alcohol), PL (Pyloric ligation), *Aegle marmelos*.

INTRODUCTION

Gastric ulcer is a very common human suffering today and is one of the most common diseases caused by an imbalance between 'damaging' factor within the lumen and 'protective' mechanisms within the gastro duodenal mucosa. Gastric ulcers are the area of degeneration and necrosis of gastric mucosa exposed to acid –pepsin secretions[1]. The normally protective gastric mucous 'barrier' against acid pepsin is deranged in gastric ulcer. There is depletion in the quantity as well as quality of gastric mucosa. Common site for ulceration are the stomach, duodenal and intestine in various infections like H. pylori and others. More recently the role of mucosal factors in peptic ulceration has received considerable attention, and the term "cytoprotection" has been introduced to encompass the physiological processes which protect gastric mucosa from acid-pepsin digestion.[2] Recent medicinal therapy with proton pump inhibitors and selective H_2 receptor blockers can efficiently cure ulcer but none of these are devoid of adverse effect and execute their action within a limit. Thus there is a necessities to the development of newer generation of phytogenic drugs. The green fruits of *A. mormelos* have digestive, stomachic and astringent properties. They are also useful in adjuvant treatment of bacillary dysentery, assisting the healing of the ulcerated mucosa of the stomach and intestine[3].

The aim of the present study was to assess the role of various mucosal offensive acid pepsin and defensive mucosal factors. Attempts were made on the necessity of nontoxic, antiulcer compound preferably from traditional medicinal plant as *Aegle marmelos* for their protection against various experimental gastric ulcer models as Pylorus ligation induced, [4]Ethanol induced, [5]Cold restraint stress induced and Aspirin induced gastric ulcers[6]. Thus the present investigation was undertaken to study the role played by mucosal offensive mucin secretion activity of the herbal drug 50% ethanolic extract of *Aegle marmelos.*

MATERIALS AND METHODS

Total 30 Sprague-Dawley rats having weight in between 150 to 180 grams were procured from the central animal house of Central Drug Research Institute Lucknow, India. These were kept in the departmental animal house at 26 ± 2°C and relative humidity 44 –56 %, light and dark cycles of 10 and 14 h

respectively for 1 week before and during the experiment for acclimatization. The animals were provided with standard rodent pellet diet (Amrut, India) and the food was withdrawn 18-24 h before the experiment, though water was allowed *ad libitum*. All studies were performed in accordance with the guide for the care and use of laboratory animals, as adopted and promulgated by the Institutional Animal Care Committee, CPCSEA, India (Reg. No. 222/2000/CPCSEA). The standard oro-gastric cannula was used for oral drug administration in experimental animals.

Acute toxicity studies

The adult male albino mice selected for acute toxicity study. The 50% ethanolic extract of fruits of *Aegle marmelos* were taken at various doses levels (100, 200, 400, 800, 1000, 1500, 2000 mg/kg body wt) dissolved in 1 % carboxymethyl cellulose orally to five mice per dose level. The control animals received 1 % carboxymethyl cellulose in distilled water (10 ml/kg) orally. The animals were observed continuously for two hour and then occasionally for further four hours and finally any mortality. Behavior (gross behavior, general motor activity, writhing, convulsion, response to tail pinching, pupil size, fecal output, water intake, feeding behavior, sedation *etc*.) of the animals and any other toxic symptoms also observed for 72 hours and the animals were kept under observation up to 14 days (OECD 423).

Criteria of assessment:-

The ulcer index was calculated by adding the total number of ulcers per stomach and the total severity of ulcers per stomach. The total severity of the ulcers was determined by recording the severity of each ulcer after histopathological confirmation as follows-

Sr. No.	Severity of ulcer	Score	Scoring symbols
1.	No ulcer	0	-
2.	Pin point ulcer and histological changes limited to superficial layers of mucosa and no congestion	1	+
3.	Ulcer size less than 1 mm and half of the mucosal thickness showed necrotic changes	2	++
4.	Ulcer size 1-2 mm with more than two-thirds of the mucosal thickness destroyed with marked necrosis and congestion, muscular is remaining unaffected	3	+++
5.	Ulcer either more than 2 mm in size or perforated with complete destruction of the mucosa with necrosis and hemorrhage, muscular is still remaining unaffected	4	++++

Plan of study and grouping of animals:-

This study was a purely experimental and conducted with the objective and knowing the effect of preventive properties of A. mormelos on aspirin induced, cold-restraint stress induced, ethanol induced and pylorus ligation induced gastric ulcers.

Animals are divided into five groups (six animals in each group). 50 % ethanolic extract of *A.marmelos* in dose of 50, 100 and 200 mg/kg and H2 receptor blocker ranitidine in the dose of 50 mg/kg were administered orally twice daily at 10AM and 16 PM respectively for five days in various model. Control group of animals received suspension of 1 % carboxymethyl cellulose in distilled water (10 ml/kg).

Group I- Ulcer Control (1 % carboxymethyl cellulose suspension)

Group II- *A.marmelos* (50 mg/kg body wt.)

Group III- *A.marmelos* (100 mg/kg body wt.)

Group IV - *A.marmelos* (200 mg/kg body wt.)

Group V - Ranitidine (50 mg/kg body wt.)

After 5 days administration of drugs, according to their respective groups and subgroups, animals go for induction of ulcer by different ways.

Data Documentation and Statistical Analysis:

It was an animal trialed and experimental research work it's all data were analyzed using appropriate statistical tests i.e. unpaired Student's *t*-test. All values of quantitative variables are expressed as percentage, Mean ± SEM and p values.

Table 1: Preventive effect of *A. marmelos* on aspirin-induced gastric ulcers

Group	Administered drugs	Dose (mg/kg)	Ulcer index (mm^2/rat)	Percent protection
I	Aspirin	200	22.6± 3.4	-
II	*A.marmelos* extract	50	14.3± 2.3	36.73
III	*A.marmelos* extract	100	8.6 ± 2.8[a]	61.95
IV	*A.marmelos* extract	200	4.2± 1.3[b]	81.42
V	Ranitidine	50	5.6± 2.9[b]	75.22

Values are mean ± SEM for 6 rats. [a] P < 0.01, compared to respective aspirin induced group. [b] P < 0.001 compared to respective aspirin induced group.

Table 2: Preventive effect of *A. marmelos* on cold-restraint stress (CRS) induced gastric ulcers.

Group	Treatment	Dose (mg/kg)	Ulcer index (mm^2/rat)	Percent protection
I	Cold-restraint stress	-	23.8 ± 3.2	-
II	*A.marmelos* extract	50	16.4 ± 1.7	20.7
III	*A.marmelos* extract	100	10.3 ± 1.8[a]	56.72
IV	*A.marmelos* extract	200	4.4 ± 1.7[b]	81.51
V	Ranitidine	50	11.2 ± 2.3[b]	52.94

Values are mean ± SEM for 6 rats, [a] P < 0.01, compared to respective CRS group, [b] P < 0.001 compared to respective CRS group

Table 3: Preventive effect of *A. marmelos* on Ethanol -induced gastric ulcer

Group	Treatment	Dose (mg/kg)	Ulcer index (mm^2/rat)	Percent protection
I	Ethanol	1ml/0.2kg	22.o ± 4.7	-
II	*A.marmelos*	50	11.6± 3.8	47.3
III	*A.marmelos*	100	7.6± 4.2[a]	65.5
IV	*A.marmelos*	200	4.4±2.6 [b]	80.0
V	Ranitidine	50	4.3 ± 2.8[b]	80.5

Values are mean ± SEM for 6 rats, [a] P < 0.05, compared to respective EtOH group, [b] P < 0.01 compared to respective EtOH group.

Table 4: Preventive effect of *A. marmelos* on pylorus ligation induced gastric ulcers:-

Groups	Treatment	Dose (mg/kg)	Ulcer index (mm^2/rat)	Percent protection
I	Pylorus ligation	-	18.3± 1.7	-
II	*A.marmelos*	100	15.2 ± 1.2	16.4
III	*A.marmelos*	200	10.5 ± 0.72[a]	42.6
IV	*A.marmelos*	400	4.2 ± 0.59[a]	77.04
V	Ranitidine	50	3.5 ± 1.2[a]	84.66

Values are mean ± SEM for 6 rats, [a] P < 0.001 compared to respective pylorus ligated group, [b] P < 0.001 compared to respective pylorus ligated group

RESULTS AND DISCUSSION

Table No. 1- Administration of *A.marmelos fruit* extract 1 h before the induction of gastric lesions by ASP, showed significant activity, and decreased the total ulcer index of by 14.3 ± 2.3 – 4.2 ± 1.3, respectively. Ranitidine decreased the total ulcer index of by 5.6 ± 2.9 (75.22% protection). Results for *A.marmelos* fruits extracts are comparable to Ranitidine at the dose of 50 mg/kg (Table-3).

Table No2- A.marmelos fruits extract at dose of 50, 100, 200 mg/kg, twice a day for 5 days prevented the acute gastric ulcers in a dose related manner. The oral administration of *A.marmelos* fruits extract in CRS induced ulcer model decreased the index of gastric lesion by 10. 16.4 ± 1.7- 4.4 ± 1.7, respectively (20.7– 81.51 % protection) in comparison to control 23.8 ± 3.2.

Table No. 3- Effects of *A.marmelos* fruits extract at dose of 50, 100, 200 mg/kg, twice a day for 5 days prevented the acute gastric ulcers in a dose related manner. The oral administration of *A.marmelos* fruits extract in EtOH induced ulcer model decreased the index of gastric lesion by 12.3 ± 3.4 - 5.1 ± 0.3, respectively (34.22 – 72.73 % protection) in comparison to control 18.7 ± 4.4.

Table No. 4- Effects of *A.marmelos* fruits extract at dose of 50, 100, 200 mg/kg, twice a day for 5 days prevented the acute gastric ulcers in a dose related manner. The oral administration of *A.marmelos* fruits extracts in P.L induced ulcer model decreased the index of gastric lesion by 11.6 ± 1.2- 4.4 ± 2.6, respectively (47.3– 80% protection) in comparison to control 22.0± 4.7

CONCLUSION

From above discussion and mentioned table and data it is clear that 50 % ethanolic extract of fruit of A. marmelos showed potent anti ulcer activity as indicated by low ulcer index and high protection percentages in dose dependent manner in different group of ulcer induced animals and possess antiulcer activity.

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