Original Article

In vivo Gastro-Protective Effects of Five Moroccan Medicinal Plants against Gastric Ulcer

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ABSTRACT

Centaurea chamaerhaponticum Ball. (Asteraceae), *Lawsonia inermis* L. (Lythraceae), *Origanum compactum* Benth. (Lamiaceae), *Punica granatum* L. (Punicaceae) and *Ceratonia siliqua* L. (Sapindaceae) are medicinal plants recommended in Moroccan folk medicine for the treatment of gastric ulcers.

The protective effects of the studied plants against gastric damage were investigated using three experimental models in rats (HCl/ethanol, pylorus ligation, and aspirin-induced ulcer). Each plant extract (250 or 500 mg/kg) was orally administered once prior to ulcer induction. The antiulcer activity was assessed by comparing the ulcer index and gastric parameters in the test group with those of the control group. As a result, all five plant extracts showed, at the high dose, a significant gastro-protective effect. *O. compactum* showed the highest ulcer protective in NSAID-induced ulcer model (86.1 % of protection), greater than that of omeprazole (79.7 %) and almost similar to that of cimetidine (84.8%). The volume of gastric secretion was decreased significantly by *C. chamaerhaponticum* (50% of gastric secretion reduction), *C. siliqua* (46.4%) and *L. inermis* (42.8%) similarly to omeprazole's antisecretory effect (50% of secretion reduction). A significant decrease in the total acidity was noticed only at the highest dose for all tested plants (percent of total acidity reduction ranged from 22.2 to 30.5 %), except for *C. chamaerhaponticum* which showed no significant modifications in both total acidity and gastric pH. Taken together, the results of this study indicate that the selected plants possess potent gastroprotective and antisecretory properties, which justify the ethno-medicinal claims.

Keywords: Moroccan folk medicine, Gastric ulcer, Antacid effect, Gastroprotective properties.

INTRODUCTION

Gastric hyperacidity and gastro-duodenal ulcer is very common global problems[1]. It is now generally agreed that gastric lesions develop when the delicate balance between gastro-protective factors and aggressive ones is lost. Major gastro-duodenal aggressive factors are gastric acid, pepsin, bile salts, and the release of reactive oxygen species in the gastric mucosa. Defensive factors, mainly involve mucus secretion and prostaglandins production[2].

Most of the prescribed antiulcer drugs involve proton pump inhibitors like omeprazole and lanzoprazol and histamine H_2-receptor blocker such as ranitidine, famotidine, and cimetidine. They are extensively used to control increased acid secretion, and acid related disorders caused by stress, NSAIDs and *Helicobacter pylori*. However, there are reports of adverse effects (i.e. headache, diarrhea, abdominal pain, nausea, dizziness, trouble awakening and sleep deprivation) of the long-term uses of such commercially available drugs[3,4]. Furthermore, long-term use of these drugs results in high costs for the treatment of chronic peptic ulcers[5,6]. In this context, research on developing plant-derived antiulcer medication as an alternative strategy for the management of gastro-duodenal ulcers were highly recommended.

In Morocco, the use of medicinal plants is an important and essential part of the culture and of the traditional health care system[7]. Therefore, this recommendation has been appropriate because of the high cost of modern antiulcer medication for the population, their unavailability in some rural areas, the multiple side effects that result from their prolonged uses, and more important, is the reliance on local population on traditional remedies.

In the present study, five plant remedies were selected based on the results of an ethnobotanical survey undertaken by our research team, which showed that the local population of Marrakech (Morocco) uses the fruits of *Ceratonia siliqua* L. (Sapindaceae), leaves of *Lawsonia inermis* L. (Lythraceae), roots of *Centaurea chamaerhaponticum* Ball. (Asteraceae), aerial part of *Origanum compactum* Benth. (Lamiaceae) and fruit peel of *Punica granatum* L. (Punicaceae) to treat gastrointestinal ailments, including ulcer. They are generally consumed as an infusion, decoction or as a powder mixed with honey (Table 1). In addition to ulcer healing properties, the chosen plants are known for other traditional uses[8,9] which several were evidence-based confirmed (Table 1). In this paper, the mentioned plants were studied in terms of their gastro-protective and anti-secretory activities in rats, using three induced gastric ulcer models (HCl/ethanol, pylorus ligation and NSAID), in order to confirm the reported traditional uses in Moroccan folk medicine.

MATERIALS AND METHODS

Drugs and chemicals

All chemicals used in the anti-ulcerogenic study (absolute ethanol, hydrochloric acid, urethane, sodium chloride, sodium hydroxide) were of analytical grade and were procured from Sigma-Aldrich, Germany. Cimetidine was obtained from Promopharm Pharmaceuticals, Casablanca (Morocco). Omeprazole was obtained from Cooper

Maroc, Casablanca (Morocco), and aspirin was obtained from Bayer Maroc, Casablanca (Morocco).

Plant materials

O. compactum, *C. chamaerhaponticum*, and *P. granatum* were collected from Marrakech region (Morocco). *C. siliqua* was collected from Demnat, (Morocco), and *L. inermis* from Taliouine (Morocco). The taxonomic identification of the plant materials was confirmed by Prof. Ahmed Ouhammou, a plant taxonomist of Faculty of Sciences-Semlalia, Cadi Ayyad University, Marrakech (Morocco). Voucher specimens of *C. siliqua*, *L. inermis*, *C. chamaerhaponticum*, *O. compactum*, *P. granatum* were deposited in the Herbarium of the Laboratory of Biotechnology, Protection and Valorization of Plant Resources, Faculty of Sciences-Semlalia (Marrakech) under the respective references OCO-022, PGR-041, CSI-038, LIN-037 and CCH-044.

Plant extraction

After collection, plants were air-dried and thereafter ground to a powder. The powdered plant materials 150 g each were exhaustively extracted with methanol-water mixture (70:30) in a Soxhlet extractor. The aqueous methanol extract of each plant was concentrated to dryness under vacuum. The residue was stored in a refrigerator at 4°C until the time of use. The yield of extraction of *C. siliqua, L. inermis, C. chamaerhaponticum, O. compactum, P. granatum* was respectively 26, 33, 24, 13.5 and 48% w/w.

Phytochemical screening

Preliminary phytochemical screening of the extract involved qualitative determinations of the following substances: anthocyanins, alkaloids, tannins, saponins, coumarins, flavonoids, terpenes and sterols. Determinations were carried out in accordance with procedures described by Harborne[10].

Dose preparation

The selection of testing doses of plant extracts and positive controls (aspirin, cimetidine and omeprazole) was done based on literature survey[4,11]. Methanol extracts were dissolved in distilled water in order to obtain the two chosen doses: 250 and 500 mg/kg body weight. Aspirin, cimetidine and omeprazole were also dissolved in distilled water. Solutions were prepared in order to obtain the administered doses of 400, 100, and 20 mg/kg body weight, respectively[4,11].

Animals

Adult Wistar rats of either sex, weighing 150-200 g were used for the anti-ulcer assay. The animals were supplied by the Animal Care Facility of the Faculty of Sciences - Semlalia, Cadi Ayyad University, Marrakech (Morocco). They were randomly assigned to different groups and a period of 5 days was allowed for adaptation on each experiment. Animals were kept under standard environmental conditions (25 ± 2°C; 12/12 h light/dark cycle). They were fed *ad libitum* with feeding pellets (Cicalim S.A., Casablanca, Morocco) and barley, and had free access to tap water. All tests were conducted in accordance with the recommendations from the declaration of Helsinki on guiding principles in the care and use of animals and after obtaining prior approval from our institution.

HCl/ethanol-induced ulcer

HCl/ethanol-induced ulcer model was performed following the method of Jorge *et al*.[11]. The necrotizing agent was prepared with HCl (0.3 M) mixed with ethanol 60% (50:50, v/v). Animals were randomly divided into thirteen groups of six

rats each. All groups of rats were fasted for 24 h, with free access to water.

One hour before the administering necrotizing agent, animals of group 1 received 10 ml/kg body weight of distilled water and served as controls. Animals of groups 2 to 11, received 10 ml/kg of respective plants extracts at doses of 250 or 500 mg/kg body weight. Group 12 received cimetidine at a dose of 100 mg/kg, and group 13 received omeprazole at 20 mg/kg. All solutions were administered orally through gastric intubation.

One hour after treatment, all animals received 1 ml of HCl/ethanol to induce gastric lesions. The rodents were sacrificed 1 h later with an overdose of urethane (i.p.). Their stomachs were excised and opened along the greater curvature. The mucosal surface was observed with the help of a magnifying lens and the extent of gastric damage was scored, according to the method described by Main and Whittle (1975), using the following scale: 0 = normal mucosa, 1 = patch length was less or equal to 1 mm, 2 = patch length was between 1 and 2 mm, 3 = patch length was over than 2 mm. The ulcer index (UI) and percent inhibition of gastric lesion formation were calculated as earlier described[4,12] by using the formula:

UI = [1 × (number of lesions of grade 1) + 2 × (number of lesions of grade 2) + 3 × (number of lesions of grade 3)] × 10^{-1}.

% Inhibition of ulceration = (Ulcer index in control – ulcer index in the test) × (Ulcer index in control)$^{-1}$ × 100.

Pylorus-ligation model

The experiment was performed following the method of Shay[13]. Animals were divided into thirteen groups of six rats each. All groups of rats were fasted for 24 h, with free access to tap water. One hour prior to pylorus ligation, animals received an oral dose of the vehicle (distilled water, 10 ml/kg), plants extracts (250 or 500 mg/kg), cimetidine (100 mg/kg) or omeprazole (20 mg/kg). The animals were anesthetized with urethane (1 g/kg; i.p.); then a small excision was done on the abdomen in order to make a ligature on the pylorus area. The abdomen was closed by suturing.

The animals were sacrificed 4 h later with an overdose of urethane (i.p.). The abdomen was opened and another ligature was placed around the esophagus close to the diaphragm. The stomach was removed and the gastric content collected in tubes to determine the total amount of gastric juice (ml) and pH values (unit). Distilled water (3 ml) was added, and the resultant solution was centrifuged at 3.000 rpm for 10 min. The total acidity of the supernatant was determined by titration to pH 7.0 with 0.01 N NaOH and expressed as mEq per liter per 100 g body weight of rats. Ulcer index and percentage inhibition of ulceration were calculated as described above.

NSAID-induced gastric ulcer

In this model, gastric lesions were induced by aspirin. The experiment was performed according to the method reported by De Andrade *et al*.[14]. After 12 h of fasting, the rats were randomly divided into thirteen groups of six animals each. The first group was given 1 ml of vehicle (distilled water), the second and the third groups were treated respectively, with cimetidine (100 mg/kg) and omeprazole (20 mg/kg). Each group of the remaining ten received one plant extract at 250 or 500 mg/kg. All treatments were administered orally. One hour after treatment, the rats received aspirin (400 mg/kg) to induce gastric ulcer. Animals were sacrificed 4 hours later by an intraperitoneal overdose of urethane. The stomachs were removed, and opened along the greater curvature. The stomachs were gently rinsed with water to remove the gastric contents and blood clots; the

ulcerative index and percentage inhibition of ulceration were calculated as described above.

Statistical analysis

The results are expressed as mean ± S.E.M. The statistical difference between the treated groups and the negative control was calculated by *SigmaStat 3.1* software, using the Student's *t-test*. The results were considered statistically significant if $p < 0.05$, and highly significant if $p < 0.001$.

RESULTS AND DISCUSSION

The antiulcerogenic effect of crude methanol extracts of five medicinal plants, well-known in Moroccan herbal medicine practice of healing gastric ulcer, was studied using three ulcerogenic models: HCl/ethanol, pylorus ligation and aspirin.

HCl/ethanol-induced ulcer model

In HCl/ethanol-induced ulcer model (Table 2), the oral administration of the HCl / ethanol solution to the control group produced characteristic necrotizing mucosal lesions confined to the glandular portion with an ulcer index of 2.26 ± 0.44. Cimetidine and omeprazole treated animals showed a significant reduction in ulcer formation in 84.5 and 60.2% of ulcer inhibition respectively. Ulcer formation was also significantly reduced in rats pretreated with tested plants, especially at the dose of 500 mg/kg. *P. granatum, O. compactum*, *L. inermis*, *C. chamaerhaponticum*, and *C. siliqua* showed a percentage of ulcer formation inhibition of 78.6, 71.3, 65.4, 55.8, and 50.7 % respectively. The dose 250 mg/kg was less efficient with a lesion formation inhibitory effect ranging from 30.8 to 59.5%.

Actually, HCl/ ethanol model, widely used in assessing anti-ulcer activity of drugs, relies on the necrotizing potential of HCl and of ethanol that leads to the formation of lesions in the gastric mucosa[15,16]. It has been suggested that the mechanism underlying these lesions may (i) involve damage to the vascular endothelium causing edema formation and lifting[17], (ii) be due to the stagnation of gastric blood flow, resulting in the appearance of hemorrhage, necrosis, and tissue injury[16,18]; (iii) as well be due to the erosion of mucus membrane, the first defending layer of the stomach tissue[19,20]. All tested plants showed great preventive properties with this model. Moreover, *P. granatum* and *O. compactum* had a higher gastro-protective effect than omeprazole. This suggests that the components present in the extracts must be suppressing gastric damage.

Pylorus-ligation model

In pylorus ligation model, ulcers are developed due to accumulation of gastric acid and pepsin which leads to auto-digestion of gastric mucosa[21]. This model remains an important procedure that shows the possible changes of biochemical parameters of gastric content after submitting the animals to the various treatments[22]. It may then point out the target of action of testing plant extracts in their gastro-protective activity.

In this experimental model, the ulcer index was significantly reduced ($p < 0.001$) among plants-pretreated animals, whether at 250 or 500 mg/kg in comparison with negative control group (Table 3). Plants gastro-protective effect was relevant, ranging up to 79.8% of ulcer protection.

Pylorus ligation for 4 hours resulted in an accumulation of 2.8 ± 0.2 ml of gastric secretions for the control group (Table 4). Meanwhile, the volume of gastric secretions of pretreated rats was decreased significantly ($p < 0.001$) by *C. chamaerhaponticum* (50% of gastric secretion reduction), *C. siliqua* (46.4%) and *L. inermis* (42.8%) when compared with the

control value. The observed reductions in gastric juice volumes were similar to omeprazole's antisecretory effect (46.4% of secretion reduction vs. control) and higher than that of cimetidine's (7% of secretion reduction vs. control) (Table 4). A significant decrease in the total acidity was noticed only at the highest dose for all tested plants (percent of total acidity reduction range from 22.2 to 30.5 %), except for *C. chamaerhaponticum* which showed no significant modifications in both total acidity (8.3% total acidity decrease *vs.* control, $p > 0.05$) and gastric pH (31.8% pH increase vs. control, $p > 0.05$). However, plants pretreatments remain less efficient than the positive controls in reducing the total acidity (52.7 and 36.1% of total acidity decrease for omeprazole and cimetidine respectively) and in increasing the gastric juice pH (122.7 and 90.9% pH increase for omeprazole and cimetidine respectively) compared to the control.

All tested plants reduced significantly the volume of gastric acid juice. Moreover, *C. chamaerhaponticum, C. siliqua, P. granatum*, and *L. inermis* significantly reduced that volume in the same manner it was done by omeprazole, a proton pump inhibitor. Therefore, these plants may claim an antisecretory property.

NSAID-inducing-ulcer

The antiulcer activity of the studied plant was also assessed using aspirin as an NSAID-inducing-ulcer model. Results (Table 5) showed a great ulcer protection by testing positive controls, cimetidine and omeprazole (84.8 and 79.7 % respectively). The pretreatment with *O. compactum* methanol extract at 500 mg/kg inhibited significantly ($p < 0.001$) the ulcer formation in the gastric mucosa of aspirin treated rats. The inhibition rate reached 86.1% and was greater than that of the positive controls. On the other hand, the ulcer formation inhibitory effect of the methanol extracts of *C. chamaerhaponticum* and *L. inermis* at 500 mg/kg were also significant (69.6% of inhibition; $p < 0.001$) but less than *O. compactum,* cimetidine and omeprazole. The extracts of *C. siliqua* and *P. granatum* exhibited in this model the lowest ulcer inhibitory effect (51.9 and 50.6%, respectively; $p < 0.001$; 500 mg/kg).

Meanwhile, *O. compactum* was the most active in preventing gastric lesions induced by aspirin. Its preventive effect was greater than that of the positive controls. In this model, aspirin, a nonsteroidal anti-inflammatory drug (NSAID), blocks the function of cyclooxygenase enzyme (COX), which is essential for the production of protective prostaglandins[23-25]. Inhibition of prostaglandin synthesis diminishes mucus secretion and therefore increases the exposure of the gastric mucosa to acid attacks causing gastric injury. Consequently, plants with antiulcer activity in this model enhance the defensive factors, by increasing the mucin synthesis through activating prostaglandin production. This was probably the case for *O. compactum* through carvacrol, its main active component, as reported by Oliveira *et al*.[26]. Saponins found also in most of screened plants (Table 6) exhibit, like tannins, a gastro-protective effect[27]. The reported antioxidant ability of both[27, 28] as well the occurrence of other natural antioxidants (flavonoids, carotenoids, etc.) in the plant extracts (Table 6) would explain, to some extent, the observed antiulcer effect.

Lesion formation in gastric mucosa results from an imbalance between defensive mucosal factors and offensive acid-pepsin secretion as well as from free radical generation[29]. Therefore, plants with antiulcer properties may be active by targeting one or several of these factors. Plants may act as antacids by neutralizing the acidity of the gastric fluid or by

inhibiting the gastric acid secretion like cimetidine (a histamine H_2-receptor blocker) and omeprazole (a proton-pump inhibitor) effects. Plants may also act as gastric membrane protectors by preventing mucus layer erosion and/or by enhancing mucosal secretion through prostaglandin synthesis induction. They can as well counterbalance the free radical oxidant effect by scavenging them.

To define the way a plant acts as a gastric ulcer healing remedy, the resort to complementary models of induced ulcer may be very informative. Models of gastric ulcers induced by necrotizing agents give an insight into the aptitude of the plant to reduce offensive acid-pepsin secretion, while models of gastric ulcers induced by non-steroidal anti-inflammatory agents inform, in general, about the ability of the plant to enhance defensive mucosal factors.

The five tested medicinal plants (*P. granatum*, *L. inermis, O. compactum, C. siliqua, and C. chamaerhaponticum*), selected on the basis of their antiulcer reputation in Moroccan traditional medicine, exhibited a real gastroprotective activity by reducing significantly the ulcer lesion formation. They showed protective effects with different degrees according to the experimental model, the specie and the tested dose. The highest tested dose was the most efficient.

The etiology of the ulcer is complex and multifactorial. The gastroprotective action of the screened medicinal plants remains also complex and with multiple-targets. Nevertheless, although the exact mechanism of action of each plant was not elucidated in this study, our findings give evidence for the traditional use of these plants as antiulcer remedies. Moreover, their antisecretory properties are of great interest since patients who need aspirin therapy to prevent cardiovascular diseases may find in them natural alternative antacids that relieve aspirin side effects.

CONCLUSION

Obtained results showed that crude extracts of *C. siliqua, L. inermis, C. chamaerhaponticum, O. compactum and P. granatum* possess significant gastroprotective and antisecretory properties which prevent gastric ulceration induced by different necrotizing agents. Further work is required to elucidate the mechanism of action with chemically identified active principles.

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Table 1. Ethnobotanical data and some reported biological activities of selected Moroccan plants species used in treating ulcer disease

Plants species (Family)	Plant vernacular name	Used Part	Mode of preparation	Other traditional properties	Evidence- based properties
Centaurea chamaerhaponticum Ball. (Asteraceae)	Tafgha	Roots	Decoction, powder	Hepatic and gastrointestinal illness[30]	No data available
Ceratonia siliqua L. (Cesalpidaceae)	Kharroub	Fruits	Decoction, powder	To treat diarrhea and bronchitis. Its pods are reputed to be energizing[9,30]	Antioxidant properties[31] Anti-proliferative effect on hepatocellular carcinoma cell line[32]
Lawsonia inermis L. (Lythraceae)	Henna	Leaves	Infusion	Antipyretic, analgesic, and anti-inflammatory activities[8,9,30]	Antipyretic, analgesic, and anti-inflammatory[33,34] Antiulcer properties[35] Antitumor activity[36] Antileishmanial activity[37] Hepatoprotective potential[38]
Origanum compactum Benth. (Lamiaceae)	Zaatar	Aerial part	Infusion	Dysenteries, colitis, gastro-intestinal affections, gastric acidity and broncho-pulmonary affections[8,9,30]	Antibacterial[39] Antioxidant[40,41] Antifungal[42] Cytotoxic activity[41,43] Antimalarial properties[41]
Punica granatum L. (Punicaceae)	Roumman	Fruit peel	Decoction, powder mixed with honey	Ulcer, diarrhea and helminthiasis diuretic properties[9,30]	Anti-salmonellose property[44] Antidiarrheal potencies[45,46] Tyrosinase-inhibition activities[47] Antioxidant properties[47,48] Antiulcer potential[4,48]

Table 2. Effect of oral administration of cimetidine, omeprazole and plants extracts on ulcer lesions induced by HCl/ ethanol in rats (n=6/group)

Treatment	Dose (mg/kg)	Ulcer Index	Percentage of inhibition (%)
Control (HCl/ethanol; 1 ml)	-	2.267 ± 0.444	-
Cimetidine	100	0.350 ± 0.182**	84.56
Omeprazole	20	0.900 ± 0.400*	60.29
P. granatum	250	0.917 ± 0.221*	59.55
	500	0.483 ± 0.168**	78.69
L. inermis	250	1.067 ± 0.095*	52.93
	500	0.783 ± 0.252*	65.46
O. compactum	250	1.300 ± 0.181	42.65
	500	0.650 ± 0.123**	71.32
C. siliqua	250	1.117 ± 0.264*	51.47
	500	1.567 ± 0.219	30.87
C. chamaerhaponticum	250	1.100 ± 0.179*	51.47
	500	1.000 ± 0.137*	55.88

Results are mean ± S.E. Statistical comparison was performed using Student's *t*-test, *: $p < 0.05$; **: $p < 0.01$; *** $p < 0.001$.

Table 3. Effect of oral administration of cimetidine, omeprazole and plants extracts on ulcer lesions induced by pylorus ligation in rats (n=6/group)

Treatment	Dose (mg/kg)	Ulcer Index	Percentage of inhibition (%)
Control	-	2.233 ± 0.098	-
Cimetidine	100	0.650 ± 0.173***	70.89
Omeprazole	20	0.800 ± 0.057***	64.17
P. granatum	250	0.750 ± 0.05***	66.41
	500	0.683 ± 0.094***	69.41
L. inermis	250	1.000 ± 0.110***	55.21
	500	0.450 ± 0.152***	79.84
O. compactum	250	1.000 ± 0.137***	55.21
	500	0.917 ± 0.101***	58.93
C. siliqua	250	0.950 ± 0.126***	57.45
	500	0.800 ± 0.159***	64.17
C. chamaerhaponticum	250	1.350 ± 0.148***	39.54
	500	0.683 ± 0.087***	69.41

Results are mean ± S.E. Statistical comparison was performed using Student's t-test, *: $p < 0.05$; **: $p < 0.01$; *** $p < 0.001$.

Table 4. Effect of oral administration of cimetidine, omeprazole and plants extracts on gastric secretion parameters in pylorus-ligated rats (n=6/group)

Treatment	Dose (mg/kg)	Gastric pH	Gastric secretion volume (ml)	Total acidity mEq/L/100g	Percentage of inhibition (%)
Control	-	2.2 ± 0.5	2.8 ± 0.2	36 ± 2.0	-
Cimetidine	100	4.2 ± 0.2***	2.6 ± 0.7	23 ± 3.0 **	7.14
Omeprazole	20	4.9 ± 0.9***	1.5 ± 0.2***	17 ± 2.0***	46.43
P. granatum	250	2.3 ± 0.2	2.5 ± 0.2	34 ± 1.0	10.71
	500	3.1 ± 0.3*	1.7 ± 0.1***	28 ± 1.7*	39.28
L. inermis	250	3.0 ± 0.2	2.2 ± 0.2	32 ± 2.0	21.43
	500	4.0 ± 0.1***	1.6 ± 0.1***	28 ± 1.0**	42.86
O. compactum	250	2.4 ± 0.1	2.5 ± 0.5	33 ± 1.0	10.71
	500	3.1 ± 0.3**	2.1 ± 0.2*	27 ± 1.0**	25.00
C. siliqua	250	3.0 ± 0.2	1.8 ± 0.3**	35 ± 3.0	35.71
	500	3.3 ± 0.4**	1.5 ± 0.1***	25 ± 2.1**	46.43
C. chamaerhaponticum	250	2.8 ± 0.2	1.8 ± 0.3*	39 ± 2.0	35.71
	500	2.9 ± 0.4	1.4 ± 0.1***	33 ± 3.0	50.00

Results are mean ± S.E. Statistical comparison was performed using Student's *t*-test, *: $p < 0.05$; **: $p < 0.01$; *** $p < 0.001$.

Table 5. Effect of oral administration of cimetidine, omeprazole and plants extracts on ulcer lesions induced by non-steroidal anti-inflammatory drug (aspirin) in rats (n=6/group)

Treatment	Dose (mg/kg)	Ulcer Index	Percentage of inhibition (%)
Control (aspirin)	400	1.317 ± 0.098	-
Cimetidine	100	0.200 ± 0.036***	84.81
Omeprazole	20	0.267 ± 0.061***	79.72
P. granatum	250	0.750 ± 0.076**	43.05
	500	0.650 ± 0.106***	50.64
L. inermis	250	0.500 ± 0.175**	62.03
	500	0.400 ± 0.173***	69.62
O. compactum	250	0.550 ± 0.150**	58.23
	500	0.183 ± 0.065***	86.10
C. siliqua	250	0.917 ± 0.087*	30.37
	500	0.633 ± 0.115**	51.93
C. chamaerhaponticum	250	0.717 ± 0.117**	45.55
	500	0.400 ± 0.129***	69.62

Results are mean ± S.E. Statistical comparison was performed using Student's *t*-test, *: $p < 0.05$; **: $p < 0.01$; *** $p < 0.001$.

Table 6. Phytochemical screening of aqueous and methanolic extracts

	C. siliqua	*L. inermis*	*O. compactum*	*P. granatum*	*Z. lotus*	*C. chamaerhaponticum*
Aqueous extracts						
Anthocyans	-	-	-	-	-	-
Leucoanthocyans	+	++	+	+++	++	-
Tannins	+++	+++	+++	+++	++	-
Flavonoids	-	-	-	+	-	+
Saponins	+++	++	+++	+++	++	+++
Alkaloids	-	-	-	+	-	+
Terpenes and sterols	-	+	-	-	-	+
Methanolic extracts						
Tannins	+++	+++	+++	+++	++	++
Flavonoids	+	-	-	-	-	+
Saponins	++	+++	+	++	+	+++
Coumarins	-	+++	-	-	-	-
Alkaloids	-	-	-	+	-	+
Terpens and sterols	-	+	+	-	+	+