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Protective Role of *Momordica charantia* L. Seed Extract against Experimentally-induced Gastric Ulcers in Rats

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ABSTRACT

The present study evaluates the antiulcer and antisecretory activity of methanolic extract *Momordica charantia* L. seed (MEMCS) using pyloric ligation and stress-induced ulcer models in Wistar albino rats. A total of four groups, each comprising six rats, were used. Ulcers were induced through pyloric ligation, and stress ulcers were generated by subjecting the animals to continuous swimming for three hours. The test animals received MEMCS at doses of 250 mg/kg and 500 mg/kg for seven consecutive days, while ranitidine served as the reference standard. Key parameters, including acid volume, free acidity, and total acidity, were analyzed. The control group exhibited significant ulcer formation and increased gastric acid secretion. In contrast, pretreatment with MEMCS at 500 mg/kg demonstrated significant gastroprotective effects, reducing ulcer formation in both ulcer models. The pyloric ligation method revealed that MEMCS (500 mg/kg) inhibited gastric acid secretion by 68.28%, free acidity by 55.66%, and total acidity by 48.88%. These findings suggest that *M. charantia* possesses potent antiulcer and antisecretory properties, likely mediated through mucosal protective mechanisms and enhanced mucosal defense.

Keywords: Antiulcer, *Momordica charantia*, Seed Extract, Pyloric ligation, *Helicobacter pylori*, Ranitidine

INTRODUCTION

It is thought that an imbalance between protective and aggressive factors leads to gastric ulcers, one of the most common disorders. Many substances, including acids, pepsin, bile acid, dietary additives, bacterial byproducts (*Helicobacter pylori*), and medications, may cause harm to the stomach mucosa [1]. Increased production of stomach acid and pepsin, decreased gastric blood flow and motility, and inhibition of prostaglandin synthesis and cell proliferative growth are all factors that these medicines have been linked to in the development of gastric ulcers [2]. Because many different chemical compounds have shown promise in the treatment of stomach ulcers, the idea of creating a novel antiulcer medication from medicinal plants is an appealing one [3]. The bitter melon, bitter gourd, or Karela in Hindi is really the scientific name for the Cucurbitaceae family member *Momordica charantia* Linn. All around India, you may find this plant [4]. Indian markets include a wide variety of dried seeds from this plant. There have been traditional uses for this plant's fruits and dried seeds in the treatment of a variety of illnesses. Glycosides, alkaloids, tannins, flavonoids, and saponins were among the phytochemicals found [5]. Producing stomach ulcers in rats by ligation of the pylorus area is an easy and dependable technique. A buildup of gastric liquid in the stomach is the root cause of ulceration [6]. When it comes to the causes of gastro-duodenal ulceration, stress is a major factor. The development of stress-induced ulcers involves increased stomach motility, vagal hyperactivity, mast cell degranulation, reduced blood supply to the gastric mucosa, and reduced prostaglandin synthesis [7]. The biological reaction of an organism to harmful stimuli, such as stress, involves intricate neurochemical pathways. When hormones, neurotransmitters, and neuromodulators undergo alterations in production, action, and degradation, pathologic ulcerations develop. Stress ulceration and plasma corticosterone modulation are processes that rely heavily on the central nervous system [8]. The method of use should include a variety of predisposing variables, since the etiopathogenesis of various ulcer models differs. The mucosal protection that non-prostanoid chemicals provide may, however, be mitigated by triggering the release of endogenous prostaglandins [9].

The aim of this study is to evaluate the antiulcer and antisecretory potential of *M. charantia* L. seed methanolic extract (MEMCS) using pyloric ligation and stress-induced ulcer models in Wistar albino rats. The objectives include investigating the protective effects of MEMCS against ulcer formation and gastric acid secretion, analyzing key parameters such as acid volume, free acidity, and total acidity, and comparing its efficacy with the standard antiulcer drug ranitidine. Additionally, the study aims to assess the ability of MEMCS to enhance gastric mucosal defense and its potential role in strengthening the mucosal barrier, thereby contributing to its therapeutic value in ulcer management.

MATERIALS AND METHODS

Plant Material and Preparation of Extract

It was at the Malegaon (BK), Baramati market when the *M. charantia* plant material seeds were gathered. Dr. Deshmukh, Head and Research Officer (Botanist) of the Department of Botany at SPMV at Sharada Nagar, Baramati, verified the seeds. It all started with a thorough washing, followed by air drying, and then a final drying in an oven set at 40–45°C. Once the seeds had dried thoroughly, they were ground into a fine powder. The methanolic extract of *M. charantia* seeds (MEMCS) was produced by first subjecting the fine powder to defatting with petroleum ether and then extracting it with hot methanol (60-65°C) using a soxhlet extractor. The essential oil was concentrated using a simple evaporation technique. Refrigeration was used to keep the semisolid extract at a temperature below 10°C in an airtight container. There was an 8% yield of extract.

Chemicals

In the research, rats were orally administered the methanolic extract of *M. charantia* seeds (MEMCS) at dosage levels of 250 mg/kg and 500 mg/kg. The current investigation used ranitidine, a typical anti-ulcer medicine, at a dosage of 50 mg/kg, which was obtained from a local pharmacy.

Animals

All of the experiments made use of Wistar albino rats weighing 150–200 g and Swiss mice weighing 20–30 g. A college in Malegaon (BK) Baramati, known as S.V.P.M., supplied the animals. The animals were kept in propylene cages and kept at a temperature of 27±3°C, relative humidity of 65± 10%, and a light-dark cycle of 12 hours with 12 hours of darkness. The animals were given a rat pellet meal (Gold Mohr, Lipton India Ltd.) and water ad libitum under strict sanitary conditions after being acclimated to the experimental room setting for one week. The Institutional Animal Ethical Committee (IAEC) gave its stamp of approval before any animal experiments were conducted. Group 1 consists of a control group, Group 2 of a standard group, Group 3 of MEMCS (250 mg/kg body weight), and Group 4 of MEMCS (500 mg/kg body weight). Each group consists of five participants.

Preliminary Phytochemical Screening

In order to identify any phytoconstituents in MEMCS, it was subjected to preliminary phytochemical screening [10].

Acute Toxicity Study

Mice weighing 20-30 g and kept in a typical environment were used to test the acute toxicity of MEMCS. In the hours leading up to the trial, the animal was allowed to fast. The toxicity experiments used the fixed dosage approach of CPCSEA, as outlined in OECD Guideline no. 420 [11].

Evaluation of Antiulcer Activity

Pylorus Ligation Method

Care was taken to prevent coprophagy when albino rats of either sex weighing around 150-200 g (pregnancy was omitted) were placed in separate animal cages and fasted for 48 hours before pyloric ligation [6]. To access the abdominal cavity, a tiny midline incision was made below the xiphoid process while the patient was under mild ether anesthetic. The pyloric section of the stomach was gently taken out and ligated to prevent tension on the pylorus or harm to its blood supply. With great care, the stomach is restored, and interrupted sutures are used to repair the abdominal wall. One hour before pyloric ligation, the medications are taken orally. They are starved and dehydrated for the four hours after surgery before being killed. By removing the stomach and allowing its contents to flow into the tube, the acidity levels (both free and total) and pH may be measured. Next, the larger curvature of the stomach is used to open the stomach and check for ulcers. According to previous studies [12, 13], the degree of ulceration may be scored from zero to five, with ten representing duodenal epithelium, twenty representing petichial / flank hemorrhages, thirty representing one or two ulcers, forty representing multiple ulcers, and fifty representing perforated ulcers. Ulcer Index is the mean score of ulcers for every animal. Removable gas should be centrifuged at 1000 rpm for 10 minutes. Pay close attention to the loudness. To make 10 milliliters of distilled water, dilute 1 milliliter of supernatant liquid using a pipette. Use a pH meter to take note of this mixture. When employing Topfer's reagent, titrate the solution against 0.01 N NaOH. Until the solution

became orange, an arbitrarily assigned score was used to rank the occurrence or severity of the lesion condition. Keep in mind that the acidity is directly proportional to the volume of NaOH. Restore the solution's pink hue by adding more titratable acid. Recall that the overall acidity is proportional to the volume of NaOH. The formula for acidity (mEq/ i/100 mg) is:

$$\text{Acidity} = \frac{\text{Vol. of NaOH} \times \text{Normality} \times 100\ (\text{mEq/i/100 mg})}{0.1}$$

Evaluate the effects of ranitidine on stomach volume, acidity, and ulcer index in comparison to the control group [4].

Forced Swim Induced Ulcers

Albino rats (male or female) weighing 150-200 g (no pregnancy included) were housed in separate cages and given a 24-hour fast (water was permitted) before being forced to swim against their will, with special attention given to avoiding coprophagy. According to a previously published procedure, rats were temporarily exposed to forced swim stress by being made to swim in a vessel that was 30 cm tall and 10 cm diameter. The water within the vessel was kept at a temperature of roughly 25°C, and the depth of the water reached up to 15 cm. This caused ulcers to form. Mice were made to swim in a container for three hours on the day of the experiment after being given a dose of test extract one hour before the test. Under profound ether anesthesia, animals were slaughtered and their stomach linings were checked for ulcers. We graded symptoms from moderate to severe, using a scale from low to high. Here are several ways ulcers are categorized: 0.5 for red coloring, 1.0 for spot ulcers, 1.5 for hemorrhagic streaks, 2.0 for ulcers that are more than 3 mm but less than 5 mm, and 3.0 for ulcers that are more than 5mm. We determined the average ulcer scores for each group in the trial and reported them as the ulcer index (UI) [14, 15].

Statistical Analysis

The Mean±SEM was used to represent the data. The data was analyzed using Graph Pad Prism v.6 software, which included a One-way ANOVA test and a test for comparison between the control and test groups. A statistically significant result was defined as a P-value less than 0.05.

RESULT AND DISCUSSION

Preliminary Phytochemical Screening

Table 1 displays the results of the first phytochemical study conducted on the methanolic extract of *M. charantia* seeds.

Table 1. Preliminary phytochemical investigation of MEMCS.

Phytochemical Constituents	Inference
Flavonoids	++
Saponin glycosides	+
Tannins and Phenolic compounds	++
Steroids	+++

+ = indicates presence; ++ = More clarity; +++ = Better response

Acute Toxicity Study

Albino mice were administered a dosage of 2000 mg/kg i.p. of MEMCS for the purpose of studying acute toxicity. There was no evidence of animal death in the extract. Therefore, the LD50 threshold was set at 2500 mg/kg. The following dosages of extract were chosen in accordance with the OECD guideline no. 420 (annexure-2d) fixed dose methods: 250 mg/kg ($1/10^{th}$ of 2500 mg/kg) and 500 mg/kg ($1/5^{th}$ of 2500 mg/kg).

Antiulcer Activity

Pyloric Ligation Method

In Figure 1, the antiulcer activity of MEMCS was seen at two dosage levels (250 mg/kg and 500 mg/kg) in rats with pylorus ligation. The effects on stomach acidity, pH, and ulcer score were represented as Mean±SEM, and for six animals, the corresponding ***P<0.001 and ***P<0.01 were compared to the control group. It demonstrated a notable impact (Table 2).

Table 2. Effect of MEMCS on different parameters in pylorus ligation induced ulcers in rat.

Treatment mg/kg	Volume of gastric secretion ml/100 g	pH	Free acidity (meq/1/100g)	Total acidity (meq/1/100g)	Mean Ulcer Index
Control	3.51 ± 1.158	2 ± 1.702	53 ± 1.812	67.5±1.153	50
MEMCS (250 mg/kg, p.o.)	3.19 ± 1.603**	3.75± 1.750**	30.75± 14.75**	44±23.55**	35
MEMCS (500 mg/kg, p.o.)	2.86 ±1.285***	4.75 ± 2.750***	37.25±3.473***	32.5±3.24***	32.5
Std. Ranitidine (50 mg/kg, p.o.)	1.91 ±0.105***	4.67 ± 0.964***	15.75±1.566***	28±2.353***	28.24

***P<0.001; **P<0.01

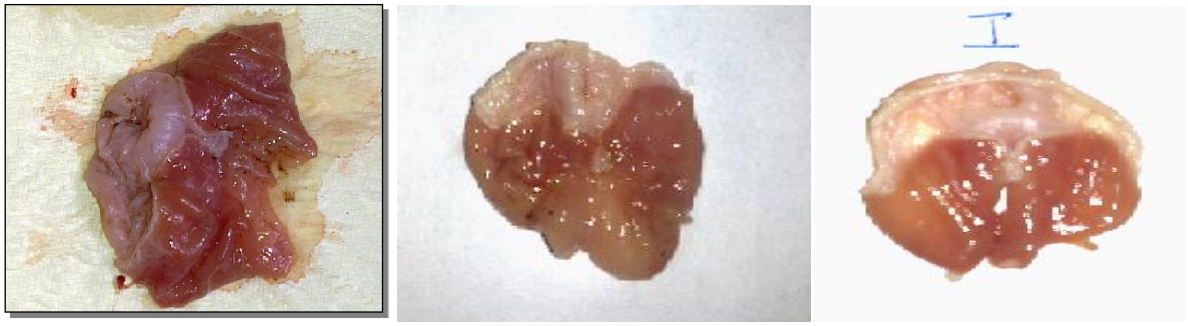

Figure 1. (from left) Ulcer in control group; Rat pretreated with MEMCS 250 mg/kg; and Rat pretreated with MEMCS 500 mg/kg.

Stress induced method

Weight Variation

During the 7-day therapy, rats given MEMCS 250 mg/kg b.w. gained significantly more weight than the control group, whereas rats given greater doses gained weight, but the difference was not statistically significant (Table 3).

Table 3. Effect of MEMCS on weight variation in rat.

Treatment	Mean wt. variation in rats during 7 days treatment (g)			
	1st day	3rd day	5th day	7th day
Control	133.12	137.3 (3.14%)	141.23 (6.10%)	134.3 (0.88%)
MEMCS (250 mg/kg)	129.74	140.65 (8.40%)	146.1 (12.60%)	139.35 (7.40%)
MEMCS (500 mg/kg)	125.97	133	133.55 (6.01%)	128.2 (1.80%)

Figure in the parenthesis are % increase / decrease wt compared with 1st wt (g)

Ulcer index

Figure 2 shows that the antiulcer activity of MEMCS was seen in stress-induced rats at doses of 250 mg/kg and 500 mg/kg, with significant effects on stomach acidity, pH, and ulcer score (mean±SEM, 6 animals, ***P<0.001, ***P<0.01) compared to the control group. By preserving mucosa, MEMCS demonstrated substantial and dose-dependent antiulcer efficacy (Table 4).

Table 4. Effect of MEMCS on ulcer index in stress induced ulcers.

Group/ Treatment	Ulcer Index	% Index
Control	8	-
MEMC (250 mg/kg)	3	62.5
MEMC (500 mg/kg)	0.5	93.75
Ranitidine (Standard)	0.5	93.75

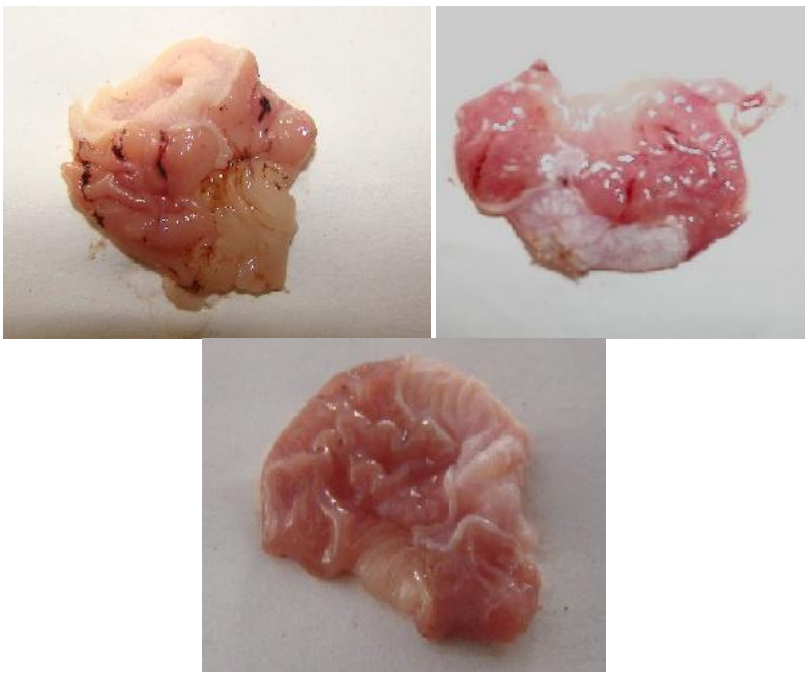

Figure 2. (from left) The control group had no ulcers, whereas the *M. charantia* L. extract groups received 250 mg/kg, 500 mg/kg, and 750 mg/kg doses, respectively, of the extract.

An imbalance between offensive (*i.e.*, acid, pepsin, and *H. pylori*) and defensive (*i.e.*, machine prostaglandin and bicarbonate) components leads to peptic ulcer disease, a severe gastrointestinal condition. Peptic ulcer disorders have traditionally been treated by focusing on lowering stomach acid production and strengthening gastric mucosal protection. The plant included phytoconstituents such as steroids, alkaloids, flavonoids, and saponins. *M. charantia* has a long history of usage in the treatment of ulcer healing, and research shows that its wide variety of phytochemical ingredients makes it a promising plant food for the creation of new treatments for a wide range of diseases. Traditional medicine makes advantage of *M. charantia*'s antiulcer properties. The results show that it has antiulcer properties.

In a dose-dependent antiulcer study of MEMCS, we used the pyrolus ligation induced ulcer model, a well-established model for the induction of gastric ulcers and increased acid secretion. In our study, rats were pretreated with MEMCS at different doses (250 mg/kg b.w. and 500 mg/kg b.w.), and the results demonstrated significant gastrointestinal protective activity by inhibiting the formation of ulcers. Standard ranitidine at a dosage of 50 mg/kg was used to compare the observed outcomes. A histaminergic mechanism involving blocked H_2 receptors may be responsible for the decrease in stomach capacity and ulceration. The current investigation tested the efficacy of a MEMCS against stress-induced ulcers in rats. Rats subjected to swimming stress for three hours prior to treatment with 250 mg/kg and 500 mg/kg MEMCS had a dose-dependent and substantial ulcer-protective effect, in contrast to the severe ulcers generated in control animals.

CONCLUSION

Early phytochemical analysis of MEMCS revealed the presence of steroids, glycosides, tannins, saponins, and flavonoids. The research used MEMCS to determine acute toxicity doses, and the LD_{50} cutoff value was used to determine dosages used to evaluate antiulcer activity. The current study's results corroborate the cytoprotective impact of stomach tissues on rat ulcers caused by stress and pyrolus ligation. Based on its effects on an experimentally produced ulcer model in rats, the current work shows that MEMCS has strong antiulcer activity.

CONFLICT OF INTEREST: No Conflict of interest is declared.

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