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Gastro protective effect of *Momordica charantia* in experimental corrosive gastric ulcer

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Abstract

The purpose of our study is to assess the gastroprotective effect of *Momordica charantia* (MC) in gastric ulcer created with corrosive matter. The rats were treated after they were given corrosive matter; in Group 1, MC oil extract gavage (1 ml), and in Group 2 famotidine was given. Group 3 was the control group and did not receive any treatment. In histopathological examination, mucosal necrosis, edema, inflammation were assessed. The healing of corrosive induced gastric ulcer was found increased in treatment groups; ulcer scores were found as 3.6 (range 1-6) in Group 1, 3.7 (range 2-6) in Group 2 and 7.5 (range 6-8) in the control group. In paired comparison, significant difference was found in both treatment groups when compared with the control group in terms of necrosis width, $p=0.024$ and $p=0.019$ for Group 1 and 2, respectively. However, no difference was found between treatment groups regarding treatment efficiency ($p=0.99$).

Keywords: *Momordica Charantia*, gastritis, corrosive, experimental

1. Introduction

Momordica Charantia (MC) is an herbaceous climbing annual plant belonged family cucurbitaceae. It bears yellow flowers, the fruit is first green and it becomes yellow-orange as it ripens. It is also known as bitter squash, bitter melon and balsam pear, it is known as "karela" in Asia [1]. MC is a traditional medicine used among the public in many countries including Turkey, India, China, East Africa and South America. Besides being eaten as fruit primarily, especially the extracted unripe fruit is also used in various therapies. Its fruits are used frequently for anti-diabetic purposes because of their hypoglycemic effects. It is traditionally used as antimycotic, antiviral, antibacterial, antihyperlipidemic, antioxidant, anthelmintic, antiemetic, degassing, purgative and it is also used in the treatment of anemia, hypertension, malaria, cholera and liver diseases. MC ripened fruits have been used externally due to their effects in accelerating wound healing and thus, it is claimed to be useful in the healing of leprosy and malign ulcer [2-11].

Peptic ulcer is among the most frequent gastrointestinal diseases in society. It is generally thought to result from a defect in mucosal barrier function. H₂ receptor blockers and proton pump inhibitors are mostly used in the treatment. However, its side effects against antisecretory agents, it's long term free of control usage and ulcer relapses after treatment are still problems. Thus, researches have started for new treatment agents that have less side effects and toxicity and higher efficiency. Especially recently, there has become an increase in the knowledge of products derived from resources that have existed for centuries in traditional medicine and as new anti-ulcer medicine in nature and it is thought that these can be effective as potential bioactive agents. Thus, the purpose of our study is to assess the gastroprotective effect of standardized oil extract of MC in ulcer model created experimentally with corrosive agent.

2. Material and methods: MC Preparation of extracts; yellow-orange MC fruits maturing in August and September are taken and their cores are purified. 500 g olive oil (acidity 0.25-0.30%) is added to the 500 g sliced fruit. After waiting 15 days at room temperature, it is stirred thoroughly and complete dissolution of the fruit provided. Finally, after being rested for 3 days, by making both coarse and fine filtration, The olive oil extract of the MC is obtained (1,2) days later (when completely dispersed in olive oil), the oil was filtered with a small fine sieve and centrifuged, and then only the oily part was prepared for use.

Healthy adult male Sprague Dawley (SD) rats, which were approximately the same, age and between 150 and 200 g were provided from Ondokuz Mayıs University Faculty of Medicine Laboratory Animals Research Center.

Experiments were conducted in accordance with the recommendations from the Declaration of Helsinki and the internationally accepted principles in the care and use of experimental animals. Ondokuz Mayıs University's Ethic Committee for Animal Use approved the protocols and all the experiments were designed to use in the least number associated with a valid statistical analysis. The animals were kept under standard conditions [humidity and light (12 hours dark, 12 hours light) and $24 \pm 2^\circ \text{C}$ heat and lighting]. Before the study, the animals were fed with a commercial diet and drinking water for 3 days. 30 adult male SD rats were grouped in four. No food was given to the groups for 24 hours before the experiment started and they were given free access to only drinking water 2 hours before the experiment. 0.2 mol/l NaOH 1 mL intragastric gavage was applied as bolus to create experimental acute chemical gastric ulceration and after the application, the animals were observed for abnormal behaviors (respiratory problems, death, etc.). In order to assess the gastroprotective effect of MC, Group 1 was compared with another treatment group (Group 2), which was given famotidine (F), another standard antisecretory agent that is known for its anti-ulcer efficacy. After intragastric corrosive agent was given through stomach intubation, therapeutical agents were given as intragastric bolus in the form of MC aqueous suspension 6 ml/kg and 50 mg/kg and 1 ml famotidine, paying attention to have the same period of time in each rat. The choice of dose and the dose chosen for application experiments were applied as the maximum dose that can be tolerated (30 g/kg body weight) and based on pretests [12, 13]. No treatment was applied in the control (C) group (Group 3) following the corrosive matter gavage, and sham group was not given corrosive agent and any treatment either. Normal gastric mucosa is presented as sham (S) group. After the laboratory animals were anesthetized with a combination of 50 mg/kg ketamine and 5 mg/kg xylazine 2 hours later, they were sacrificed. Their stomachs were taken out quickly bordered by pylorus and esophagogastric junction. In order to assess gastric mucosal lesions macroscopically, the stomach was washed with physiological saline solution by gastrotomy along the greater curvature of the stomach and the lesions were examined; ulcer characteristics, sizes and shapes were noted down and scoring was made according to the method explained by Schiantarelli [14] (Table 1, Picture 1).

Gastric lesions were scored with ulcer score described by Schiantarelli *et al.* [14]: 0 = normal mucosa, 1: hyperemic mucosa or up to 3 small patches, 2: 4 to 10 small patches, 3: more than 10 small or up to 3 medium-sized patches, 4: 4 to 6 medium-sized patches, 5: more than 6 medium-sized or up to 3 large patches, 6: 4 to 6 large patches, 7: 7 to 10 large patches, 8: more than 10 large patches or extensive necrotic zones. "Small" was lesion up to 2 mm across (max. diameter), "medium-sized" between 2 and 4 mm across and "large" more than 4 mm across.

For histopathological assessment, gastric tissue samples were fixed with 10% buffered formalin for 48 hours, and then they were dehydrated and embedded in paraffin wax. Later, they were stained with hematoxylin eosin using traditional method with light microscope under 5 micron section thickness slides and they were examined in terms of changes such as necrosis, edema and inflammation. Necrosis in mucosal layers (mucosa, submucosa, lamina propria, muscularis propria) and necrosis size (width and depth) were assessed in terms of edema and inflammation (Picture 2). Ulcer area in 3 dimensional measurement in mm^3 calculated with cylindrical volume; $\pi \cdot r^2 \cdot h$ (π : 3.14, r : radius [1/2 width], h : depth of ulcer in greatest measurement) (Table 1)

Statistical analyses were performed with SPSS 18.0 for windows. Data were presented as mean \pm standard deviation (SD), as frequency (%). The Shapiro–Wilk test was used to analyze normal distribution assumption of the quantitative outcomes. Results were evaluated using the parametric One Way ANOVA tests for comparison between groups. To compare two groups, we used Tukey test for normally distributed data. The frequencies were compared, using the Pearson Chi-square. The test for one proportion was used. A p value less than 0.05 was considered as statistically significant.

3. Results

In macroscopic assessment, when compared with the control group, a significant decrease was found in both groups, which were treated with MC extract and famotidine (Picture 3). Average ulcer scores were found as 3.6 (range 1-6) in Group 1 treated with MC, as 3.7 (range 2-6) in Group 2 treated with famotidine and as (range 6-8) in Group 3, the control group.

In histopathological assessment, no difference was found between groups in terms of the presence of necrosis, the size (width and depth) of necrosis, necrosis extension in muscular layer, presence of edema in submucosa and inflammation; difference was found between groups in terms of the width of the necrosis ($p=0.011$), however, no difference was found in terms of depth. In paired comparisons with the control group, necrosis width was found to be less in treatment group; the difference between Group 2 and 3 was significant ($p=0.019$) and the difference between Group 1 and 3 was also significant (0.024).

In Group 2, a moderate deterioration was found in submucosal edema layer and surface epithelium; in Group 1, a mild deterioration was found in submucosal edema layer and surface epithelium. However, no difference was found between both treatment groups (Group 1 and 2) in terms of gastroprotective effect ($p=0.99$).

When the groups were examined in terms of the number of rats, which had submucosal edema and those, which did not have submucosal edema, no statistical difference was found between Groups 1, 2, and 3 ($p=0.754$, $p=0.070$: KG, $p=1.000$, respectively). When the groups were examined in terms of the number of rats, which had inflammation and those that did not have inflammation, no difference was found. Histopathological examination results of ulcer tissue supported the macroscopic results; when compared with the control group, MC oil extract and famotidine showed a significant decrease in ulcer scores. These results showed that MC could be effective cytoprotectively in necrotizing agent-induced ulcer. In the control group, which did not receive treatment, histological examinations showed substantial damage in stomach mucosa, extensive edema in submucosal layer, necrotic lesions with increased depth in mucosa and deterioration in surface epithelium (Picture 2).

Ulcer score was 3.5 ± 1.5 (1-6) in F group; 3.63 ± 1.18 (2-6) in MC group and 7.5 ± 8.78 (6-8) in C group, and ulcer score was found to be less in the treatment groups when compared with control group ($p=0.001$)

Microscopically area of the ulcer volume is calculated using the three-dimensional *cylindrical volume* $\pi \cdot r^2 \cdot h$ formulation. The ulcer volume was found to be less in the treatment groups when compared with control group ($P = 0.034$) but there was no statistically significant difference between treatment groups of F and MC ($p=0.657$) (Figure 3).

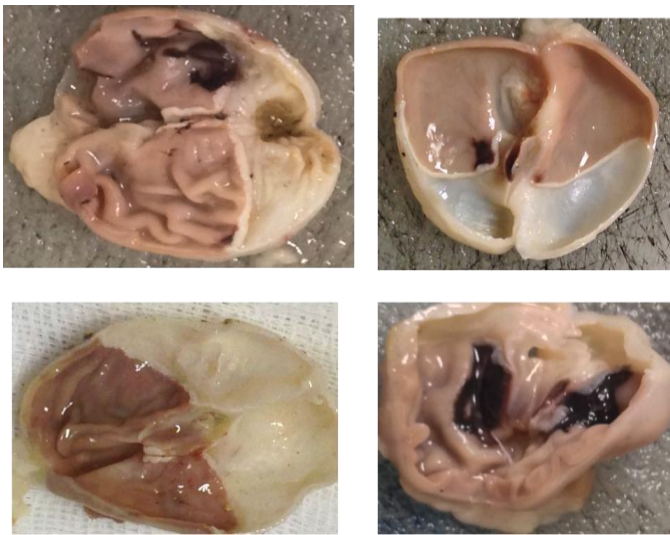


Fig 1: Macroscopic evaluation of stomach lesions in rats; A, B. Hemorrhagic necrosis of the gastric mucosa and moderate damage to the mucosa are seen in the treated groups (Group1[MC] and Group 2 [F]); C. The control group © shows damage to the stomach mucosa and diffuse necrosis; D. Normal gastric mucosa of rat.

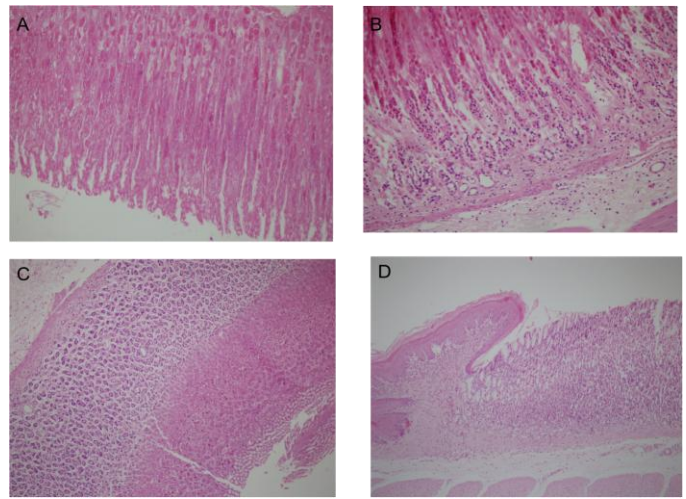


Fig 2: A. Full-thickness necrosis of lamina propria in the Group 2[F], H-E x200; B. 2/3 necrosis of lamina propria and subsequent inflammation of [MC] group, H-Ex200; C. Necrosis of the lamina propria in Control Group group, H-Ex100; D. Esophagogastric junction followed by stomach wall without pathologic finding in S group, H-Ex100.

Table 1: Macroscopically examination results and Schiantarelli ulcer scores of gastric lesions induced by 0.2 mol NaOH in rats after treated with MC extract and famotidine, and ulcer scores in control group

Group	N	Size (mm) mean±SD	Ulcer score* mean±SD(min-max)	3D Ulcer volume** (mm ³) mean±SD(min-max)
F	10	6,30±3,401	3,5±1,5 (1-6)	76.6317 ± 85,3 (1,57-226,08)
MC	8	6,25±2,315	3,63± 1,18 (2-6)	43.0278125 ± 40.17(3,8-117,8)
C	8	10,31±2,577	7.5±8,78 (6-8)	159.021375 ± 157.35(35,3-353,2)
Total	26	7,52 ±3,336	4.76±5,21	91,6427 ± 93,57450 (1,57-353,25)
p		0.011	0.001	0.034

*:Schiantarelli *et al.* (14), **:3D Ulcer Volume; Ulcer area in 3 dimensional measurement in mm³ calculated with cylindrical volume; πr^2h (π :3.14, r: radius [1/2 width], h: depth of ulcer in greatest measurement

F: Treatment group with Famotidine, MC: Treatment group with Momordica Charantia, C: Control group

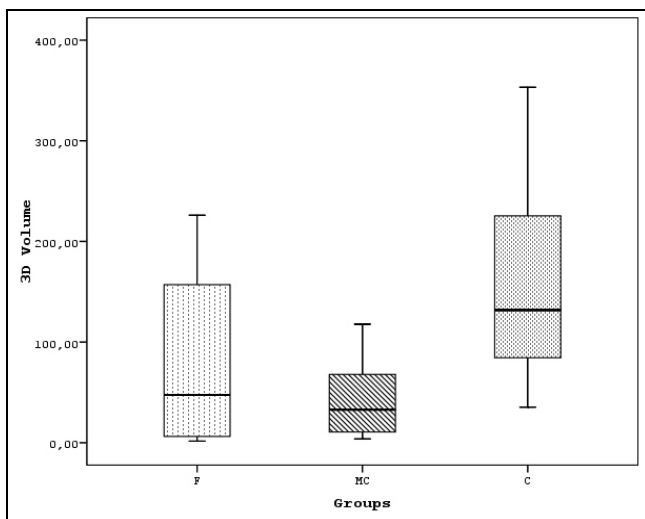


Fig 3: Comparison of the groups according to ulcer volume that was calculated by microscopically measurements.

F: Treatment group with Famotidine, MC: Treatment group with Momordica Charantia, C: Control group
3D Ulcer Volume**: Ulcer area in 3 dimensional measurement in mm³ calculated with cylindrical volume; πr^2h (π :3.14, r: radius [1/2 width], h: depth of ulcer in greatest measurement

4. Discussion

The imbalance between defensive factors and ulcerogenic factors are known to play a basic role in the development of gastric ulcer. While the effect mechanism is not known clearly, studies suggest that MC suspension plays an

important role as a defense factor against gastric mucus gastric mucosal damage and that its antioxidant characteristics can be effective [5]. MC fruits are reported to prevent the development of Helicobacter pylori, which is the organism responsible for the development of gastric and duodenal ulcer and in addition, they are reported to be effective in decreasing hydrochloric acid production [10]. In traditional medicine in Turkey, 1 tablespoon of MC extract is taken orally every morning 30 minutes before breakfast for the treatment of stomach and duodenal ulcers. As an alternative, it is also recommended to prepare and used by being mixed with pure honey in the form of paste with fresh fruit or dried fruit powder [1, 2, 9].

Studies have researched the physical and chemical components of MC and they have reported lipid, protein, zinc, copper, iron, magnesium, calcium and phosphor among its chemical components. Flavonoids, alkaloids and many chemical compounds are also reported among its components [3, 15, 16]. Phenolic components are momordicin, charantin specific ones, while gallic acid, p-coumaric acid, ferulic acid, caffeic acid, chlorogenic acid, catechin, benzoic acid, gentisic acid, tannic acid are others [16-18]. Oleic, linoleic acid, conjugated linoleic acid have been reported in its content with gas chromatography-mass spectroscopy [16, 19]. Conjugated linoleic acid is reported to have strong antitumor effect in human tumor cell. It has been reported have high levels of Vitamin E, lutein xanthophyll, beta-carotene and carotenoid. Its hypoglycemic effects, antioxidant characteristics and antioxidant efficacy have been found [20]. It is not known which components are effective in its therapeutic effect

against ulcer. However, the efficacy of flavonoids in its content has been shown to decrease the formation of stomach ulcer [15, 21]. In addition, steroids such as beta-sitosterol and carotenoids are thought to decrease the development of gastric ulcer [1, 21, 22]. Charantin is the active form of MC and new studies can be conducted to find out the effects of Charantin on stomach and duodenum ulcers [21]. The present study presents the gastroprotective efficiency of MC oil extract in corrosive ulcer model, different from other ulcer models. MC was compared with the treatment the efficiency of which is known and although no statistically significant difference was found between the two treatment groups in terms of gastroprotective effect, a minimal decrease was found in ulcer score with MC and necrosis depth was found to be less in MC group.

5. Conclusion

The present study has shown the protective effect of MC oil extract in corrosive stomach ulcers created with NaOH. As a conclusion, we believe that MC is worth being taken into consideration as an alternative treatment for ulcer and the results can be supported with new researches.

6. Declaration of interest: The authors report no conflicts of interest.

7. Funding: This research did not receive any specific funding.

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