



RESEARCH ARTICLE

Effect of *Hypericum perforatum* Extract on Gastric Ulcer Development in Rat Models

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ABSTRACT

Gastric ulcer is a serious condition that results from the tearing of the stomach mucosa. A physiological equilibrium is maintained between mucosal defense and aggressive factors. In this study, the effectiveness of medicinal plant (*Hypericum perforatum*) in the management of gastric ulcers was compared to that of omeprazole, a well-known drug for gastric ulcers. This study involved numerous study groups of male rats comprising the following: The first group (control group exposed to *Helicobacter pylori* and fed with normal animal feed), the second group (rats exposed to *H. pylori* and treated with two doses (of 250 mg/kg and 500 mg/kg) of aqueous *H. perforatum*), and the third group (rats exposed to *H. pylori* and treated with 20 mg/kg of omeprazole). The outcome of the study demonstrated that a high dose of 50.65% *H. perforatum* prevents the development of stomach ulcers. The group treated with omeprazole revealed a formation of stomach ulcers (24.50%). A high dose of the aqueous plant extracts showed greater effectiveness in preventing gastric ulcer formation compared to the lower dosage.

Keywords: Gastric ulcer, antibacterial activity, *Helicobacter pylori*, gastrointestinal tract, peptic ulcer

INTRODUCTION

A highly mobile, spiral-shaped, Gram-negative bacteria called *Helicobacter pylori* colonizes the intestines of 50–80% of people around the globe.^[1] The bacterium *H. pylori* damage the gastric mucosa most commonly by causing gastritis, peptic ulcer disease, or even gastric cancer.^[2] Gastric ulcer is a condition of the stomach lining that has common symptoms such as vomiting, burning, dull abdominal pain, headache, weight loss, low oral resistance, stenosis, perforation, and stomach bleeding.^[3]

The focus has been on natural plants for the management of many human disease conditions partially because certain pharmaceutical medicines are highly harmful to the patient or cause adverse effects.^[4] Moreover, in terms of cure and disease prevention, plant products are inexpensive and more affordable contributors to improving human health.^[5]

Hypericum perforatum is a *Hypericaceae* commonly known as St. John's Wort. It has been used as a form of treatment for different diseases in various Eastern countries. Nevertheless, scholars suggest that it is used to cure mental illnesses caused by demonic forces among the ancient Greeks. The plant grows well in temperate open disturbed regions.^[6]

Conventionally, omeprazole is used as a drug for the treatment of conditions where the stomach excretes large quantities of acid. It prevents the activity of a particular enzyme mechanism located within the acid-secreting stomach cells (in the stomach),^[7] thus, preventing acid production. Omeprazole

is used to control heartburn, acute gastritis, duodenitis, esophagitis attributable to recurrence of gastrointestinal material, peptic ulcer, and other secretory diseases.^[8]

Aim of Study

This research is aimed at comparing the effectiveness of *H. perforatum* and omeprazole in gastric ulcer treatment using male albino rats as the disease model.

MATERIALS AND METHODS

Extraction of the Aerial Part of *H. perforatum*

Fresh aerial plants (stem, leaf, flower, fruit, and seed) of *H. perforatum* collected from Khabat (district of Erbil city in the western region of the Kurdistan Region, Iraq) were

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extracted for the study. The aerial part of the plant with a high presence of flowers and buds was collected in August 2020 and air-dried in the shade.

The extraction process followed a modified method previously used by.^[9] The dried and pulverized aerial parts of the flower (25 g) were soaked in 250 mL of water (at 85°C) for high-dose extraction and 25 g in 500 mL for low-dose extraction. The mixture was kept for 24 h before filtering with Whatman Number 1 Filter Paper. Finally, the filtered extract was kept inside a sterile cup in the refrigerator until used.

Omeprazole

Omeprazole is the class of medicines that have been used to treat disorders including peptic ulcers because they act as proton-pump inhibitors. Omeprazole inhibits the acid-forming enzymes in the stomach wall. The output of the stomach acid is reduced by blocking these enzymes and thus, the stomach can be healed. Omeprazole served as the standard anti-ulcer agent in this study; it was procured from Happy Pharmacy in Erbil City. The medication was administered to the rats by mouth at the dose of 20 mg/kg body weight following suspension in distilled water (5 mL/kg).^[10]

Experimental Animals

Forty-eight male albino rats were used for the experiment; the body weight of the rats was 160 ± 20 g at 7–9 weeks old. The rats were randomly allocated to four groups, each group of 12 rats was purchased from Zakho University and housed hygienically in ventilated cages. The rats were fed on a standard diet for 1 week in the Animal House Unit of the College of Education at Salahaddin University-Erbil.

Induction of Gastric Ulcer by *H. pylori*

Gastritis was induced by feeding rats with the bacterium *H. pylori* that were collected from biopsy samples from clinical patients. The rats were fed for 1 week on a basal diet in the Animal House Unit, College of Education at Salahaddin University-Erbil. In this study, the rats were kept from food in the morning and afternoon, then, inoculated with the plant extracts and immediately inoculated with $1 \text{ mL } H. pylori$ suspension (5×10^8 – 5×10^{10} CFU/mL) using gavage twice daily at 4 h intervals for 3 straight days. The rats were left on normal feeding for 15 days to observe the effect of the plant extracts on *H. pylori* activity.^[11] Before inoculating the animals with the plant extract and *H. pylori*, they were subjected to stool antigen tests to ensure no pre-infection with *H. pylori*. In the last period of prevention, the rats were anesthetized through intramuscular injection of mixed xylazine–ketamine (1:9) as a single dose in the same syringe. The stomach of each rat from each group was removed and dissected for observation.

Gross Gastric Lesions Evaluation

Ulcers located in the gastric mucosa, parallel to the long stomach axis, emerged as elongated bands of hemorrhagic lesions. Thus, the damage was studied in each gastric mucosa specimen. In the measurement of the ulcer region (UA), the total of the lesion areas for each stomach was summed, wherein the sum of small squares $\times 4 \times 1.8 = \text{UA mm}^2$ as

earlier described by.^[12] The inhibition percentage (I %) was estimated using the formula: ^[13]

$$(I \%) = ([\text{UA control} - \text{UA treated}] / \text{UA control}) \times 100\%$$

Measurement and Evaluation of Acid Content of Gastric Juice (pH)

The pH level of the rat stomach was individually recorded for evaluation of the pH level of all the groups of rats; this was done to know the effect and correlation of the plant extract with pH level.

Microbiological Analysis

Microbiological analysis was directly carried out on the day of sample collection. Stool antigen and blood antibody tests were done on all the rat groups using strip *H. pylori* antigen and antibody tests; this was done to determine the *H. pylori* infection status of the rats.

RESULTS AND DISCUSSION

Effect of *H. perforatum* Extract and Omeprazole on Gastric Lesion Development

The anti-ulcer effect of *H. perforatum* extract against gastric lesion model caused by *H. pylori* is reported in Table 1. The

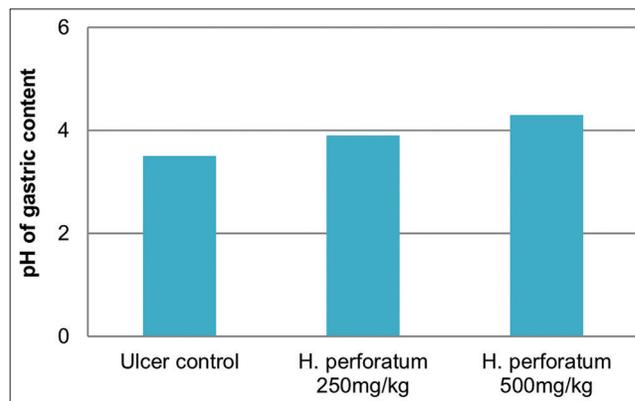


Figure 1: The pH level of gastric content of rats treated with *Hypericum perforatum* extract and omeprazole compared to the control group

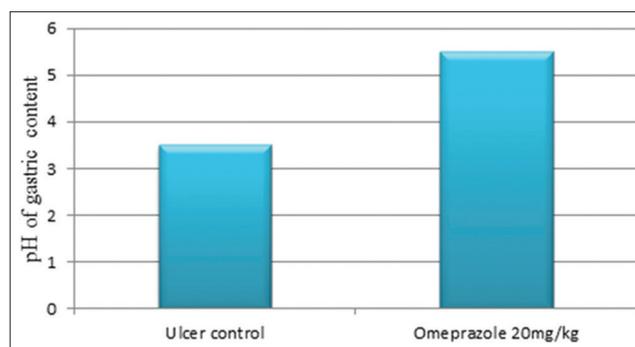


Figure 2: Effect of omeprazole antibiotic drugs on pH of gastric content

Table 1: Effect of aqueous extract of *H. perforatum* and omeprazole on gastric ulcer production and gastric ulcer development in albino rats

Animal group	Prevention (5 mL/kg) dose	Ulcer Area (mm ²) Mean \pm SEM	Ulcer Inhibition %
1	Ulcer control group	815.00	0
2	High-dose <i>H. perforatum</i>	402.20	50.65
	Low-dose <i>H. perforatum</i>	611.45	24.97
3	Omeprazole	615.25	24.50

H. perforatum: *Hypericum perforatum*

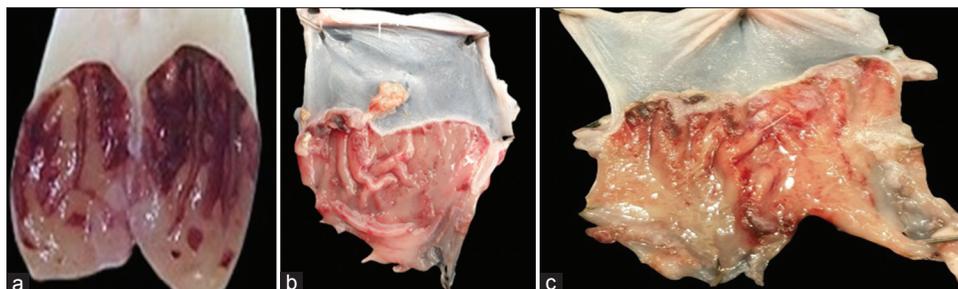


Figure 3: Stomach changes in different rat groups: (a) control group, (b) treated with *Hypericum perforatum* extract, (c) treated with omeprazole

results showed that the ulcer area of the rat's stomach with a high dose (500 mg/kg) of *H. perforatum* extracts was inhibited at the rate of 50.65% compared with the ulcer control group.

Table 1 also showed the anti-ulcer effect of omeprazole in the *H. pylori*-induced gastric ulcer rat models. The findings demonstrated that the rats' stomachs were protected by omeprazole while receiving *H. pylori* solution, thereby showing a decrease in gastric ulcer formation rate by 24.50% compared to the control group.

Effect of *H. perforatum* Extract and Omeprazole on the Gastric pH Level

When compared to the non-treated control group in Figure 1, the stomach contents' acidity in the experimental mice treated with *H. perforatum* was increased. The experimental rats treated with omeprazole showed an increase (5–5.5) in the gastric contents' acidity when compared to the control group (3.5). The acidity of the gastric juice of the group treated with *H. perforatum* extract, however, ranged from 4 to 4.5 see Figure 2.

Evaluation of Stomach Color Changes in Gastric Ulcer Rat Models Treated with *H. perforatum* and Omeprazole

The color of the stomach is one of the parameters considered in the study; the color of the stomach of *H. perforatum*-treated rats significantly changed when compared with the control group. A bright white color was found in the stomach of the rats treated with *H. perforatum*, whereas a pink-to-red color was found in the stomach of omeprazole-treated rats. The control group's stomach was totally dark red because of the ulcer and inflammation caused by *H. pylori*, while the color of the protected rat stomachs changed significantly [Figure 3].

Gastritis is among the most prominent clinical symptoms of *H. pylori* infection; *H. pylori* forms widely visible black hemorrhagic

injuries on the stomach mucosa. In this study, the plant extract showed a 50.65% inhibition rate of the formation of stomach ulcers compared with the control group at the concentration of 500 mg/kg and 24.97% inhibition at the concentration of 250 mg/kg. However, a previous study^[14] also reported the effectiveness of *H. perforatum* on gastroprotection in rat animal models. As an antibacterial agent, omeprazole, a standard drug used to treat gastric ulcers, plays a major role in preventing gastric ulcer disorders in male albino rat animal models, especially gastric ulcers caused by *H. pylori*. According to the current study results, the stomach of mice infected with *H. pylori* and treated with omeprazole showed an observable reduction in gastric ulcer development at the rate of 24.50% compared to the control group. The stomach mucosa of the rats exposed to *H. pylori* solution showed noticeable black hemorrhagic lesions.

The outcome of this study agrees with the report by^[15] which showed a healing rate of 61% in a study group that received 20 mg of omeprazole within 4 weeks during a study with 68 patients receiving concurrent NSAIDs. This is significant because a high percentage of patients in the omeprazole groups were free of symptoms and ulcers. In the 4th week, the healing rate was 61% in the group receiving omeprazole 20 mg, and a significant number of patients in the omeprazole group had no symptoms or ulcers.

CONCLUSION

The present study demonstrated that the development of gastric ulcers following active *H. pylori* induction can be prevented significantly using medicinal plants, such as *H. perforatum*. *H. perforatum* can serve as a natural alternative to omeprazole (a chemical agent) in the prevention of gastric ulcer formation in people that have been exposed to *H. pylori*.

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