

Evaluation study of the anti-ulcer activities of *Cuminum cyminum* Seed extract against ethanol-induced gastric ulcer in rats.

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Abstract

A herbaceous and pharmaceutical plant *Cuminum cyminum* L is one of crop and famous international spice seed after black pepper. This work was conducted to evaluate the effect the plant seeds extract against ulcer in the stomach. To achieve this goal, fifty-five rats were isolated into five gatherings. Individually, every one of the studied rats was pre-treated by oral administration with water and omeprazole and 20 mg, 250, 500 and 800 mg per kilogram of plant extracts to rat for 60 min. After that the rats were treated with ethanol to induce gastric mucosal damage. After a period for another 60 min, the rats were anesthetized and sacrificed.

The results obtained showed that the control group had severe mucus damage, whereas the rats treated with the seed extract showed a broad tolerance in a dose-dependent manner. Further, *Cuminum cyminum* seeds extract (CCSE) brought about the high level of pH of the gastric environment and mucus production. In this way, it tends to be inferred that hydrous concentrate on *Cuminum cyminum* uncovers an enemy of ulcer undertaking in protection from ethanol by means of keeping up via maintaining the acid-base balance of gastric content.

Keywords: Anti-ulcer, *Cuminum cyminum*, mucus, submucosa.

Introduction

Cuminum cyminum L is a herbaceous and therapeutic plant and one of the most established and common seed flavor worldwide after dark pepper¹. Cumin is notoriety predominance from Latin America to Africa and all over Asia². In spite of the fact that cumin was initially embedded in Iran where today it is additionally developing in Uzbekistan, Turkey, Tajikistan, Morocco, Egypt, India, Mexico, Syria, Bulgaria, Cyprus and Chile, where India is the more noteworthy maker and shopper of cumin seed in the world³. Cumin is a bloom minimal herbaceous plant 30–50 cm long and is gathered by hand. It is a yearly plant, with a slim, fanned stem 20–30 cm tall. It produces blue-green

direct leaves and finely confined. The pink or white blooms are borne in little organization umbels^{4,5}.

Produced substances from cumin (in 2 g of seeds) are incorporated: water 0.16 g; a few calories: starches 0.88 g, protein 0.36 g, dietary fiber 0.22 g, add up to fat 0.44 g, soaked fat 0.04 g, polyunsaturated fat 0.06 g, monounsaturated fat 0.28 g, Fiery remains 0.16g, a few nutrients, for example, nutrient A 25.40 IU, nutrient E 0.02 mg, thiamin (B1) 0.02 mg, niacin (B3) 0.10 mg, niacin equiv 0.10, nutrient C 0.16 mg, folate 0.20µg and nutrient K 0.11µg; it contained a few minerals: e.g. calcium 18.62 mg, copper 0.02 mg, press 1.32 mg, magnesium 7.32 mg, manganese 0.06 mg, phosphorus 9.98 mg, potassium 35.76 mg, selenium 0.10µg, sodium 3.36 mg and zinc 0.10 mg.⁶ Phytochemicals examination displayed that *Cuminum cyminum* contained: alkaloid, anthraquinone, flavonoid, coumarin, protein, glycoside, saponin, tannin, tar and steroid⁷. Cumin plant contains incredible proportions of B-complex supplements like supplement B6, niacin, thiamin, riboflavin and another fundamental enemy of oxidant nutrients, for example, nutrient C, vitamin E, and nutrient.

Seeds of this plant are rich wellspring of various flavonoid phenolic enemies of oxidants like carotenes, zeaxanthin, and lutein. Natural acids (aspartic, citrus, tartaric, propionic, malic, ascorbic, maleic, oxalic and fumaric acids) were separated from seeds of cumin⁸. The past pharmacological investigations demonstrated that *Cuminum cyminum* applied mitigating, antimicrobial, insecticidal, antioxidant, analgesic, anticancer, antidiabetic, antiplatelet hypotensive, bronchodilatory, immunological, prophylactic, hostile to amyloidogenic, aldose reductase, anti-osteoporotic, alpha-glucosidase and tyrosinase inhibitory impacts, focal anxious and defensive impacts⁹. The enthusiasm for natural developed plants is extending in the nations¹⁰. Traditionally, different plants have been connected to treat an assortment of illnesses including gastric ulcers.

An ulcer is a damage or ulcer regularly identified in the mucous layer or skin of the body. In the digestive system, the ulcer in the duodenum and gastric ulcers is frequently analyzed and is an irritating ailment that influences a substantial extent of the total populace¹¹. The absence of insurance against gastric acid is a typical reason for gastric ulcer¹². Past investigations have demonstrated that the most

widely recognized reasons for this issue are related to inflammation, smoking and stress, nutritional deficiencies and alcohol consumption¹³.

The medications utilized in the treatment of gastric ulcers are against acids, anticholinergics, proton siphon inhibitors, and H2-receptor rivals. There are unnumbered reactions caused by these allopathic medicines¹⁴ demonstrating the requirement for more viable and safer anti-gastric ulcer agents with less unfavorable impacts. In this unique situation, metabolites determined of plants utilized in conventional medication have given a critical promise to the revelation of recover helpful medications¹⁵. Omeprazole is the most imperative inhibitor of the proton pump, which is often used as an anti-acid treatment and to lessen issues identified with gastric acid discharge for around 15 years¹⁶. Omeprazole has displaced benzimidazoles and it stops corrosive outflow by following up on the hydrogen-potassium exchanger (H⁺: K⁺-ATPase) for the apical plasma film of the gastric mucosa¹⁷.

Omeprazole is extremely particular for the proton siphon and can change into a functioning structure inside the acid development zone. Dynamic inhibitors start to interface with the SH (thiol) group of the proton pump, hence stifling the acid development¹⁸.

Material and Methods

Plant material and preparation of the extract: *Cuminum cyminum* seeds were purchased from a regional herbal store in Erbil, Iraq. Seeds samples were dried in shade and pursued by drying and changed over into powder. 100 grams of exact powder was absorbed in 500 ml of refined water in a cone-shaped cup and blended for 15 minutes, at that point left for 3 days.

Following 3 days, the blend was sifted utilizing a fine muslin by centrifuging at 3000 rpm for 15 minutes. The filtered solution was put in the oven at 40° to get powder. The dry concentrate was then disintegrated in distilled water and orally drenched to rats in concentrations of 250, 500 and 800 mg/kg (5 ml/kg body weight)¹⁹.

Experimental Animals: Twenty-five male adult animals were obtained from the animal homes, College of Veterinary Medicine/ the University of Baghdad. Animals were preserved under standard environmental conditions and had free entrance to standard feed and water. They were saved under perception for around fourteen days before the start of the experiment. Housing conditions and *in vivo* tries were affirmed in concurrence with the rules and bearings set forward in the "Manual for the Consideration and Utilization of Research center Animals," prepared by the National Foundation of Sciences and dispersed by the National Establishment to well being.

Omeprazole: In this present investigation, omeprazole was utilized as the reference against ulcer medicate, and was

gotten off the local Pharmacy. The medication was orally provided for the rats in concentrations of 20 mg/kg body weight (5 ml/kg)²⁰.

Antiulcer Experiment: The ethanol ulcer enlistment examination of the examination was taken depending on the technique depicted in untimely studies²¹. *Rattus norvegicus* (150– 200 g) were taboo of sustenance for (48 h) before the analysis was driven all together for the stomach to be unfilled, anyway they were empowered free landing to drink water up until the point that 2 h before starting the experiment^{10,21}. All creatures were treated by orogastric intubations. The rodents were parceled self-assertively into 5 gatherings, each including 5 rodents; they were treated as showed up in table 1.

Table 1
Design of the antiulcer experiment

Groups	Treatments	Concentrations
Group (1) Normal	Water	-
Group (2) (positive control group)	Omeprazole	20 mg/kg, 5 ml/kg
Group (3) LD	CCSE	250mg/kg, 5 ml/kg
Group (4) MD	CCSE	500mg/kg, 5 ml/kg
Group (5) HD	CCSE	800mg/kg, 5 ml/kg

Gastric Ulcer-Induction by Absolute Ethanol and Tissue Sample Collection: The creatures were hungry for 48 h before the examination, yet they were empowered free Entry to drink water up till 2 h before the experiment. A gastric ulcer was actuated by managing total ethanol orally 5 ml/kg. The medications were directed to various gatherings 30 min before ethanol. 2 hours after ethanol association, all creatures were anesthetized by chloroform (SIGMA-ALDRICH). The rodents were surrendered and their stomachs were associated of above and down to spare the gastric juice for evaluating the gastric corrosive; by then the stomachs were dismantled out and studied in formalin 12% for histological examination.

Measurement of Acid in Gastric Juice: Stomach was opened along the more noticeable recurring pattern. Tests from gastric substance were tried for hydrogen particle focus by pH-meter using (3540) pH Conductivity Meter (JENWAY-Japan).

Measurement of Mucus Production: The gastric bodily fluid generation creation was evaluated in each the guinea pig submitted to pre-eminent ethanol-prompted gastric mucosal harm. The gastric mucosa of all rodents was gently scratched using a glass slide and the bodily fluid picked up was measured using accuracy electronic balance²².

Histological Preparation: A histological examination was proficient after the assessment of ulcer hurt. The stomachs were constant 12% of cradled formalin. Tissue preparing

(lack of hydration, cleaning, infiltration) was done normally using mechanized tissue processor (Leica TP1020).

The tissues were embedded in paraffin wax using Leedohisto embedder. The introduced tissues were isolated with a microtome to convey (5 μ m) paraffin wax tissue sections. By then, the territories were recolored with eosin and hematoxylin sought after by mounting with DPX mounting media. After that specifically, the mounting areas were oppressed for minute examination utilizing light magnifying instrument (AmScoop microscope eyepiece camera, China).

Statistical Analysis: Data are presented as the mean \pm SE from 5 rats per group. Statistically significant differences between the treatments were tested by the Duncan's Multiple

Range Test. Probability (p) values less than 0.01 were considered significant.

Results

Total Evaluation of Gastric Lesions: Present outcomes demonstrated that animals treated with *Cuminum cyminum* seed extract demonstrated a noteworthy diminishing in ulcer development compared with the control group. The animals beforehand treated with plant extract altogether diminished mucosal harm yet at the same time few folds saw in rats that already treated concentrations 250 and 500 mg/kg (Figure 1C and D). Convergence of (800 mg/kg) from CCSE watched full insurance of the mucous layer in the stomach with nearly smoothing of the mass of mucous in the stomach as in Figure 1E.

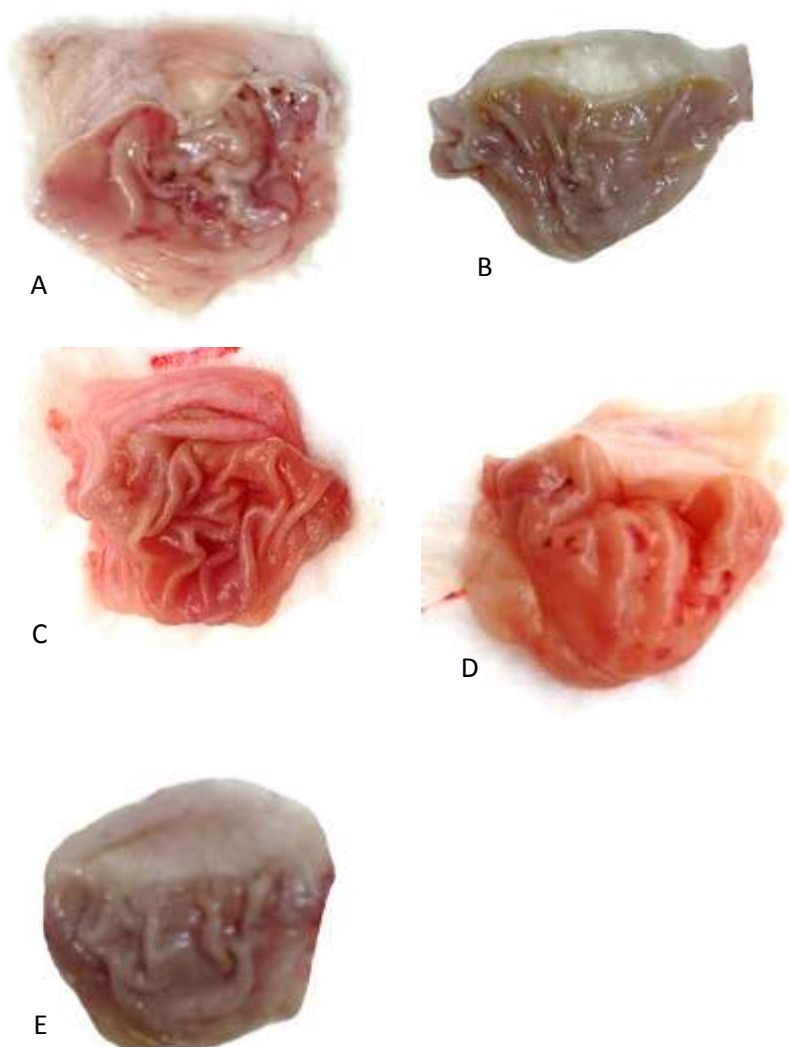


Figure 1: Plainly visible appearance, of the gastric mucosa in the rodent. A, before-treated with (5 ml/kg) of water (control gathering). intense harms were found in the gastric mucosa. B, pre-treated with (5 ml/kg) of Omeprazole (20 mg/kg). Damage to the gastric mucosa was milder appeared differently in relation to the injuries found in the ulcer control gathering. C, Pre-treated with (5 ml/kg) of CCSE (250 mg/kg). humble wounds with collapsed of gastric mucosa were seen. D, Pre-treated with (5 ml/kg) of CCSE (500 mg/kg). No damages with fallen of gastric mucosa were seen. F, pre-treated with (5 ml/kg) of CCSE (800 mg/kg). Assurance of gastric mucosa was more prominent and lower crumbled of gastric mucosa were seen

pH of Gastric Content and Mucus Production: Effect of CCSE on mucus production and gastric acidity in the ethanol-resulting gastric injury is shown in table 2. The infectious substance is essentially reduced ($P \leq 0.01$) in pre-treated rats with 250, 500 and 800 mg/kg CCSE, and the omeprazole group compared with that of the ulcer control group. Rats pre-treated with 800 mg/kg and omeprazole of CCSE view a significant decrease in acidity compared to the 250 and 500 mg/kg group, as shown in table 2. The production of mucus from the gastric mucosa increased significantly ($P \leq 0.01$) in pre-treated mice with 250, 500 and

800 mg/kg and omeprazole compared to the control group as in table 2. On the other hand, there was no noteworthy qualification in the production of known mucus between omeprazole and 800 mg/kg of CCSE collection.

Histological Evaluation of Gastric Lesions: Histological areas appeared in the negative control bunch before treatment with water causing moderately serious damage to the gastric mucosa., edema and leucocytes penetration of the submucosal layer (Figure 2B).

Table 2
Effect of CCSE on pH of gastric content and mucus in rats.

Animal Group	Pre-treatment (5 ml/kg dose)	pH of gastric content	Mucus content
1	Water (Ulcer control)	3.7±0.05 d	0.316±0.01 e
2	Omeprazole (20 mg/kg) (positive control)	6.9±0.10 a	0.630±0.00bc
3	LD (250 mg/kg)	4.3± 0.19 c	0.481±0.02d
4	MD (500 mg/kg)	5.54±0.08 b	0.606±0.02c
5	HD(800 mg/kg)	6.89±0.22a	0.674±0.00ab

All data expressed in mean ± SD.

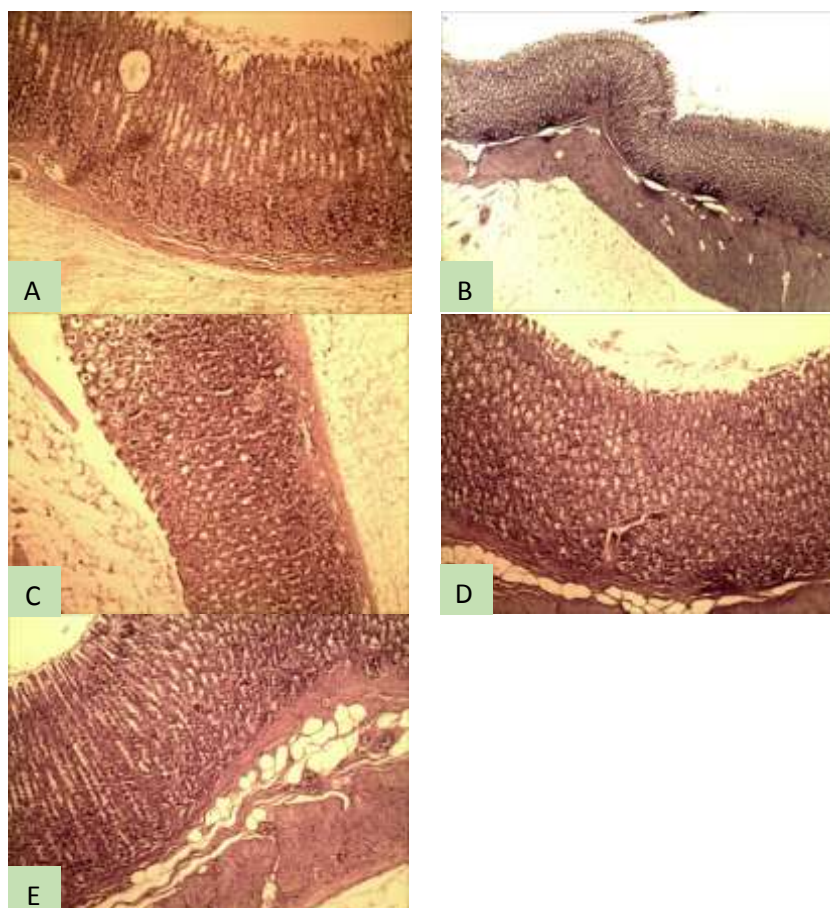


Figure 2: A histological segment of gastric. mucosa in rodents. A. pre-treated with (5 ml/kg) of water (ulcer control gatherings). There was intense turmoil to the surface epithelium, or mucosal damage, and edema of the submucosa layer with leucocytes invasion. (E&H recolor 100X). B. pre-treated with 5 ml/kg from Omeprazole (20 mg/kg). It demonstrates the leucocytes invasion. C. pre-treated with (5 ml/kg) of CCSE (250 mg/kg). D. pre-treated with 5 ml/kg from CCSE 500 mg/kg. E. pre-treated with 5 ml/kg of CCSE (800 mg/kg). It demonstrates a typical cytoarchitecture of gastric mucosa, with no neurotic changes.

Discussion

In the current study, we have evaluated the protective effects on the induced gastric ulcer and antisecretory property of *Cuminum Cyminum*, which is an important plant in herbal medicine practice. Gastric ulcers and hyperacidity are global issue at present. It has been agreed that the progress of this ulcer occurs when the balance between the insurance factors and the attacking is lost. Major forceful aggressive components are acid, bile salts, pepsin, and *Helicobacter pylori*. Defensive factors mainly include mucus-bicarbonate secretion and prostaglandins²³. Hypersecretion of gastric acid is an obsessive circumstance, which occurs because of uncontrolled emission of hydrochloric acid from the parietal cells of the gastric mucosa out of the proton pumping H⁺K⁺ATPase²⁴.

In this work, omeprazole is used as positive control. A large portion of the antisecretory drugs like proton pump inhibitors (omeprazole) and histamine H₂-receptor blocker (famotidine, ranitidine etc.) are widely used to check for expanded acid secretion and acidity problems caused by stress but there are reports of reactions and bounce back over the long term²⁵.

Intragastric administration of absolute ethanol to experimental animals is an excessively utilized model to instigate gastric ulceration. Ethanol is responsible for unsettling influences in gastric discharge modifications in the penetrability, damage to the mucosa, free radical production, and gastric mucus depletion. A generation of free radicals was created through the continuous release of superoxide anion and hydroperoxy free radicals through metabolism of ethanol²⁶. The ulcer can be caused by ethanol, which causes the flow of blood to stop, which adds to the migration of dead tissue²⁷. Ethanol causes gastric ulcers spread in vast areas: infection characterized by continuous leakage and expansion of blood stasis at the edge of the ulcer accompanied by edema, congestion of the surface epithelium and inflammatory invasion²⁸.

CCSE serves as gastric cytoprotectants by attenuating or prohibition mucosal injuries. Cumin oils enjoy high-strength cells because of the presence of mono-terpene alcohols, essential flavors, , flavonoids and other polyphenolic molecules²⁹.

The dietary supplement of cumin has kept the episode of rodent colon disease prompted by a colon-particular cancer-causing agent and furthermore diminishing the action of β -glucuronidase and mucinase enzymes. In cumin-colon treated rats, the levels of cholesterol/phospholipids rate, cholesterol, and 3-methylglutaryl COA reduces action were diminished³⁰. The other restraint exercises of dietary cumin in rodents are benzopyrene-prompted for stomach tumorigenesis, 3-methyl-4-dimethylaminoazobenzene incited hepatomas and 3-methylcholanthrene actuated uterine cervix tumorigenesis³¹.

A few logical investigations found that the phytoconstituents such as flavonoids, tannins, terpenoids, and saponin were liable for gastroprotective agents³². Tannins have as an antiulcer factor by its astringency favorable position and vasoconstriction impacts. Because of the deposition of small-scale proteins on the ulcer site, a moderate layer was shaped which averts gut emissions and shields the mucosa from poisons and some other aggravations. The untimely study has prescribed that these above dynamic mixes had ability to animated mucus, prostaglandin and bicarbonate emission and invigorate with the backsliding impacts of responsive oxidants in gastrointestinal³³. Therefore CCSE has anti-ulcer movement, might be because of the essence of terpenoids, flavonoids, and tannins. There are many works that have looked for gastric ulcer repair by testing the derived extract from plants. However, the concentrated focus of herbal extracts seems to be a distinct therapeutic alternative to resist or improve successful effect because of the multiple activities they can exert simultaneously (i.e. antiulcerogenic, antioxidant, antibiotic, antiinflammatory, angiogenic and cytoprotective).

Conclusion

The present study completed that the anti-ulcer action of CCSE could securely ensure the gastric mucosa against ethanol-prompted harm. It is might be ascribed to antisecretory, cytoprotective and antioxidant quality This safety has been shown to be dependent on the dose that is identified by low gastric ulcers due to lack or obstruction of edema and the permeation of leucocytes in the sub-mucosal layers and protection was most notable at a dose of 800 mg/kg leaf extract. This insurance could have returned to the adjust between acid-base creation in the stomach and the presence of tannins, flavonoids, and triterpenoids.

Further studies are needed to identify the minerals responsible for ulcer reduction from *Cuminum cyminum* seeds extract.

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