Antiulcerogenic activity of hydroalcoholic extract of *Achillea millefolium* L.: Involvement of the antioxidant system

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**Abstract**

*Achillea millefolium* L. is a member of the Asteraceae family that is commonly referred to as “yarrow” and has been used in folk medicine against several disturbances including skin inflammations, spasmodic and gastrointestinal disorders, as well as hepatobiliary complaints. **Aim of the study:** In the present study, we evaluated the efficacy of a hydroalcoholic extract from the *Achillea millefolium* (HE) for gastroprotective properties and additional mechanism(s) involved in this activity. **Material and methods:** Rats were treated with HE and subsequently exposed to both acute gastric lesions induced by ethanol P.A. and chronic gastric ulcers induced by 80% acetic acid. Following treatment, glutathione (GSH) levels and superoxide dismutase (SOD) activity were measured. The activity of myeloperoxidase (MPO) and histological and immunohistochemical analysis were performed in animals with acetic acid-induced gastric ulcers. **Results:** Oral administration of HE (30, 100 and 300 mg/kg) inhibited ethanol-induced gastric lesions by 35, 56 and 81%, respectively. Oral treatment with HE (1 and 10 mg/kg) reduced the chronic gastric ulcers induced by acetic acid by 43 and 65%, respectively, and promoted significant regeneration of the gastric mucosa after ulcer induction denoting increased cell proliferation, which was confirmed by PCNA immunohistochemistry. HE treatment prevented the reduction of GSH levels and SOD activity after acetic acid-induced gastric lesions. In addition, HE (10 mg/kg) inhibited the MPO activity in acetic acid-induced gastric ulcers. **Conclusions:** The results of the present study indicate that the antioxidant properties of HE may contribute to the gastroprotective activity of this extract.

**1. Introduction**

*Achillea millefolium* L. is a member of the Asteraceae family that is commonly referred to as “yarrow”. *Achillea millefolium* has been used in folk medicine against several disturbances including skin inflammations, spasmodic and gastrointestinal disorders, and hepatobiliary complaints. Phytochemical studies carried out with *Achillea millefolium* have identified several components, including essential oils, sesquiterpenes, and phenolic compounds such as flavonoids and phenolicarboxic acids. Moreover, the presence of sesquiterpenes, azulene, flavonoids such as apigenin, luteolin and rutin sustains the pharmacological activity of *Achillea millefolium* (Kocevar et al., 2008). Different preparations of *Achillea millefolium* have demonstrated anti-inflammatory, antitumor, antimicrobial, liver protective, and antioxidant properties (Goldberg et al., 1969; Tozyo et al., 1994; Gagdoli and Mishra, 1995; Tunon et al., 1995; Lin et al., 2002; Candan et al., 2003). In addition, our laboratory previously reported the potent gastric anti-secretory and gastroprotective activity of an aqueous extract of *Achillea millefolium* in models of acute (Baggio et al., 2002) and chronic gastric injury (Cavalcani et al., 2006).

Gastric ulcer is one of the major gastrointestinal disorders, which occur due to an imbalance between the offensive (gastric acid secretion) and defensive (gastric mucosal integrity) factors (Laine et al., 2008). There is evidence for the participation of reactive oxygen species (ROS) in the etiology and pathophysiology of human gastric ulcer development (Repetto and Llesuy, 2002). Many
studies have shown that ROS are involved in several models of gastric injury, such as ethanol, gastric lesions caused by stress, acetic acid, and the use of non-steroidal anti-inflammatory drugs (Das and Banerjee, 1993; Oda basoglu et al., 2006; Ineu et al., 2008; Ishihara et al., 2008). These results indicate the involvement of antioxidant targeting enzymes in gastric injury models and the discovery of drugs that also possess free-radical scavenging activity. In this context, we have investigated the antioxidant mechanisms involved in the gastroprotective effects of the hydroalcoholic extract of Achillea millefolium (HE).

2. Material and methods

2.1. Botanical material

Achillea millefolium L. plants were collected in July 2007 in the Botanical Garden of Universidade Paranaense (UNIPAR), Campus Umuarama (Brazil) at 430 m altitude above sea level (52°3’47”–55’–W53’18”48’). Dr. Mariza Barion Romagnolo identified botanical material (Department of Botany, UNIPAR, Campus Umuarama, Brazil), and a voucher specimen was deposited at the Campus Umuarama Herbarium under number 1896.

2.2. Preparation of the hydroalcoholic extract (HE)

The hydroalcoholic extract (HE) of aerial portions of the plant was prepared by maceration with 90% ethanol at room temperature (1:1, v/v), initially for 48 h and thereafter until exhaustion. The hydroalcoholic extract obtained was filtered and concentrated under vacuum (at 50 °C) and stored at −20 °C. The concentrated extract (yield of 17.4%) was diluted in distilled water immediately before use.

2.3. Animals

Experiments were conducted using female Wistar rats (180–220 g), housed under standard laboratory conditions (12 h light/dark cycle, temperature 22 ± 2 °C) with free access to food and water. The rats were deprived of food for 16 h prior to the start of experiments. The study was conducted in accordance with the Ethical and Practical Principles of the Use of Laboratory Animal guidelines and the experimental protocol was approved by the Institutional Ethics Committee of the Universidade Federal do Paraná (CEEA/UFPR; approval number 161).

2.4. Induction of acute gastric lesion

Rats were orally treated with vehicle (water, 0.1 ml/100 g of body weight), omeprazole (40 mg/kg), ascorbic acid (500 mg/kg) or HE (30, 100 and 300 mg/kg) 1 h before intragastric administration of ethanol P.A. (0.5 ml). The animals were sacrificed 1 h after HE administration (Robert et al., 1979). The stomachs were removed and the area of ulceration (mm²) was measured by planimetry using the program Image Tool 3.0.

2.5. Induction of chronic gastric ulcer

Chronic gastric ulcers were induced with acetic acid as described previously, with modifications (Okabe et al., 1971; Okabe and Amagase, 2005). Briefly, rats were anesthetized with xylazine/ketamine (7.5 mg/kg and 60 mg/kg, i.p., respectively). The abdomen was opened, the stomach was exposed and the 80% glacial acetic acid (0.5 ml) was instilled into a cylinder (6 mm of diameter) and applied to the serosal surface of the stomach for 1 min. The acetic acid was removed by aspiration and the area of contact was washed with sterile saline. 48 h after the induction of ulcers, rats were treated orally with omeprazole (40 mg/kg), ascorbic acid (250 mg/kg), HE (0.1, 1 and 10 mg/kg) or vehicle control (water, 0.1 ml/100 g of body weight), twice a day for 7 days. One day after the final treatment, the animals were sacrificed, the stomachs removed, and the extent of the gastric lesion was measured as the total injured area (mm³) = length (mm) × width (mm) × depth (mm).

For histological evaluation, gastric ulcers were fixed in Alfac solution for 16 h. After fixation, the tissue samples were dehydrated with alcohol and xylene. Immediately after the dehydration, each sample was embedded in paraffin wax, sectioned at 5 μm and stained with hematoxylin/eosin. The gastric sections were observed and photographed under a stereomicroscope at 25-fold magnification.

2.6. Immunohistochemistry

Proliferating cell nuclear antigen (PCNA) was used to determine proliferating cells in acetic acid–induced ulcers. Paraffin-embedded sections were deparaffinized in xylene and hydrated through standard graded ethanol solutions. Sections were rinsed 2 times for 5 min each in PBS (pH 7.4), incubated in H₂O₂ solution for 10 min to inactivate endogenous peroxides and then heated in citric acid sodium solution in microwave oven at 100 °C to retrieve antigen for 10 min. Blocking of nonspecific reaction was performed with blocking solution (1% BSA and 0.3% Triton X-100 in PBS) for 30 min. The sections were then incubated overnight at 4 °C with goat anti-PCNA (at 1:100; Santa Cruz Biotechnology Inc., CA, USA). After that, slides were rinsed in PBS (pH 7.4) and the sections were incubated in secondary antibody at room temperature for 2 h. After washing, the immunoreacted cells were then developed utilizing avidin-conjugated horseradish peroxidase (HRP) with diaminobenzidine (DAB) as substrate (BD Biosciences, San Diego, CA, USA). Finally, the specimens were counterstained with hematoxylin. PCNA-containing cells were identified by the presence of a dark reddish-brown chromogen. The nuclear-positive staining cells were observed under microscope (×400).

2.7. Preparation of subcellular fractions of stomachs

Tissue samples of stomachs were homogenized with 200 mM potassium phosphate buffer, pH 6.5. The homogenate was used to measure the GSH levels and then centrifuged at 9000 × g for 20 min. The supernatant was used for the determination of SOD activity and the pellet was used to determine the activity of MPO.

2.8. Determination of glutathione content

GSH levels in gastric mucosa were determined by the method of Sedlak and Lindsay (1968). Aliquots of tissue homogenate were mixed with 12.5% trichloroacetic acid, vortexed for 10 min and centrifuged for 15 min at 9000 × g. The supernatant was reserved, and TRIS buffer (0.4 M, pH 8.9) and 5,5′-dithiobis(2-nitrobenzoic acid) (DTNB, 0.01 M) were added to it. Absorbance was measured using a spectrophotometer at 415 nm with a microplate reader. The procedures were performed at 4 °C, and the individual values were interpolated into a standard curve of GSH and expressed as μg of GSH/g of tissue.

2.9. Determination of enzymatic activities of SOD

SOD activity was measured according to Marklund and Marklund (1974) and Gao et al. (1998). Measurements were based on the capacity of SOD to inhibit pyrogallol autoxidation. Pyrogallol (1 mM) was added to buffer solution (200 mM Tris HCl–EDTA, pH 8.5) and supernatant aliquots, and then vortexed for 1 min. The
reaction was incubated for 20 min at room temperature, stopped with the addition of 1 N HCl and centrifuged for 4 min at 18,700 × g. The absorbance of the resulting supernatant was measured at 405 nm using a spectrophotometer. The amount of SOD that inhibited the oxidation of pyrogallol by 50% (relative to the control) was defined as a unit of SOD activity.

2.10. Determination of MPO activity

The activity of MPO (a marker of neutrophil infiltration) was measured according to Bradley et al. (1982) and modified by De Young et al. (1989). The pellet was re-suspended in 1 ml of 80 mM potassium phosphate buffer (pH 5.4) containing 0.5% hexadecyltrimethylammonium bromide (HTAB), and it was centrifugated at 11,000 × g for 20 min at 4 °C. MPO activity in the supernatant was determined at 620 nm in presence of H₂O₂ and TMB. MPO activity in tissues was expressed as units of milli optic density (mO.D.)/g of tissue.

2.11. DPPH free-radical scavenging assay

2,2-Diphenyl-1-picrylhydrazyl (DPPH) is a stable free radical that has been widely used as a tool to estimate the free-radical scavenging activity of antioxidants. The reduction capacity of the DPPH radical was determined by the decrease of absorbance induced by antioxidants, according to Blois (1958) and Chen et al. (2004), with a few modifications. The reaction system consisted of 750 μl of HE diluted to different concentrations (3, 10, 30 and 300 μg/ml) and 250 μl of DPPH methanolic solution. After 5 min, the absorbance was measured at 517 nm using a spectrophotometer. Ascorbic acid (50 μg/ml) was used as positive control and distilled water was employed as negative control.

2.12. Drugs and reagents

The following substances were used: hexadecyltrimethylammonium bromide, 3,3′,5,5′-tetramethylbenzidine, hydrogen peroxide, glutathione, pyrogallol, 5,5′-dithiobis(2-nitrobenzoic acid) and 2,2-diphenyl-1-picrylhydrazyl (all from Sigma, St. Louis, USA), acetic acid, sodium acetate, N,N-dimethylformamide, ascorbic acid, xylene, formaldehyde, trichloroacetic acid and absolute ethanol (Vetec, Rio de Janeiro, Brazil) and methanol (Tédia Brazil, Rio de Janeiro, Brazil).

2.13. Statistical analysis

Data were expressed as means ± standard error of mean with 6–10 animals per group. Differences between means were determined by one-way analysis of variance (ANOVA) followed by post hoc Bonferroni’s test. Differences from Veh group (*P < 0.05, **P < 0.01 and ***P < 0.001).

3. Results

3.1. Effect of HE on gastric lesions induced by ethanol

Oral administration of HE (30, 100 and 300 mg/kg), 1 h before the induction of gastric lesions with ethanol P.A., significantly reduced lesion area by 35, 56 and 81%, respectively, compared to the control group (87.1 ± 6.3 mm²) (Fig. 1A). Omeprazole (40 mg/kg, p.o.) and ascorbic acid (500 mg/kg, p.o.) have been previously demonstrated to inhibit ethanol-induced gastric lesion formation and so they were used as positive controls of lesion inhibition. Omeprazole and ascorbic acid inhibited the gastric lesions in 72 and 35%, respectively (Fig. 1A).

3.2. Effect of HE on gastric ulcers induced by 80% acetic acid

The results show that oral administration of HE (1 and 10 mg/kg) reduced the gastric ulcer formation caused by 80% acetic acid exposure by 43 and 65%, respectively (Fig. 1B). The positive controls for lesion inhibition, omeprazole (40 mg/kg, p.o.) reduced the gastric ulcer size by 69% when compared to control group (146.7 ± 6.8 mm²) (Fig. 1B). However, ascorbic acid (250 mg/kg, p.o.) treatment did not reduce the acetic acid-induced gastric lesion formation.

Histological analysis of the gastric ulcers showed extensive deep damage induced by acetic acid (Fig. 2A and E). Slices from ulcers treated with HE (1 and 10 mg/kg, p.o.) (Fig. 2C, D, G and H) and omeprazole (40 mg/kg, p.o.) demonstrated a regenerated mucosa (Fig. 2B and F).

These results were confirmed by PCNA immunohistochemical analysis, where the HE (10 mg/kg) treatment increased the number of proliferating cells in 112 ± 18% when compared to control group (Fig. 3). However, PCNA expression in the omeprazole group (40 mg/kg, p.o.) was not different from control group (Fig. 3).

3.3. Effects of HE on antioxidant system

Administration of ethanol P.A. decreased GSH levels and SOD activity by 51% and 37%, respectively, when compared with untreated controls (Table 1). The treatment of animals with HE (300 mg/kg, p.o.) prevented the decrease in GSH levels and SOD activity. Omeprazole (40 mg/kg, p.o.) prevented decreased SOD activity but failed to affect GSH levels, while ascorbic acid (500 mg/kg, p.o.) increased the levels of glandular GSH and SOD.
activity by 45% and 43%, respectively, when compared to ethanol-induced lesion controls (Table 1).

In gastric ulcers induced by acetic acid, GSH levels decreased by 54% and SOD activity decreased by 33% (Table 2). Oral administration of HE (10 mg/kg, p.o.) restored the GSH levels and SOD activity to baseline levels. Omeprazole (40 mg/kg, p.o.) and ascorbic acid (250 mg/kg, p.o.) also restored the GSH levels and SOD activity (Table 2).
3.4. Effects of HE on MPO activity

The chronic gastric ulcer induced by acetic acid increased MPO activity by 82% when compared to untreated controls (1.3 ± 0.4 μM/g of tissue). HE (10 mg/kg, p.o.), omeprazole (40 mg/kg, p.o.) and ascorbic acid (250 mg/kg, p.o.) inhibited MPO activity by 68, 42 and 60%, respectively (Fig. 4).

3.5. Effect of HE on free-radical DPPH

In the DPPH test, HE (3, 10, 30 and 300 μg/ml) scavenged the DPPH radicals with IC50 value of 30.9 (19.3–49.5) μg/ml and an inhibition of 72%. Ascorbic acid was used as a positive control, and it was able to reduce DPPH levels by 75% (Fig. 5).

4. Discussion

In the present study, we demonstrated that oral administration of the hydroalcoholic extract from Achillea millefolium (HE) effectively protects the animals against acute gastric lesions caused by ethanol and chronic gastric ulcer induced by acetic acid. These results are in accordance with previous studies obtained with aqueous extract of A. millefolium that presented potent anti-secretory and gastroprotective activity in several models of acute and chronic...
The difference between groups was determined by ANOVA followed by Bonferroni’s test.

### Table 1
Effects of HE on the quantity of GSH and SOD in rats with gastric ulcer induced by ethanol P.A.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>GSH (µg GSH/g tissue)</th>
<th>SOD (U SOD/g tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veh/Veh</td>
<td>1572 ± 38</td>
<td>2.7 ± 0.1</td>
</tr>
<tr>
<td>Veh/ethanol</td>
<td>764 ± 14***</td>
<td>1.7 ± 0.2**</td>
</tr>
<tr>
<td>Omeprazole (40 mg/kg)</td>
<td>1036 ± 133***</td>
<td>3.6 ± 0.1***</td>
</tr>
<tr>
<td>Ascorbic acid (500 mg/kg)</td>
<td>1394 ± 69**</td>
<td>3.0 ± 0.1**</td>
</tr>
<tr>
<td>HE (30 mg/kg)</td>
<td>434 ± 61***</td>
<td>2.6 ± 0.1</td>
</tr>
<tr>
<td>HE (100 mg/kg)</td>
<td>763 ± 71***</td>
<td>2.6 ± 0.2</td>
</tr>
<tr>
<td>HE (300 mg/kg)</td>
<td>1187 ± 85**</td>
<td>2.5 ± 0.1</td>
</tr>
</tbody>
</table>

The difference between groups was determined by ANOVA followed by Bonferroni’s test.

- *P < 0.05 as compared with Veh/ethanol.
- **P < 0.01 as compared with Veh/ethanol.
- ***P < 0.001 as compared with Veh/ethanol.

### Table 2
Effects of HE on the quantity of GSH and SOD in rats with gastric ulcer induced by 80% acetic acid.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>GSH (µg GSH/g tissue)</th>
<th>SOD (U SOD/g tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veh/Veh</td>
<td>1595 ± 99</td>
<td>3.0 ± 0.1</td>
</tr>
<tr>
<td>Veh/Acetic acid</td>
<td>728 ± 33***</td>
<td>2.0 ± 0.1*</td>
</tr>
<tr>
<td>Omeprazole (40 mg/kg)</td>
<td>1229 ± 109</td>
<td>3.9 ± 0.1***</td>
</tr>
<tr>
<td>Ascorbic acid (250 mg/kg)</td>
<td>1329 ± 120**</td>
<td>3.9 ± 0.3**</td>
</tr>
<tr>
<td>HE (1 mg/kg)</td>
<td>1224 ± 95*</td>
<td>2.9 ± 0.2</td>
</tr>
<tr>
<td>HE (10 mg/kg)</td>
<td>1597 ± 177***</td>
<td>2.9 ± 0.2</td>
</tr>
</tbody>
</table>

The difference between groups was determined by ANOVA followed by Bonferroni’s test.

- *P < 0.05 as compared with Veh/acetate acid.
- **P < 0.01 as compared with Veh/acetate acid.
- ***P < 0.001 as compared with Veh/acetate acid.
- #P < 0.05 as compared with the Veh/Veh.
- ##P < 0.01 as compared with the Veh/Veh.
- ###P < 0.001 as compared with the Veh/Veh.

Effect of HE on the quantity of MPO in gastric damage induced by 80% acetic acid in the experimental groups: vehicle/vehicle (Veh/Veh – water/water), vehicle (Veh – acetic acid/water), omeprazole (Omepr – 40 mg/kg p.o.), ascorbic acid (AA – 250 mg/kg p.o.) and HE (10 mg/kg p.o.). The results are expressed as mean ± S.E.M. Statistical comparison was performed using analysis of variance ANOVA followed by post hoc Bonferroni’s test. Differences from Veh/Veh group (**P < 0.001), difference from Veh group (**P < 0.001).

**Fig. 4.** Effect of HE on MPO activity. The graph represents the activity of MPO in gastric damage induced by 80% acetic acid in the experimental groups: vehicle/vehicle (Veh/Veh – water/water), vehicle (Veh – acetic acid/water), omeprazole (Omepr – 40 mg/kg p.o.), ascorbic acid (AA – 250 mg/kg p.o.) and HE (10 mg/kg p.o.). The results are expressed as mean ± S.E.M. (n = 8). Statistical comparison was performed using analysis of variance ANOVA followed by post hoc Bonferroni’s test. Differences from Veh/Veh group (**P < 0.001), difference from Veh group (**P < 0.001).

**Fig. 5.** The effect of HE (3, 10, 30 and 300 µg/ml) or ascorbic acid (AA, 50 µg/ml) on the ability to scavenge the free-radical DPPH. The results are expressed as mean ± S.E.M. Statistical comparisons were performed using analysis of variance ANOVA followed by Bonferroni’s post hoc test. Difference from Veh group (**P < 0.001).

Glutathione is the major NP-SH of gastric mucosa and it, therefore, constitutes one of the most important cytoprotective mechanisms against lesion formation (Cubben et al., 2001), while SOD-mediated catalysis of superoxide radical anion (O₂⁻) into less noxious hydrogen peroxide (H₂O₂) represents the first line of antioxidant defense. In our experiments, the GSH levels and SOD activity were significantly reduced after ethanol administration, and this reduction was prevented by pretreatment with ascorbic acid (P < 0.001) and HE (P < 0.05). Moreover, we hypothesized that HE could be acting as a scavenger of free radicals because the chemicals employed to induce ulceration invoke damage by reactive oxygen species. Interestingly, the HE (300 µg/ml) presented a comparable profile of action with ascorbic acid in reducing (P < 0.001) the levels of free-radical DPPH, suggesting a direct scavenger activity. In fact, it is well known that the reduction of the DPPH molecule by Achillea extracts is related to the presence of flavonoids and tannins (Giorgi et al., 2009; Tuberoso et al., 2009). Furthermore, the treatment of animals twice a day for seven days with HE and omeprazole significantly reduced the size of acetic acid-induced gastric ulcers. In this model, the antioxidant assays showed the same profile as the antioxidant system of ethanol-induced gastric lesions. In addition, in agreement with our data, Ishihara et al. (2008) showed that gastric ulcers induced by acetic acid have reduced SOD activity. Oral treatment with HE (1 and 10 mg/kg), omeprazole and ascorbic acid restored the acetic acid-dependent decrease in GSH levels (P < 0.05, 0.001, 0.05 and 0.001, respectively) and SOD activity (P < 0.05, 0.001, 0.001, 0.001, respectively). Unfortunately, the phytochemical components responsible for the antioxidant effect of hydroalcoholic extract of A. millefolium in gastric ulcers are currently unknown; however, preliminary studies demonstrated the presence of flavonoids such as apigenin, luteolin and rutin, which show powerful antioxidant properties, in this plant (Kocevar et al., 2008; Giorgi et al., 2009; Tuberoso et al., 2009). Therefore, the contribution of these chemicals to the antioxidative capability of HE remains to be evaluated.
It has been shown that the application of acetic acid on the surface of theserosa produces a gastric ulcer in rats that is very similar to the human gastric ulcers in terms of location, severity and chronicity and which undergoes a similar healing process (Okabe and Pfeiffer, 1972). The ulcer results from tissue necrosis triggered by mucosal ischemia, free-radical formation, and cessation of nutrient delivery, all of which are caused by vascular and microvascular injury such as thrombi, constriction, or other occlusions (Tarnawski, 2005). Ulcer healing is a complex process that involves deep tissue damage in the gastric mucosa after administration of acetic acid. The treatment with DE significantly regenerates the gastric mucosa, which is similar to observations for animals treated with omeprazole. Moreover, cell proliferation plays an important role in wound healing (Tarnawski, 2005) and it was shown that PCNA, a tissue marker of cell proliferation, was increased during healing of gastric mucosal injury (Sun et al., 2003). We observed that HE treatment increased the number of PCNA-positive cells, suggesting that HE treatment could promote gastric cell regeneration and proliferation.

Recent studies have shown that the excessive recruitment and metabolic activation of neutrophils generates free radicals in several models of gastric damage resulting in inflammation-dependent tissue damage (Fialkow et al., 2007). The MPO enzyme is present in neutrophils and acts in the presence of superoxide anion and chloride anion (Cl⁻) to form the hypochloric acid (which is toxic to bacteria); but is also harmful to host tissues (Halliwell and Gutteridge, 1986). In this study, we observed that the treatment with HE decreased (P < 0.001) the activity of MPO, suggesting a reduction of neutrophil infiltration into ulcerated tissue. This lack of activity may contribute to the reduction of neutrophil-dependent ROS formation and therefore block the gastric inflammatory process induced by acetic acid.

Collectively, the results of the present study demonstrate that the gastroprotective effects in rat stomach induced ulcers promoted by a hydroalcoholic extract of A. millefolium (HE) could be attributed to antioxidant properties of this plant. However, further studies are required to investigate the active compound(s) and precise mechanisms involved in the effects produced by A. millefolium.

References


