Hydroalcoholic Extract of *Matricaria cha*momilla effectively reduces inflammation induced by xylene in rat

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Abstract

Introduction: Due to side effects of antiinflammatory drugs such as dexamethasone and indomethacin, there is a less tendency to use them. On the other hand, the use of medicinal plants has been common in the treatment of inflammation since ancient times and also, using of the plants is increasing. Present research investigated the antiinflammatory effect of the hydroalcoholic extract of capitols of *Matricaria chamo*milla (*M. chamo*milla) in rat.
Materials and methods: The hydroalcoholic extract of capitols of *M. chamomilla* [(at the doses of 500, 1000 and 1500 mg/kg BW (body weight)] and dexamethasone and indomethacin (at the dose of 15 mg/kg BW) were intraperitoneally injected to the rats. The weights of the ears of animal after induced inflammation by xylene and then, after the mentioned treatments were set as indices of antiinflammatory effects.
Results: Hydroalcoholic extract of the capitols of *M. chamomilla* at the dose of 1500 mg/kg BW significantly reduced the xylene induced inflammation in the rats ($P<0.01$). Also, hydro-alcoholic extract of the herb at the doses of 500, 1000, and 1500 mg/kg BW significantly reduced the acetic acid induced inflammatory pain ($P<0.001$).
Conclusion: The extract of the capitols of *M. chamomilla* have antiinflammatory effects that is comparative to the antiinflammatory effects of traditional antiinflammatory drugs such as dexamethasone and indomethacin.

Keywords: Matricaria chamomilla, Inflammation, Rat

Introduction

Inflammation is a local response of tissue to injury or infection (1, 2). Generally, the inflammatory diseases include osteoarthritis, lupus erythematosus, asthma and rheumatic disorders such as arthritis and rheumatic fevers (3). The inflammation, especially its chronic type is among the common complication of many diseases leading to immunodeficiency condition in the body (4).
Following tissue damage in bacterial infections, the inflammatory mediators are released from mast cell. The inflammatory mediators include histamine, quinines, and prostaglandins and leukotrienes many of them acting as chemotaxis factors. Chemotaxis factors are produced in

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damaged area and cause migration of white blood cells to that area. The definite symptoms of inflammation include heat, pain, and swelling. These symptoms are resulted from increased blood flow and vascular permeability in affected area. These symptoms help to phagocytic white blood cells to reach the general circulation of body and then enter into affected tissue (1, 2). The long-term use of medications that are used to suppress inflammatory reactions will lead to complication such as ulcers of stomach and intestines and subsequently anemia (3). Furthermore, some plants also have antiinflammatory compounds that can be used in treating many types of chronic inflammations, skin infections, rheumatoid pains, fever and infections (5). Chamomile is one of the important herbs in herbal medicine (6).

Chamomile with the scientific name, *Matricaria chamomilla* (*M. chamomilla*), is one type of chicory or Asteraceae star flower. Chamomile is a yearling, short stature and durable with a fragrant smell that grows in meadows and sandy lands. This has simple or branched and more or less hairy stem and small flowers like pearl. Egyptians, Romans and Ancient Greeks used chamomile to treat sunstroke, fever and colic (7, 8).

Nowadays, chamomile is used to treat many diseases including spasticity (9) and tumor (10). Typical cases of the using chamomile in traditional medicine include the use of chamomile as relieving pain, treating diseases of the skin (psoriasis, eczema), bronchitis and cold, cough, fever, healing wound and treatment of digestive problems. Extract of this plant due to its carminative and antispasmodic properties, is used for digestive disorders and stomach ulcer (7, 8).

Chamomile extract is blue-colored, due to the presence of lipophenolic compound called camazoline (11). Chamomile contains compounds such as coumarin phytosterol, flavonoid and acrolein (14-12). The high concentrations of coumarin are converted into 3 and 4-coumarin epoxide in rat which is toxic for kidneys and lungs and leads to death. However, coumarin is metabolized and converted into a less toxic substance called 7-hydroxy coumarin in humans (15, 16). Flavonoids found in chamomile have antiviral, anti-allergic, anti-cancer and anti-oxidative effect (17-20). Flavonoids also prevent the oxidation of low density lipoprotein (LDL) and thus, restrict formation of atherosclerotic plaques (21). In the present research, at first inflammation was induced by using xylene and acetic acid in experimental matured male rats and then, antiinflammatory effects of this herb were compared with the common antiinflammatory drugs namely, dexamethasone and indomethacin.

Materials and methods

For the preparation of extract, capitols of chamomile herb (*Matricaria chamomilla L.*) were collected from Ilam province in Iran and after identifying the exact taxonomic species, the capitols was dried at 25°C in the shade and then powdered by mechanical mill. The extraction then was carried out by using a rotary machine. After that, 50g of the capitols powder was weighed and dissolved in 320 ml of 96% ethanol and 80 ml of distilled water in a soaked Scott and incubated in an incubator with shaking (140 rpm) at 34 °C for 72 hours. The obtained solution was passed through a Whatman 1 filter paper, then, the ethanol fraction of the solution was evaporated from herbal extract by using a rotary machine equipped with a vacuum pump. The obtained extract was placed for 5 days into oven. The condensed extract of herb was maintained into a sterile Falcon at 4 °C (22). Experimental adult male small rats (Wistar race) with weight limit of 150 to 200 grams were purchased from Iran Pasteur Institute and maintained in experimental good conditions with 23 ± 2 °C controlled temperature, light cycle of 12 h light and 12 hours of darkness as well as the relative humidity of 40-60%.

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Animals had continuous access to water and food. Each animal only was tested once. Animals were intraperitoneally treated with herbal extract in different doses, dexamethasone and indomethacin drugs and physiological serum. The treated volume of substance was 0.2 ml in all groups.

In each groups, 10 rats that were randomly selected, were investigated. The studied groups were as follow:

The control and sham groups which treated by physiological serum (saline)

The experimental groups 1, 2, and 3 which received the herbal extract at doses of 500, 1000, 1500 mg/kg BW, respectively

The experimental groups 4 and 5 which received dexamethasone and indomethacin at a dose of 15 mg/kg BW

Antiinflammatory test of xylene: In this experiment, xylene was used for creating inflammation in the ear of rats. Firstly, rats were treated intraperitoneally with 0.2 ml of the hydroalcoholic extract of chamomile herb capitols at doses of 500, 1000 and 1500 mg/kg BW. After 15 minutes, 0.03 ml of xylene was rubbed on anterior and posterior surfaces of right ear of all animals except control group. 2 hours later, the animal was killed and 7 mm-sections were taken from both left and right ears by using the punch cork of 7 mm and weighed. Difference of weight between two ears showed the amount of inflammation (23).

The analgesic test of acetic acid: In this test, acetic acid was used to create sensation of pain in rats. Firstly, rats were treated intraperitoneally with 0.2 ml of at doses of 500, 1000 and 1500 mg/kg BW. 30 minutes later, 0.2 ml acetic acid 1% was injected intraperitoneally at all animals except control group. 5 minutes later, the number of abdominal extensions (due to pain) in the bodies of the rats was counted. Then, the numbers of the extensions were compared with those of them in the control group (24).

Data analysis

Data were presented as mean ± SD and analyzed by using one-way ANOVA. A $P < 0.05$ was considered statistically significant.

Results

Differences of the weight of ears in various experimental groups of the rats after treatments are shown in Table 1.

Drug(mg/kg)	Weight difference of two ears (mg)
Control group (normal saline)	0.66±0.14*
Sham group (normal saline)	5.93±0.22
Dexamethasone group (15 mg/kg BW)	0.69±0.07*
Extract group 1(500 mg/kg BW)	6.04±0.29
Extract group 2(1000 mg/kg BW)	5.51±0.27
Extract group 3(1500 mg/kg BW)	0.76±0.09*

Table 1. The mean and standard deviation for weight difference of two ears in groups in xylene test.
*compared to sham group $P < 0.01$.

Intraperitoneal injection of hydroalcoholic extract of the capitols of chamomile herb at dose of 1500 mg/kg BW caused a significant reduction in induced edema by xylene. Dexamethasone intraperitoneal injection at dose of 15 mg/kg BW caused a significant decrease in induced edema by xylene among rats (Figure 1).

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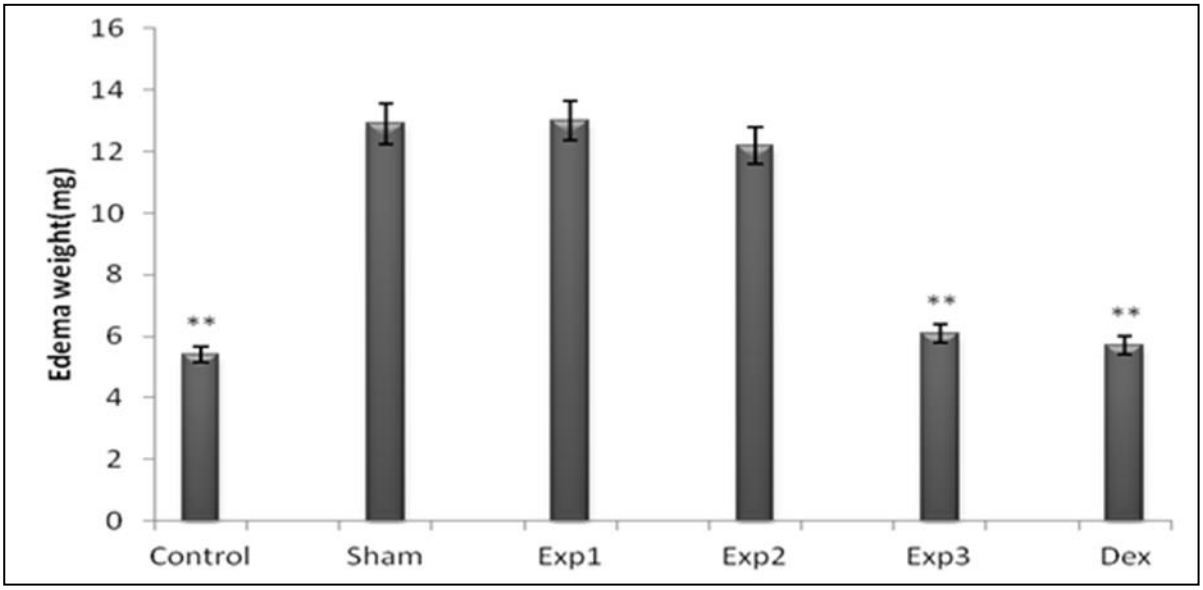

Figure 1. Intraperitoneal injection of hydroalcoholic extract of capitols of chamomile herb at doses of 500(Exp1), 1000(Exp2) and 1500(Exp3) mg/kg BW and dexamethasone at dose of 15 mg/kg BW (Dex) on induced edema by xylene test among rats.

Also, intraperitoneal injection of hydroalcoholic extract of capitols of chamomile herb at doses of 500, 1000 and 1500 mg/kg BW and indomethacin at dose of 15 mg/kg BW(Indo) resulted in a significant decrease in induced inflammatory pain by acetic acid test among rats (Figure 2).

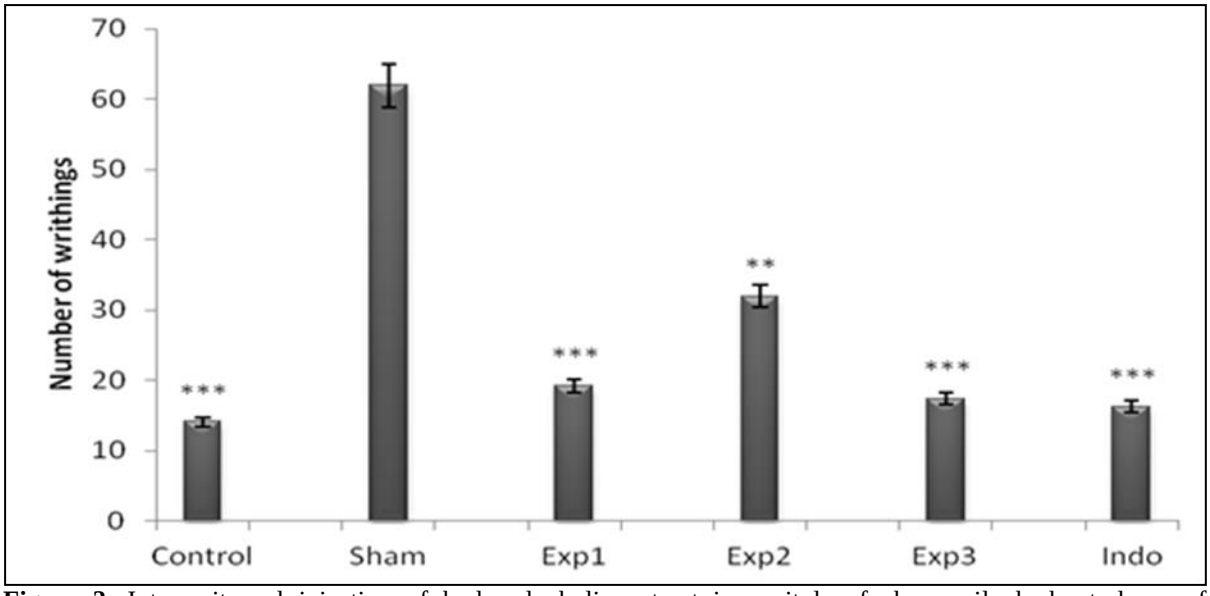

Figure 2. Intraperitoneal injection of hydro-alcoholic extract in capitols of chamomile herb at doses of 500(Exp1), 1000(Exp2) and 1500(Exp3) mg/kg BW and indomethacin at dose of 15 mg/kg BW(Indo) on induced inflammatory edema by acetic acid among rats.

Discussion

The results of present research showed that hydroalcoholic extract of the capitols of chamomile herb caused a significant decrease in induced inflammation by xylene test. Dexamethasone also caused a significant reduction in induced

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inflammation by xylene test. The induced model of edema by xylene test is a prototype to evaluate the anti-inflammatory activity of different compounds.

Xylene anti-inflammatory activity is conducted through activation of phospholipase A_2 that causes to create arachidonic acid from membrane phospholipids. Arachidonic acid causes to synthesize involved prostaglandin, prostacyclin and thromboxanes in inflammatory activity (2). Chamomile extract has been made from 120 types of chemical composition including their camazolins, flavonoids and coumarins and camazoline, Apigenen and Bizabolol can be named among the most important active components found in that (25). The relationship between existing flavonoids in plants with strong anti-inflammatory effects has been demonstrated (26).

Flavonoids are polyphenolic natural compound that are included one of enzyme inhibitors synthesizing nitric oxide and inhibit the production of NO. Flavonoids cause to decrease intracellular calcium by inhibiting the activity of N-methyl-D-aspartate receptors and subsequently decreases activity of enzyme synthesizing calcium-dependent nitric oxide and phospholipase A_2 is reduced and thus, show their anti-inflammatory effects with reduction of NO and prostaglandins.

Flavonoids inhibit prostaglandin E production from Arachidonic acid in response to inflammatory stimuli by inhibiting cyclooxygenase enzyme (27). Given that prostaglandins have an effect in creating the inflammation and intensifying pain and originate from arachidonic acid, probably flavonoids of chamomile herb playing role in creating the anti-inflammatory effect (28).

The results of present research showed that Hydroalcoholic extract in capitols of chamomile herb causes a significant reduction in induced inflammatory pain by acetic acid test. The abdominal contractions are associated with sensitivity of nociceptors to compounds such as prostaglandins. The tissue damage causes the release of compounds such as prostaglandins, bradykinin, serotonin, substance P and histamine. These mediators are released from damaged areas and stimulate nociceptors (1).

In abdominal contractions test, the injected acetic acid intraperitoneally causes to increase prostaglandins including $PGF_{2\alpha}$ in level of peritoneal liquid and involves a part of the peritoneal receptors and causes to create inflammatory pain by induction of capillary permeability. Although, this test is fully specialized yet, it is a very sensitive method to show the complex analgesic effects (1).

The associated abdominal contractions with pulling acetic acid induced hind legs is a model of visceral pain and is widely used for determining central and peripheral analgesia. In addition to prostaglandins, other several inflammatory mediators such as Tumor necrosis factor-α (TNF-α), IL-8 and IL-1B also is related to Noisy Septor response to acetic acid in adult male rat.It was also reported that the associated abdominal contraction with pulling acetic acid-induced hind legs depends on macrophages activity and peritoneal mast cells (29).

Conclusion

Based on present findings in this research, it can be concluded that the hydroalcoholic extract of the capitols of *M. chamomilla* has quite evident anti-inflammatory and analgesic properties. In this way, the extract may be further studied in clinical trials platforms.

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