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ORIGINAL ARTICLE

Comparative efficacy of chamomile against omeprazole in aspirin-induced gastric ulcer in rats

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Abstract The aim of the study was to compare the efficacy of chamomile versus omeprazole in the treatment of aspirin-induced gastric ulcer in rats. Animals were randomly assigned into three groups A, B and C (n=10 each). Aspirin (200 mg/kg, intragastric (i.g.)) was administered for three consecutive days, and then, two animals from each group were euthanized and formed the aspirin-induced gastric ulcer control group. The remaining animals (n=8 in each group) were administered with the following treatments: normal saline 9 % (0/5 mL, i.g.) (group A), omeprazole (2.3 mg/kg, i.p.) (group B) or chamomile decoction (25 mL/kg, i.g.) (group C) daily for 2 weeks. Histological analysis of tissue harvested from rats in groups B and C showed no significant difference, since ulcers in both treatment groups were completely cured. The results of this study suggest that chamomile could be used for the treatment of nonsteroidal anti-inflammatory drug-induced ulcers as an inexpensive alternative to omeprazole.

Keywords Aspirin · Chamomile · Nonsteroidal anti-inflammatory drug-induced ulcers · Omeprazole

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Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) possess excellent analgesic, anti-pyretic and anti-inflammatory effects and are widely accepted in daily practice for the treatment of arthritis (Dehpour et al. 1994), headache (Wiklund 1999) and joint and muscle discomfort associated with various disorders (Lacy 2001). Despite their good efficacy, NSAIDs are associated with gastrointestinal (GI) toxicity and gastroduodenal ulcer formation (Saggioro et al. 1991; Wiklund 1999), which may be accompanied by anaemia from the resultant blood loss (Dehpour et al. 1995). NSAIDs are considered the most important class of drugs which may affect the GI tract; these GI side effects may be seen in 2–30 % of patients (Handerson and Lander 2000). Daily use of NSAIDs significantly increases the risk of ulcer disease 10- to 20-fold (Graham 1989). Of patients on NSAID therapy for only 1–2 weeks, 60–100 % develop mucosal haemorrhage and superficial erosions (Raskin 1999).

Ancient Greek physicians described babone or chamomile as having strong healing properties especially of gastric ulcers. Although the anti-ulcer effect of chamomile extract is well established, there are no studies evaluating its efficacy in comparison with omeprazole. As an inexpensive agent with few side effects in the treatment of NSAID-induced ulcers, this study was conducted to compare the effect of chamomile decoction with those of omeprazole in rats.

Materials and methods

Animals

Thirty Wistar albino rats, approximately 2 months of age and weighing 150–200 g, were obtained from the Pasture Institute.

Animals were maintained under standard laboratory conditions with alternating light and dark cycles of 12 h each. During the study, they had access to standard laboratory pellets and tap water *ad libitum* and were housed in suitable and adequate conditions that fulfil the animal house guidelines.

Drugs

Chamomile (*Chamaemelum nobile*) root was purchased from a local herbal store. The plant was identified by a pharmacognosy professor. Aspirin (Jalinos Drug Company, Iran) and omeprazole (Exir Drug Company, Iran) were used as comparative agents.

Preparation of chamomile decoction

The dose of chamomile (babone) root was chosen depending on the literature (Al Hashem and Saeedi 1568). Hot water extract of the dried root administered by gastric intubation to mice at a dose of 1.589 g/kg was found to be inactive on stress-induced ulcers (Yamazaki and Shirota 1981). So, a higher dose (2.5 g/kg) was chosen and prepared. Five grams of finely chopped dried chamomile root was soaked in 100 mL of distilled water and boiled for about 30 min to 50 mL. After boiling, the preparation was left to steep for 10 min and then filtered into a clean container. The concentration of the final solution was 100 mg/mL. The decoction was prepared using a relatively longer extraction time (30 min) and a cooling time of 10 min, as recommended by the Soviet pharmacopoeia (USSR State Pharmacopoeia 1987). The freshly prepared (Hanrahan 2001) decoction of chamomile root (100 mg/mL) was given to the rats in aliquots of 25 mL/kg by intragastric (i.g.) route, corresponding to a dose of 2.5 g/kg.

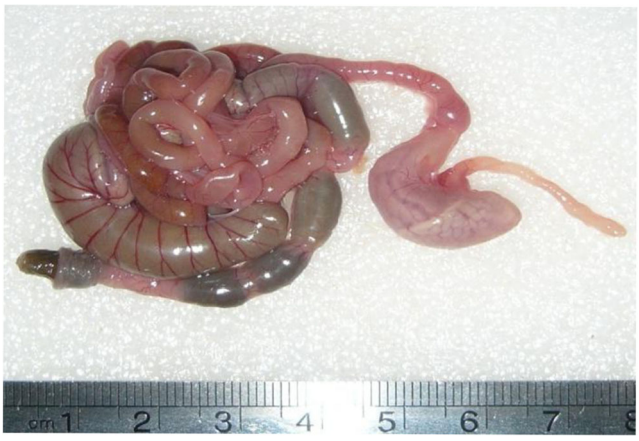

Fig. 1 **a** Autopsy of animals

Table 1 Grade of lesions based on the scoring system of Schmassmann et al. (1998)

Degree of ulceration	Score
Healthy tissue	0
Inflammation and haemorrhage	1
Erosion and haemorrhage	2
Erosion and middle ulcer	3
Severe ulcer and bleeding	4

Vehicle

The chamomile decoction was prepared with distilled water. Aspirin was dissolved in 0.2 M HCl (1.5 mL for each 100 mg of drug). Omeprazole was dissolved in its specific solvent solution ready for injection (Stewart et al. 1987; Kastrup et al. 1998).

Treatment groups

Animals were randomly allocated into three groups (n= 10), and gastric ulcerations were induced in all animals according to the method described by Asano et al. (1990) by i.g. aspirin (200 mg/kg) administration for three consecutive days. After 3 days, two animals were terminated from each group to act as ulcer formation controls. Experiments were initiated following a 24-h fasting with water ad libitum. The remaining animals underwent the following treatments:

Group A: Saline (0.9 %NaCl; 0.5 mL, i.g.)
Group B: Omeprazole (2.3 mg/kg, i.p.)
Group C: Chamomile decoction (2.5 g/kg, i.g.)

Histopathological examination

Animals in all groups were sacrificed by a lethal dose of ketamine on the 14th day of the experiment. To

Table 2 Grade of lesions of the four treatment groups

	Aspirin	Group A	Group B	Group C
Case 1	4	4	1	1
Case 2	4	4	0	1
Case 3	3	4	1	2
Case 4	4	2	1	1
Case 5	4	4	2	2
Case 6	3	3	1	2
Case 7		3	2	1
Case 8		4	2	2

assess the gastric lesions produced by aspirin, the stomach, plus part of the duodenum, was removed by laparotomy from all animals (Eastwood and Quimby 1982) (Fig. 1). The stomach of each animal was opened along the greater curvature, emptied of its contents, washed with water and stored in 10 % formalin solution (Bauer et al. 1986; Kuwayama et al. 1991; Segmai et al. 1996). For light microscopic evaluation, gastric tissue samples were fixed in 10 % formaldehyde and processed routinely for embedding in paraffin. Paraffin sections were stained with haematoxylin and eosin to indicate histological degeneration (Wang et al. 1989; Kuwayama et al. 1991). The size of lesions was measured using a light microscope and graded according to the scoring system of Schmassmann et al. (1998) (Tables 1 and 2).

Statistical analysis

All results were expressed as mean ± standard deviation. All the statistical analyses were done by the Fisher's exact test and $P<0.05$ was considered significant.

Results

Aspirin-induced gastric ulcer formation

Aspirin-induced gastric ulcer formation was confirmed by histopathological examination (Fig. 2).

Treatment group

In the treatment group, histopathological examinations showed no significant difference between chamomile decoction and omeprazole regarding aspirin-induced ulcer treatment; ulcers in all treatment groups were completely cured (Figs. 3 and 4). The results of this study suggest that *C. nobile* can be used for the treatment of NSAID-induced ulcers as an inexpensive alternative to omeprazole.

Discussion

This study was undertaken to investigate the healing effect of chamomile versus omeprazole on aspirin-induced gastric ulcers. The outcome showed that chamomile is just as effective as omeprazole but has fewer complications as an herbal medicine compared to NSAID drugs.

In 2010, Atsushi Oyagi and his group evaluated the protective effects of a gastrointestinal agent containing Korean red ginseng (KRG) on mice. KRG is a ginseng that has been cultivated and aged for 4–6 years or more and goes through an extensive cleaning, steaming and drying process. It contains more than 30 types of saponin components and has been reported as having various biological properties, such as anti-fatigue action, immune restoration and neurovegetative effect. The purpose of their study was to assess the effects of a KRG-containing drug (KRGCD) on mouse model of gastric ulcers. KRGCD (100 and 300 mg/kg, p.o.) significantly

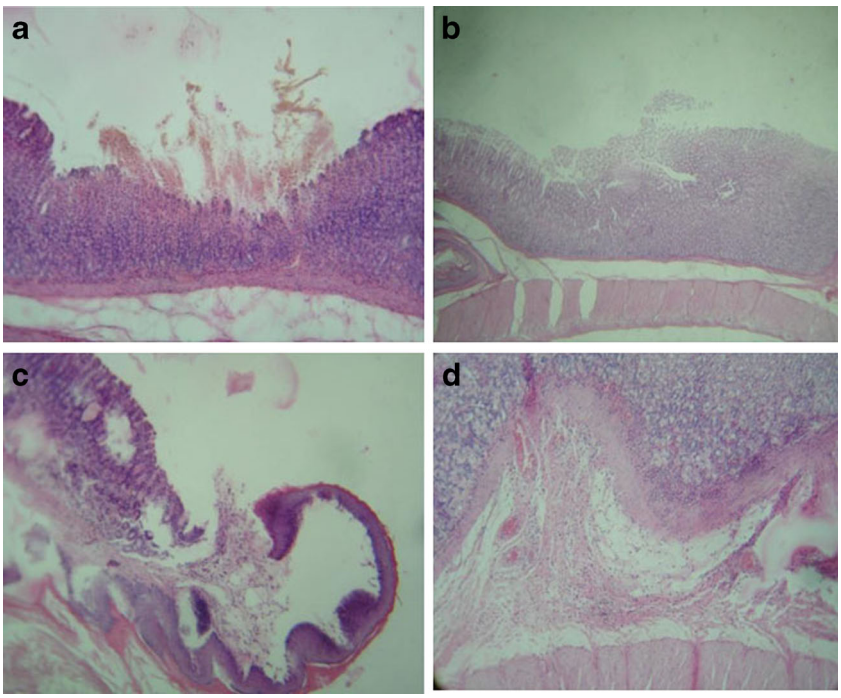

Fig. 2 Severe gastric ulcer formation observed in rats administered with aspirin (200 mg/kg, i.g.). **b** Minimal changes observed at the gastric mucosa of the chamomile-treated group. **c** Migration of inflammatory cells and hyperaemia in the glandular gastric margin with mechanical gastric changes. **d** Migration of inflammatory cells and hyperaemia in the gastric mucosa

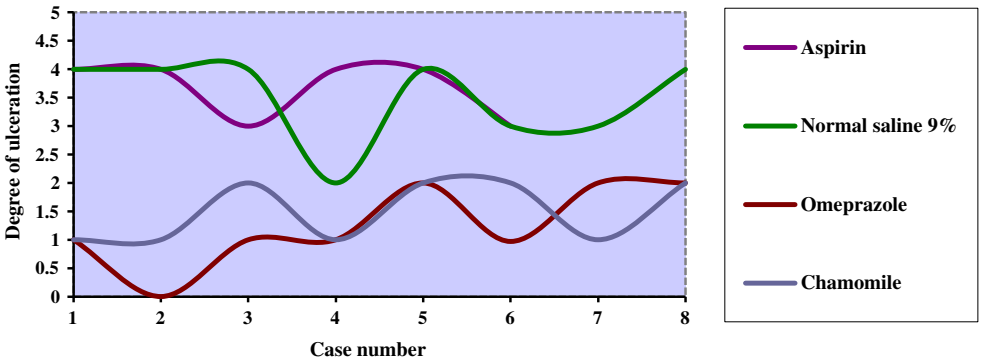

Fig. 3 Line graph presentation of the degree of ulcer in rats administered with aspirin, normal saline 9 %, omeprazole and chamomile

decreased ethanol- and indomethacin-induced gastric ulcers compared with the vehicle-treated (control) group and also decreased the level of thiobarbituric acid-reactive substance and increased gastric mucosal blood flow when compared with the control group. These results suggest that the gastroprotective effects of KRGCD on a mouse ulcer model can be attributed to its ameliorating effect on oxidative damage and improving effect of gastric mucosal blood flow.

In a separate study, the influence of cyclodextrin complexation with NSAIDs on NSAID/cold stress-induced gastric ulceration in rats was evaluated by Ibrahim and colleagues in 2010. The aim of their study was to evaluate the ability of β-cyclodextrin (β-CD) or hydroxypropyl β-cyclodextrin (HP-β-CD) to ameliorate the induction of gastric ulcers by a NSAID, indomethacin or piroxicam, in rats exposed to restraint and hypothermic stress at 4 °C. Rats treated with indomethacin or piroxicam in the presence of either β-CD or HP-β-CD exhibited normal tissues, suggesting that β-CD and HP-β-CD can act as protective agents against gastrointestinal disorders produced by restraint and cold stress, even with the added stress of either indomethacin or piroxicam.

In a separate study, Al-Hashem investigated the gastroprotective effects of aqueous extract of *Chamomilla recutita* against ethanol-induced gastric ulcers. However, daily treatment of rats with the maximum angiotensin-converting enzyme (ACE) dose led to an increase in GSH levels. Histological examination revealed that ACE treatment alleviated or completely resolved ethanol-induced degenerative alterations, including disorganization of cell nuclei and gland morphology with erosion in the gastric mucosa and interrupted muscularis mucosa.

This study provides evidence for the regulation of ACE-mediated gastroprotection against ethanol-induced ulceration by GSH. Long-term usage of NSAIDs has a prevalence for complications associated with gastric ulcers; chamomile as a natural medicinal herb has the same effects but without complications of conventional chemical drugs such as omeprazole.

Conclusion

There is a growing interest in traditional, cheaper, herbal-based medicines, which are seen to have fewer side effects than some conventional therapeutic drugs. However, robust scientific data on the efficacy of these herbal- and plant-based medicines are often lacking.

This study sets out to investigate how the long-term usage of NSAIDs, and the resulting prevalence of gastric ulcers, might be ameliorated by using the herbal medicine chamomile. Our results show that the efficacy of chamomile is comparable with the conventional NSAID, e.g. omeprazole, but without the reported side effects.

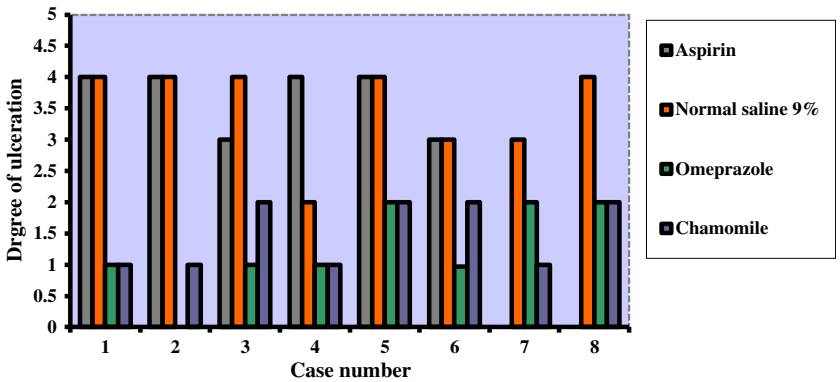

Fig. 4 Bar graph presentation of the degree of ulcer in rats administered with aspirin, normal saline 9 %, omeprazole and chamomile

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