The effect of *Matricaria Chamomilla* on the treatment of ibuprofen-induced gastric ulcers in male rats

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Original Article

Abstract

Introduction: Formation of gastric ulcer is a multifactorial process so that vascular changes, mucous secretion, gastric acid and gastrointestinal tract mucous biochemistry are involved in gastric ulcers. Despite therapeutic properties, ibuprofen as a non-steroidal anti-inflammatory drug (NSAID) can cause mucosal lesions in the stomach. In this study, the effect of *Matricaria Chamomilla* on the treatment of ibuprofen-induced gastric ulcers in animal models was examined.

Methods: In this experimental study, 18 male Wistar rats were divided into three groups of six rats. The gastric ulcer group received normal saline after inducing ulcers. Two experimental groups received *Matricaria Chamomilla* powder dissolved in normal saline after inducing ulcers. The animals were starved for 48 hours and then a single dose of ibuprofen (400mg/kg) was administrated orally. The animals were followed for two weeks to induce gastric ulcers. After inducing ulcers, the animals were treated orally with two doses of *Matricaria Chamomilla* (250 and 500mg/kg) for 10 days. At the end of the study, the animals were evaluated in terms of the number and extent of gastric ulcer. The data were analyzed with the help of SPSS using ANOVA and the nonparametric Kruskal-Wallis H test. $P \leq 0.05$ was considered as the significance level.

Results: The results showed that the mean number and surface area of gastric ulcers in the group receiving 500mg/kg of *Matricaria Chamomilla* were significantly decreased in comparison with the gastric ulcer group ($P < 0.01$). However, no significant difference was found between the group receiving 250mg/kg of *Matricaria Chamomilla* and the gastric ulcer group.

Conclusion: *Matricaria Chamomilla* caused a dose-dependent gastric ulcer healing effect in animals.

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Introduction:

Peptic ulcers, especially gastric ulcers may be due to increased acid secretion or for different reasons such as non-steroidal anti-inflammatory drugs (NSAID), alcohol consumption, long hunger, poor eating habits and intense and continuous stresses. Non-steroidal anti-inflammatory drugs are of the most prescribed antibiotics in the world. Many

studies show a relationship between consumption of NSAIDs and the incidence of gastric ulcers in western societies (1,2).

Bleeding and gastric mucosal lesions are the most common side effects while taking NSAIDs as one of the main problems in medical science so that the non-steroidal anti-inflammatory drugs are the second cause of peptic ulcers after Helicobacter pylori (3).

Treatment of gastric ulcers by chemical drugs such as omeprazole, metronidazole and ranitidine is costly and is associated with side effects and problems such as an autoimmune phenomenon and the potential recurrence of lesions after treatment discontinuation. For this reason, there is a massive effort to find most effective natural ingredients and herbs for the treatment of gastric ulcers (4).

Matricaria Chamomilla is among medicinal plants in traditional medicine with various effects. Today, *Matricaria Chamomilla* is used over the world to treat a variety of diseases including the treatment of inflammation of the skin (5) and tumors (6).

Matricaria Chamomilla is used in traditional medicine as a pain reliever, antispasmodic and anti-inflammatory drug and for the treatment of skin diseases (psoriasis and eczema), bronchitis and the common cold, cough, fever, wound healing and gastrointestinal problems (7,8).

According to the results of some research on laboratory animals, mucilage and phenolic acids found in *Matricaria Chamomilla* play a substantial role in appetite stimulation in addition to reducing inflammation and spasms.

Matricaria Chamomilla extract is composed of 120 chemicals including chamazulenes, flavonoids and coumarins. The most important active components in *Matricaria Chamomilla* include chamazulene, apigenin and bisabolol (9). According to literature, chemical components in the *Matricaria Chamomilla* extract have anti-inflammatory and antibacterial effects as well as antioxidant activity (10,11). *Matricaria Chamomilla* is rich in flavonoids as effective antioxidants in neutralizing oxygen radicals (12). According to Karbalaeidoust *et al.* (13), oral intake of *Matricaria Chamomilla* extract at a dose of 400mg/kg in rats with ethanol-induced gastric ulcers improved the number and area of ulcers as well as the therapeutic index. Therefore, in this study, the effect of oral intake of 250 and 500mg/kg of *Matricaria Chamomilla* powder on ibuprofen-induced gastric ulcers in rats is investigated (14).

Methods:

In this study, male Wistar rats weighing 140±20g were prepared from the animal house of Shahid Bahonar University and were kept in the same center. The animals were kept at a constant temperature of 22±2°C throughout the day during 12 hours of light and 12 hours of darkness. Food and water were provided without limitation. A total number of 18 rats were randomly divided into 3 groups of 6 rats including the gastric ulcer group and two experimental groups receiving 250 and 500mg/kg of *Matricaria Chamomilla*. The rats were tested as follows:

The animals were starved for 48 hours in special cages with wire floor to induce ulcers. During this period, the animals were fed with water containing 2.0% NaCl and 2% sucrose to prevent dehydration (22). After this period, animals received orally (gavage) a single dose of 400mg/kg ibuprofen (Daroupakhsh Co.). The animals were followed for two weeks to induce ulcers (Figure 1).

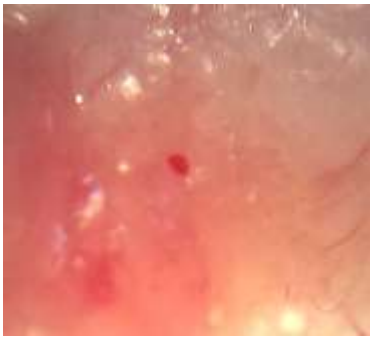

Figure 1. The ulcer caused by ibuprofen in the stomach of rats

After inducing ulcers in the gastric ulcer group, the animals received orally 2ml normal saline daily. The animals in the *Matricaria Chamomilla* 250 group received orally 250mg/kg of *Matricaria Chamomilla* powder in normal saline daily. The

rats in the *Matricaria Chamomilla* 500 group received orally 500mg/kg of *Matricaria Chamomilla* daily.

Gastric ulcer examination: After removal of the stomach from the body (Figure 2), it was cut from the large curve. Then, it was washed by normal saline and placed on the glass slides. The surface area and the number of ulcers were determined using a light microscope with a calibrated lens. Finally, the therapeutic index was calculated for each group of animals.

Figure 2: The stomach of normal rat

The data obtained from different groups were analyzed with the help of SPSS using ANOVA, Tukey post-test and the nonparametric Kruskal-Wallis H test. $P \leq 0.05$ was considered as the significance level. Data were expressed as mean±SEM.

Results:

At the end of the treatment period, the number of animals in each group with gastric ulcers was determined and shown in Table 1.

The mean surface area and the number of ulcers in the groups receiving *Matricaria Chamomilla* and in the gastric ulcer group were determined and the results are shown in Table 2. The therapeutic index was calculated for different groups as shown in Table 2. The therapeutic index is calculated by the following formula:

$$\text{Therapeutic index} = \frac{\text{The number of ulcers in the intervention group} - \text{The number of ulcers in the control group}}{\text{The number of ulcers in the control group}}$$

Table 1. The number of animals in each group with gastric ulcer at the end of the experimental period

Group	The number of animals with gastric ulcer	Percentage of animals with gastric ulcer (%)
Ulcer	6	100
Matricaria Chamomilla (dose: 250 mg/kg)	6	100
***Matricaria Chamomilla* (dose: 500 mg/kg)**	4	66

Table 2. The mean number and size of gastric ulcers (mm^2) and therapeutic index in the studied groups

Group	Number of ulcers (Mean±SEM)	Ulcer area (mm2) (Mean±SEM)	Therapeutic index (TI)
Ulcer	3.8±0.4	19.8±3.6	0
Matricaria Chamomilla (dose: 250 mg/kg)	2.5±0.5	16.3±1.5	34%
***Matricaria Chamomilla* (dose: 500 mg/kg)**	**1.1±3.3	***4.6±1.5	71%

** a significance level of $P<0.01$ with ulcers *** a significance level of $P<0.001$ with ulcers and at dose of 250 mg/kg.

Conclusion:

According to the results, the use of *Matricaria Chamomilla* at a dose of 500 mg/kg in animals with gastric ulcers reduced the ulcer size significantly in comparison with the gastric ulcer group ($P<0.001$). The ulcer size in the animals receiving a dose of 500 mg/kg showed a significant decrease in comparison with those receiving a dose of 250 mg/kg ($P<0.01$). There was not a significant difference between the number of ulcers in

animals receiving 250 and 500mg/kg of *Matricaria Chamomilla*. The use of *Matricaria Chamomilla* at a dose of 500 mg/kg significantly decreased the number and surface area of ulcers and increased the therapeutic index as compared with the gastric ulcer group. *Matricaria Chamomilla* at a dose of 250mg/kg reduced gastric lesions but it was not statistically significant. In a study by Amr *et al.*, after ulcer induction by ethanol, *Matricaria Chamomilla* extract was orally administered for 7 days at different doses (100, 200, 300 and 400mg/kg). The results showed a decrease in the surface area of gastric ulcers at the highest dose as compared to lower doses. This is consistent with our results (13). The results also showed that *Matricaria Chamomilla* reduces gastric secretion which can improve gastric ulcers (15-16), but it was not measured due to the limitation of our study.

Literature confirms the presence of flavonoid compounds in *Matricaria Chamomilla* with antioxidant properties. Nowadays, flavonoids are known as an important class of natural antioxidants due to numerous OH functional groups in their structure and their ability to neutralize oxygen free radicals (17,18). Flavonoids in *Matricaria Chamomilla* are of the flavonol and flavone types and are found in free form or as glycosides. Luteolin, as a component of *Matricaria Chamomilla,* is able to eliminate ROS generated in the process of inflammation in inflamed lung tissue where ROS increases (19). The effect of *Matricaria Chamomilla* on gastric ulcer healing may be due to its antioxidant effect. The effect of *Matricaria Chamomilla* extract on acute experimental gastric ulcers in rats has been reported. According to Khayyal *et al.*, apiaceae plants like oregano, lemon balm and *Matricaria Chamomilla* alone or with angelica, mint and licorice show an anti-ulcer activity (20).

Due to the involvement of oxidative stress mechanism in the pathogenesis of NDAIDs-induced gastric ulcers (2), an increase in the antioxidants level with the consumption of *Matricaria Chamomilla* may have a significant role in ulcer healing (21-24).

According to the results of this study, the beneficial effect of *Matricaria Chamomilla* at a dose of 500 mg/kg is confirmed for the treatment of ibuprofen-induced gastric ulcers. *Matricaria Chamomilla* at a dose of 250mg/kg caused ulcer healing but the effect was not significant and further studies are needed to evaluate its mechanism.

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بررسی اثر گیاه بابونه بر درمان زخم معده ناشی از ایبوپروفن در موش صحرایی نر

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چکیده

مقدمه: *ایجاد زخم معده فرآیندی چند عاملی است که در پیدایش آن تغییر عروق، ترشح مخاطی و اسید معده و بیوشیمی مخاط لوله‌ی گوارش دخیل است. ایبوپروفن به عنوان داروی ضدالتهاب غیراستروئیدی (NSAID) با وجود خواص در مانی، می‌تواند باعث آسیب‌های مخاطی در معده شود. در این مطالعه سعی شده است تا اثر گیاه بابونه در درمان زخم معده ایجاد شده توسط ایبوپروفن در مدل حیوانی مورد بررسی قرار گیرد.*

روش کار: *در این مطالعه تجربی، ۱۸ سر موش صحرایی نر نژاد ویستار به ۳ گروه ۶ تایی تقسیم شدند. گروه زخم معده که پس از ایجاد زخم، نرمال سالین دریافت کرد و دو گروه تجربی بعد از ایجاد زخم پودر بابونه حل شده در نرمال سالین دریافت کردند. حیوانات ۴۸ ساعت گرسنه نگه داشته شدند و سپس تجویز ایبوپروفن با تک دوز ۴۰۰mg/kg از طریق خوراکی صورت گرفت. حیوانات دو هفته پیگیری شدند تا زخم معده ایجاد شد. پس از ایجاد زخم حیوانات با دو دوز ۲۵۰ mg/kg و ۵۰۰ گیاه بابونه به مدت ۱۰ روز از طریق خوراکی تحت درمان قرار گرفتند. در پایان مطالعه، حیوانات از نظر تعداد و وسعت زخم معده مورد بررسی قرار گرفتند . داده‌های به دست آمده از گروه‌های مختلف با استفاده از نرم‌افزار آماری SPSS و آزمون ANOVA و پس آزمون Tukey و همچنین آزمون غیر پارامتری Kruskal-Wallis H مورد بررسی قرار گرفتند و $P \leq 0.05$ به عنوان سطح معنی‌داری در نظر گرفته شد.*

نتایج: *نتایج بدست آمده از این تحقیق نشان می‌دهد که میانگین تعداد و مساحت زخم‌های معده در گروه دریافت کننده بابونه با دوز ۵۰۰ در مقایسه با گروه زخم معده به طور معنی‌داری (P< ۰/۰۱) کاهش داشت، ولی گروه دریافت کننده دوز ۲۵۰ در مقایسه با گروه زخم معده معنی‌دار نبود.*

نتیجه‌گیری: *گیاه بابونه به صورت وابسته به دوز باعث بهبود زخم معده در حیوانات می‌شود.*

کلیدواژه‌ها: *بابونه، ایبوپروفن، زخم معده، موش صحرایی*

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