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Protective effects of esomeprazole, curcumin, chitosan, and curcumin-chitosan mixture on ethanol-induced gastric mucosal injuries in female rats

Jenan Mahdi Jawad Al-Kawaz[1,*], Hussein Jasim Obaid Al-Harbi[1], Fakhir Magtoof Al-Zubaidy[2]

[1]Department of Biology, College of Science, University of Babylon, Hillah, Iraq
[2]College of Pharmacy, University of Babylon, Hillah, Iraq

***Corresponding author:** Jenan Mahdi Jawad Al-Kawaz, Department of Biology, College of Science, University of Babylon, Hillah, Iraq; Tel.: +964-(0)7732954719
E-mail: sci.jinan.mhadi@uobabylon.edu.iq

Abstract

Gastric ulcer is the most common health concern due to alcohol consumption, smoking, and physiological stress. An ethanol-induced gastric ulcer in an animal model resembles the pathophysiology of the human ulcer. The present study attempted to detect the protective effects of esomeprazole, curcumin, chitosan, and a mixture of curcumin and chitosan on ethanol-induced gastric ulcers in female rats. The present study included 60 rats with an average weight between 179.1 and 180.3 g, divided into two control groups and four treated groups (esomeprazole, curcumin, chitosan, and mixture), where each group included 10 rats. All groups were treated for 30 days. In order to induce a gastric ulcer, absolute ethanol (2 mL/rat) was given orally to all groups (except the negative control ones) after a period of fasting of 20 h. All animals were sacrificed 5 h later. The gastric ulceration was studied by comparing the volume and the pH of the gastric juice, the ulcer index as well as the protective index. Our results revealed a significant decrease (P<0.05) in the values of the ulcer index and the volume of gastric juice in the esomeprazole-, curcumin-, chitosan-, and mixture-treated rats as compared to those of the positive control group. The value of the gastric juice pH exhibited a significant increase (P<0.05) in these same groups.

KEYWORDS
gastric ulcer, esomeprazole, curcumin, chitosan, rat

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1. INTRODUCTION

Peptic ulcer is a common disorder of the entire gastrointestinal tract, although it occurs mainly in the stomach and the proximal duodenum [1]. Alcohol-induced gastric lesions cause a dysfunctionality of the gastric defence factors, the mucosal circulation, and the mucus secretion. The consumption of ethanol could lead to necrotic lesions in the gastric mucosa *via* various mechanisms, including the generation of a direct necrotic lesion, which in turn lowers the defence system, the secretion of bicarbonate, and the mucus formation.

The mucus gastric layers are considered a crucial factor in the protection against gastrointestinal injuries. Mucosal secretion has also been known as a key defensive factor in the prevention of gastric lesions. The produced gastric mucus is usually evaluated by the amount of gastric mucosal secreted [2].

The present study aimed at comparing the protective effects of esomeprazole, of curcumin, of chitosan, and of a curcumin-chitosan mixture on ethanol-induced gastric ulcers in female rats.

2. MATERIALS AND METHODS

Experimental Animals: The animals used in this study were adult female rats obtained from different sources in the city of Hillah.

Experimental design: Animals were randomly divided into six main groups: one control group and five treated groups (n=10 each) as follows: (i) control group (given distilled water at 2 mL orally through a stomach tube for 30 days, then subdivided equally into subgroup 1 that was immediately sacrificed, and to subgroup 2 that was sacrificed after 19 h of fasting with access to water *ad libitum* and then receiving orally 2 mL of ethanol that was given for 5 h), (ii) acetic acid group (given 2 mL of 0.1M / 0.06% acetic acid, orally through a stomach tube, for 30 days, then subdivided equally into subgroup 1 that was immediately sacrificed, and to subgroup 2 that was sacrificed after 19 h of fasting with access to water *ad libitum* and then receiving orally 2 mL of ethanol that was given for 5 h), (iii) esomeprazole-treated group (given esomeprazole at a dose of 40 mg, orally through a stomach tube, for 30 days, then subdivided equally into subgroup 1 that was immediately sacrificed, and to subgroup 2 that was sacrificed after 19 h of fasting with access to water *ad libitum* and then receiving orally 2 mL of ethanol that was given for 5 h), (iv) curcumin-treated group (given curcumin at a dose of 40 mg/kg, orally through a stomach tube, for 30 days, then subdivided equally into subgroup 1 that was immediately sacrificed, and to subgroup 2 that was sacrificed after 19 h of fasting with access to water *ad libitum* and then receiving orally 2 mL of ethanol that was given for 5 h), (v) chitosan-treated group (given chitosan at a dose of 150 mg/kg, orally through a stomach tube, for 30 days, then subdivided equally into subgroup 1 that was immediately sacrificed, and to subgroup 2 that was sacrificed after 19 h of fasting with access to water *ad libitum* and then receiving orally 2 mL of ethanol that was given for 5 h), and (vi) curcumin-chitosan mixture-treated group (given a curcumin-chitosan mixture containing 40 mg/kg of curcumin and 150 mg/kg of chitosan, orally through a stomach tube, for 30 days, then subdivided equally into subgroup 1 that was immediately sacrificed, and to subgroup 2 that was sacrificed after 19 h of fasting with access to water *ad libitum* and then receiving orally 2 mL of ethanol that was given for 5 h).

Measurement of the gastric ulcer index: The gastric ulcer index was estimated according to a previously described method [3].

Measurement of the pH and the volume of the gastric juice: The stomach of each euthanized rat was immediately dissected, and the gastric content was collected in sterilized tubes. The pH of the gastric juice was determined by a pH paper, and the gastric juice was then centrifuged for 10 min at 3,000 rpm so as to isolate the aqueous phase. The volume of the centrifuged gastric juice was measured by a graduated cylinder and was expressed as mL.

Statistical analysis: The Statistical Package for Social Science (SPSS) version 23.0 (SPSS, Chicago, USA) was used for the undertaking of the statistical analysis of the data.

3. RESULTS

An overview of the protective effects of esomeprazole, curcumin, chitosan and curcumin-chitosan mixture on the ulcer index, the protective index, as well as the volume and the pH of the gastric juice in female rats treated for 30 days, is provided in Table 1.

4. DISCUSSION

The exposure to ethanol produced gastric lesions by penetrating and digesting the gastric wall due to its proteolytic and hydrolytic action as well as due to endothelial cell damage as a result of the reduction in blood circulation [4]. The results of the present study showed that the oral administration of absolute ethanol (2 mL/rat) for 5 h can induce a gastric ulcer. A significant decrease (P<0.05) was noticed in the gastric ulcer index in the groups pretreated with esomeprazole, curcumin, chitosan, or the curcumin-chitosan mixture, with the protective index being equal to 64.58%, 45.83%, 62.5%, or 64.58%, respectively, as compared with that of the ulcer control group. This may reflect the gastroprotective effects of esomeprazole, curcumin, chitosan, and the curcumin-chitosan mixture on the gastric mucosa. This finding is in agreement with those of Xie *et al*. [5] who have shown that esomeprazole decreases the ulcer index in rats.

The significant decrease in the ulcer index in the group pretreated with curcumin in this study may be due to its antioxidant activity. The antioxi-

dant or free radical scavenging ability of curcumin arises from the phenolic OH group or from the CH_2 group of its b-diketone moiety. Free radical-mediated peroxidation of membrane lipids and oxidative damage of cellular molecules are believed to be associated with various chronic pathological complications such as cancer, ulcers, and other inflammatory diseases. Curcumin is assumed to play a vital role against these pathological conditions, and could be a potent antiulcer agent [6].

Table 1. Protective effects of esomeprazole, curcumin, chitosan and curcumin-chitosan mixture on the ulcer index, the protective index, as well as the volume and the pH of the gastric juice in female rats treated for 30 days. Notes: different letters indicate significant differences (P<0.05) among groups; n=5 for each group.

Groups	Ulcer index	Protective index (%)	Gastric juice volume (mL)	Gastric juice pH
distilled water (negative control group)	0.00±0.00 ^{a}	100	1.30±0.20 ^{ab}	5.40±0.25 ^{ab}
distilled water + ethanol (positive control group)	4.80±0.49 ^{b}	0.00	3.80±0.26 ^{e}	3.00±0.32 ^{c}
0.1 M acetic acid (negative control group)	0.00±0.00 ^{a}	100	1.60±0.19 ^{abc}	5.00±0.32 ^{ab}
0.1 M acetic acid + ethanol	3.00±0.45 ^{c}	37.5	3.60±0.25 ^{e}	3.60±0.25 ^{c}
esomeprazole 40 mg	0.00±0.00 ^{a}	100	1.00±0.16 ^{a}	5.60±0.5 ^{a}
esomeprazole 40 mg + ethanol	1.70±0.30 ^{d}	64.58	2.00±0.16 ^{bcd}	5.20±0.37 ^{ab}
curcumin 40 mg/kg	0.00±0.00 ^{a}	100	1.10±0.19 ^{a}	5.20±0.37 ^{ab}
curcumin 40 mg/kg + ethanol	2.60±0.51 ^{cd}	45.83	2.30±0.37 ^{cd}	4.60±0.51 ^{b}
chitosan 150 mg/kg	0.00±0.00 ^{a}	100	1.10±0.19 ^{a}	5.40±0.25 ^{ab}
chitosan 150 mg/kg + ethanol	1.80±0.37 ^{d}	62.5	2.50±0.27 ^{d}	5.00±0.32 ^{ab}
mixture (curcumin 40 mg/kg - chitosan 150 mg/kg)	0.00±0.00 ^{a}	100	1.00±0.27 ^{a}	5.80±0.20 ^{a}
mixture (curcumin 40 mg/kg - chitosan 150 mg/kg) + ethanol	1.70±0.30 ^{d}	64.58	1.90±0.33 ^{bcd}	5.20±0.37 ^{ab}

Wallace [7] has demonstrated that the mechanism by which chitosan prevents gastric mucosa damage may be due to its adhesion activity, which prevents direct contact of the injured mucosa with the physiological environment of the stomach and prevents the proliferation of microorganisms at the wound site. In addition, it inhibits the enzyme activities responsible for the synthesis of the microorganisms' cell wall at the injured site. The antiulcer action of the curcumin-chitosan mixture in this study may be related to the potent multi-target antioxidant, anti-inflammatory, gastroprotective, and ulcer-healing actions attributed to curcumin and chitosan [8,9].

The data presented in Table 1 clearly demonstrate a significant increase (P<0.05) of the gastric juice volume in the ethanol group, that may be due to the direct effects of ethanol on the gastric mucosa, as ethanol is known to cause gastric injuries *via* several pathways, including dehydration, which disrupts mucosal cell barriers and exerts cytotoxicity. This cytotoxicity contributes to the recruitment of reactive oxygen species-releasing leukocytes and inflammatory cytokines, all of which may contribute to cellular apoptosis. Interestingly, the nuclear factor-kappa B plays a key role in the relationship between these disparaging events [10].

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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