

Comparative effect of garlic (*Allium sativum*), onion (*Allium cepa*), and black seed (*Nigella sativa*) on gastric acid secretion and gastric ulcer

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Abstract: Protective roles of raw and boiled garlic (*Allium sativum*) and onion (*Allium cepa*) in comparison with black seed (*Nigella sativa*) on acidified ethanol-induced gastric ulcers and gastric acid secretion in rats in vivo have been investigated. Raw or boiled *Nigella sativa*, garlic, or onion significantly inhibited histamine stimulated acid secretion, whereas on basal acid secretion, onion and garlic significantly stimulated secretion but *Nigella sativa* had no effect. Raw *Nigella sativa* and garlic showed a significant decrease in the ulcer index when compared with the control at all doses (0.25 g/kg, 0.5 g/kg, and 1 g/kg) tested, whereas onion-only, at doses of 0.5 g/kg and 1 g/kg, significantly reduced the ulcer index. Boiled *Nigella sativa* showed equal potency to raw *Nigella sativa* in decreasing ulcer index, but boiled garlic and onion showed reduced potency. The results of this study demonstrate the protective role of raw *Nigella sativa*, garlic, and onion against ethanol-induced gastric ulcers and gastric acid secretion. Boiling did not affect the protective effect of *Nigella sativa* on gastric ulcers.

Keywords: *Nigella sativa*, onion, garlic, acid ulcer

Introduction

Nigella sativa (NS) (black seed or black cumin), garlic, and onion have been used as food and for medicinal purposes since ancient times. *Nigella sativa* Linn., a plant belonging to the family Ranunculaceae, is cultivated throughout India, Pakistan, and countries bordering the Mediterranean Sea and other tropical countries, and grows as a small herb.¹⁻³ This plant is one of the most widely studied.⁴ In fact, these common food plants are a rich source of several nutrients that are used in the treatment and prevention of a number of diseases, including cancer, coronary heart disease, obesity, diabetes, hypertension, and disturbances of the gastrointestinal tract.⁵⁻⁷ Similarly, garlic (*Allium sativum*) and onion (*Allium cepa*) are among the oldest of all cultivated plants and form an important dietary and medicinal role. Garlic has been used as a spice, food, and folklore medicine for over 4000 years.⁸ Garlic has been mentioned many times in the Codex Ebers, an Egyptian medical papyrus dating to about 1500 BC, regarding its effectiveness for a variety of ailments, including heart problems, headache, bites, worms, and tumors.⁹ In China, garlic and onion tea have long been recommended for many ailments, including fever, headache, cholera, and dysentery. More recent studies have shown garlic to be effective in lowering serum cholesterol^{10,11} and to have protective effects against stroke, coronary thrombosis,^{12,13} atherosclerosis,^{14,15} platelet aggregation,^{16,17} infections, and vascular disorders.¹³ Garlic has also been reported to have fibrinolytic activity in both humans¹⁸ and

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experimental animals.¹⁰ Similarly, onion has been shown to have serum cholesterol-lowering properties^{10,11} and to have protective effects against platelet aggregation induced by epinephrine, adenosine diphosphate, or arachidonic acid.^{16,19,20} Some studies have shown the gastroprotective effect of NS oil,^{21,22} and one study²³ has shown garlic to be protective against ethanol-induced gastric ulcers. However, there is a paucity of studies of garlic on gastric ulcers, and no information is available on the effects of onion on the gastrointestinal tract. Similarly, there is a paucity of studies on gastric acid secretory effect of garlic, onion, and NS. Therefore, our main aim was to investigate the protective role of raw or boiled garlic and onion on acidified ethanol-induced gastric ulcers and histamine-stimulated gastric acid secretion in rats and to compare them with either raw or boiled NS.

Materials and methods

Male Wistar rats (weighing 200–225 g) were fasted for 24 hours in wire mesh cages to avoid coprophagy. The rats were obtained from the animal facilities of the Faculty of Medicine and Health Sciences of the United Arab Emirates (UAE) University.

Materials

Onion, NS, and garlic were obtained from the local market. Hydrochloric acid (HCl), ethanol, and histamine were obtained from Sigma (St Louis, MO).

Gastric acid secretion measured in vivo

Four groups of six rats were used for the experiment. Rats were initially anesthetized with urethane (1.5 g/kg) intraperitoneally. Following general anesthesia, a laparotomy was immediately performed followed by the insertion of a polyethylene tube at the pyloric end of the stomach. This tube was used to collect exudates from the stomach. An orogastric tube was inserted in the stomach via the esophagus. This tube was used to perfuse the stomach with saline (pH 7) at a constant rate of 7 mL/min⁻¹ at 37°C. Following perfusion, effluent samples were collected and titrated against 0.01 M NaOH every 15 minutes for acid secretion. After basal acid output for 1 hour, saline, raw, or boiled homogenized water extracts (5 minutes) of test drugs (either NS, onion, or garlic; six rats for each dose) at neutral pH was administered orally to the animals. Thirty minutes later, histamine (2 mg/kg⁻¹) was administered as a bolus injection. Acid output was monitored continuously for 2 hours thereafter. The acid output was

calculated and expressed as μmol (15 min⁻¹). This study had an ethical clearance from the Ethical Committee of the UAE University.

Antiulcer activity

Rats were divided into four groups of six to seven animals for each experiment. Each group received either neutral pH physiologic saline (1 mL) or water extract of either raw or boiled (5 minutes) homogenized NS, garlic, or onion (0.25 g/kg, 0.5 g/kg, or 1 g/kg; six rats for each dose) by gastric gavage. After 30 minutes of the treatment, 1 mL of acidified ethanol (60% ethanol with 150 mM HCl), an ulcerogenic agent, was administered orally to the animals. The animals were sacrificed 1 hour later by overdosing with pentobarbital. The abdomen was incised, and the stomachs removed, cut open along the greater curvature, and rinsed with saline to remove any adherent particles and mucus. The open stomach was spread on a sheet of cork so as to have a clear view of gastric lesions in the gastric mucosa. The total lengths of hemorrhagic lesions, which were approximately 1 mm in length and formed in the glandular portion of the gastric mucosa, were taken as ulcer index. An observer who was unaware of the drug treatments confirmed the ulcer index. The percentage reduction of the ulcer index in the drug-treated groups was calculated from the saline-treated groups.

The use of 60% ethanol in 150 mM HCl to produce an ulcerogenic effect was based on earlier observation that ethanol 50% and over provided a reproducible model of gastric damage.^{24,25}

Statistical analysis

The results are mean plus standard error of the mean. Differences were compared using one-way analysis of variance. Significance differences were determined by paired Student's *t*-tests. Significance was set at $P < 0.05$.

Results

Effect of either raw or boiled NS, garlic, or onion on gastric acid secretion

Figure 1 shows the effect of gastric gavage of either raw NS (0.25 g/kg), garlic (0.5 g/kg), or onion (0.5 g/kg) on gastric acid secretion administered 30 minutes before histamine ($n = 6$). There was an initial significant ($P > 0.001$) increase in basal acid secretion by both onion and garlic followed by significant ($P > 0.01$ – 0.001) inhibition of histamine-stimulated gastric acid secretion after 45–90 minutes of administration. NS did not inhibit basal gastric acid secretion

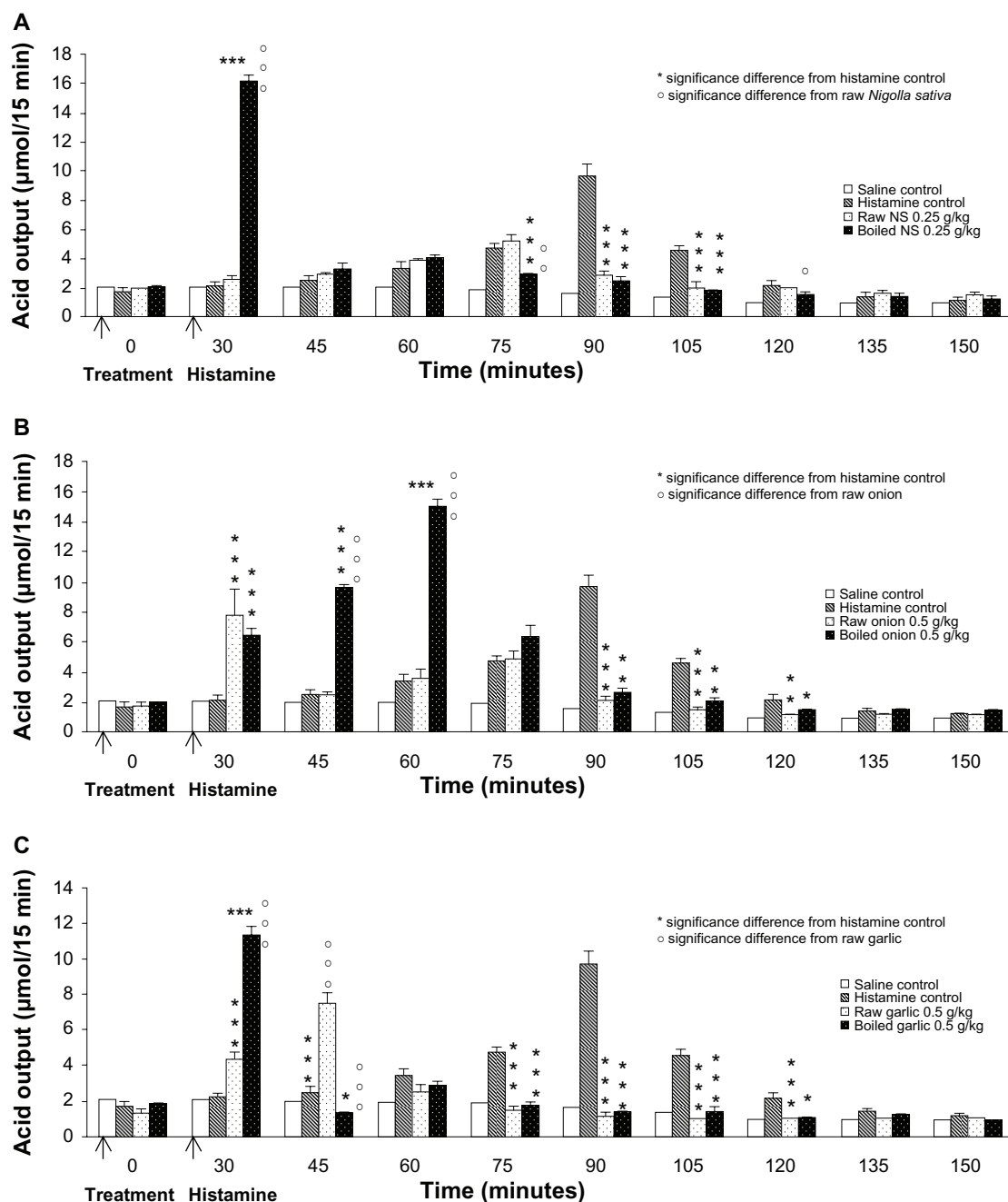


Figure 1 Effect of raw and boiled *Nigella sativa* (0.25 g/kg) (A), onion (0.5 g/kg) (B), and garlic (0.5 g/kg) (C) on gastric acid secretion in the stomachs of rats administered 30 minutes before histamine.

Notes: The results are mean \pm standard error of the mean of six experiments. Significant difference * $P > 0.05$, ** $P > 0.01$, *** $P > 0.001$ for histamine control; $^{\circ\circ\circ}P > 0.001$, $^{\circ\circ}P > 0.01$, $^{\circ}P > 0.05$ for boiled from raw *Nigella sativa*, onion, and garlic.

but inhibited histamine-stimulated acid secretion after 60–75 minutes of histamine administration. There was some visual observation increase in salivary secretion after the administration of garlic and onion.

After boiling the test food products in water for 5 minutes, there was an initial significant ($P > 0.001$) increase in basal acid secretion by onion, garlic, and NS followed by significant ($P > 0.01$ – 0.001) inhibition

of histamine-stimulated gastric acid secretion after 45–90 minutes of administration.

Effect of either raw or boiled NS, garlic, or onion on acidified ethanol-induced gastric ulcer

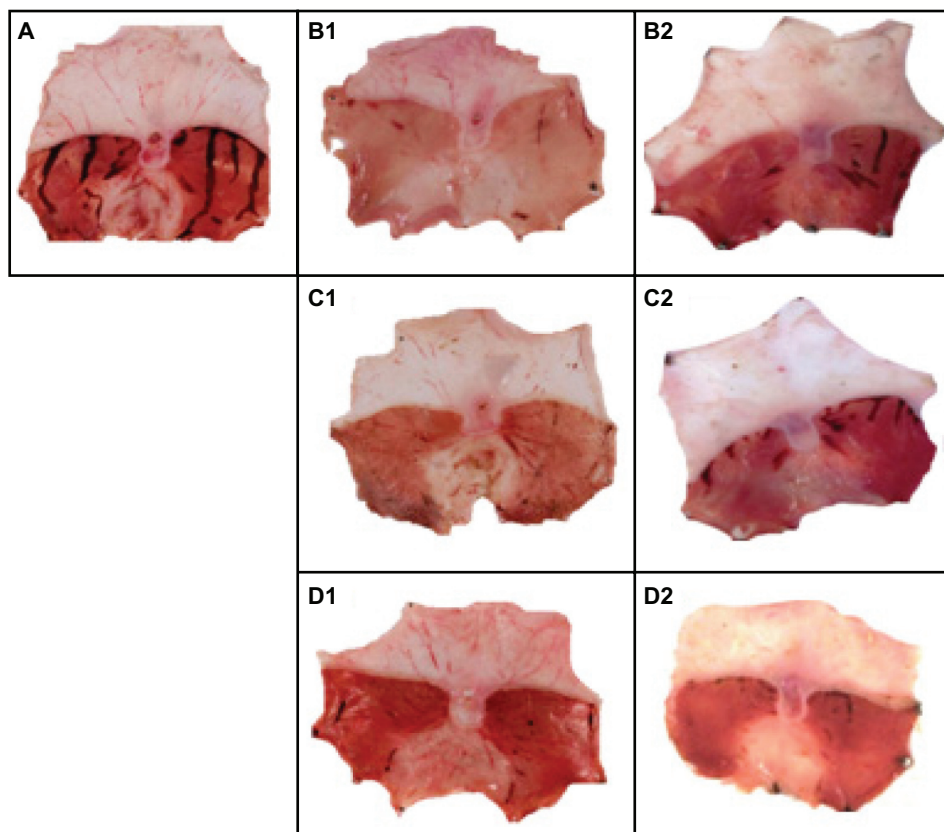
Table 1 summarizes the results of the ulcer study, and Figure 2 shows the photo microns of the effects of either raw or

Table 1 Effect of administration of either raw or boiled *Nigella sativa*, onion (*Allium cepa*), or garlic (*Allium sativum*) on acidified ethanol-induced ulcer in rats (n = 7)

Groups	Dose of the substance	Ulcer index (mean \pm standard error of the mean)		P-value		
		Raw	Boiled	Control vs raw	Control vs boiled	Raw vs boiled
Control	10 mL/kg	126.5 \pm 11.5	126.5 \pm 11.5			
<i>Nigella sativa</i>	0.25 g/kg	13.7 \pm 5	47.8 \pm 19.1	0.000	0.001	0.952
	0.5 g/kg	24.5 \pm 7.1	45.3 \pm 4.3	0.000	0.000	0.018
	1 g/kg	15.3 \pm 4.37	3.8 \pm 2.17	0.000	0.000	0.002
Onion	0.25 g/kg	142.3 \pm 19.05	72.2 \pm 13.3	0.493	0.013	0.018
	0.5 g/kg	35.5 \pm 9.75	75 \pm 16.0	0.000	0.165	0.001
	1 g/kg	40.4 \pm 10.4	75 \pm 16.04	0.000	0.026	0.101
Garlic	0.25 g/kg	34.3 \pm 12.2	35.5 \pm 14.4	0.000	0.005	0.031
	0.5 g/kg	7.7 \pm 2.9	37 \pm 3.7	0.000	0.000	0.031
	1 g/kg	14.5 \pm 2.7	33.5 \pm 3.7	0.000	0.000	0.049

boiled NS, onion, and garlic on acidified ethanol-induced gastric ulcers. Acidified ethanol administration at a dose of 10 mL/kg caused gastric ulceration (UI, 126.5 \pm 11.5) in all the animals tested (n = 7) (Table 1, Figure 2). Administration of either raw NS or garlic at all doses significantly reduced the formation of ulcers when rats were given acidified ethanol ($P < 0.001$).

However, onion was found to reduce the ulcer index only at doses of 0.5 g/kg and 1 g/kg. By comparing the mean ulcer index in all doses of the three preparations, a dose of 0.5 g/kg was found to be the most potent in both onion and garlic, as it showed the least ulcer formation (see Figure 2). As for NS, the dose of 0.25 g/kg showed the highest potency (see Figure 2).

**Figure 2** Photomicrographs of stomachs showing the effect of acidified ethanol in (A) control, 1 (raw) and 2 (boil); (B) *Nigella sativa* treated, (C) onion treated, and (D) garlic treated.

Notes: Micrographs are the results of six to seven such experiments.³ Figures B, C, and D show the most potent doses (0.5 g/kg in onion and garlic, 0.25 g/kg in *Nigella sativa*) and the most effective in reducing the stomach ulcers in the raw at least. In the boiled, the higher doses were more effective in reducing stomach ulcers (not shown).

Administration of boiled NS at both doses, 0.5 g/kg and 1 g/kg, significantly ($P < 0.001$) reduced the mean ulcer index similar to the raw NS. Boiled garlic similarly ($P < 0.001$) reduced the mean ulcer index, but the reduction (37.0 ± 8.7) was much less when compared with the raw garlic (7.7 ± 2.9) at both doses of 0.5 mg/kg and 1.0 mg/kg. Boiled onion at a dose of 0.5 g/kg did not significantly reduce the mean ulcer index (72 ± 16) when compared with the control (126.5 ± 11.5). At 1 g/kg, boiled onion significantly ($P < 0.05$) reduced the mean ulcer index (75.0 ± 16.04) when compared with the control but was reduced to a lesser degree when compared with raw onion (40.4 ± 10.4). Figure 2 shows the differences in the protective effect of the food herbs on ethanol-induced ulcers. The protective effect was reduced but not abolished.

Discussion

This study investigated the effects of NS, garlic, and onion on gastric acid secretion and gastric ulcers induced by acidified ethanol. NS had no effect on basal acid secretion but inhibited histamine-stimulated gastric acid secretion. The effect of NS is similar to another report by Rajkumar et al,²⁶ who did the experiment on pyloric ligated stomachs of rats rather than by gastric perfusion. Additionally, Rajkumar et al²⁶ used alcoholic extract of NS rather than saline extract, and no gastric acid secretory stimulant was used. However, El-Dakhankhny et al²¹ found no significant change in free acidity and peptic activity by NS. As far as the authors are aware, we are the first to report this inhibitory effect of NS on acid secretion by using the gastric perfusion method.

The initial increase in acid secretion by onion and garlic on gastric acid secretion could be due to a cholinergic mechanism since Vasudevan et al,²⁷ when working with aqueous spice extracts administered by an intragastric route, increased acid secretion and a cholinergic mechanism was proposed. Other investigators²⁸ reported a digestive-stimulating action of spices mixed with onion and found that bile secretion, bile acid, and pancreatic enzymes were significantly increased in spices containing onions. Rafsanjani et al²⁹ found an increase in basal acid secretion and a decline in pentagastrin-stimulated acid secretion in rats treated with garlic extracts, which is similar to our results, although we used histamine as the stimulant. They attributed this stimulatory effect to the special components in garlic that either increase parietal or chief cell activities through cholinergic mechanisms. Additionally, we had observed an increase in salivary secretion (visual observation) when the rats were administered, showing that cholinergic mechanisms could be involved.

Our ulcer results show that administration of acidified ethanol produced 100% ulcer induction in rats with a mean ulcer index of 126.5 ± 11.5 . It is well known that ethanol causes ulcers and is known to produce gastric mucosal damage within 1–3 minutes of its instillation into the gut, which lasts more than 2 hours by causing areas of focal hyperemia and hemorrhage.³⁰ We have also shown in our previous studies that ethanol causes gastric damage in rodents.^{31,32}

The results of this study clearly showed that raw NS has a gastroprotective effect against gastric ulcers induced by acidified ethanol. The results are in line with previous reports that NS^{21,22} protects against ethanol-induced ulcers. El-Dakhankhny et al²¹ demonstrated that gastric mucin content and glutathione S-transferase (GST) levels were significantly higher and gastric mucosal histamine levels reduced when rats were pretreated with NS oil. An increase in glutathione levels leads to an increase in prostaglandin E₂ (PGE₂) levels, because glutathione is a cofactor in some steps of PGE₂ synthesis.³³ In addition, thymoquinone, the main constituent of NS, has been shown to be gastroprotective against ethanol-induced gastric mucosal injury.^{34,35} Fiorucci et al³⁶ investigated the role of hydrogen sulfide (H₂S) in a rat model of nonsteroidal anti-inflammatory drug gastropathy and concluded that H₂S has a physiologic role in regulating the gastric microcirculation and gastric mucosal protection. Thus, raised gastric mucin, GST, thymoquinone, and H₂S and reduced mucosal histamine could be the mechanism of gastroprotective effect of NS in our study.

Raw garlic and onion showed similar activities in protecting the gastric mucosa against ethanol-induced gastric ulcers. Both were comparable with NS, though NS was more potent (0.25 g/kg for NS against 0.5 g/kg for garlic and onion). The protective effect of garlic is in line with one report that shows garlic to be protective against ethanol-induced gastric ulcer.²³ The gastroprotective effect of onion in this study was remarkable though not totally unexpected. The gastroprotective effect of onion observed in this study is, as far as the authors are aware, the first report of its kind, although onion is known for its other biologic effects such as promoting cardiovascular health by decreasing atherosclerotic or thrombotic disease in populations with increased onion intake.^{37,38} The antiplatelet activity of onion and garlic is determined in part by the native concentration of organosulfur compounds.³⁹ As, initially, raw onion and garlic were used in this study, it was interesting to discover the mechanism of their protective effects on the gastric mucosa against ulcers in the present study. One of the mechanisms suggested was its effect on

the cyclooxygenase activity. Garlic extracts have been shown to decrease serum thromboxane (TX) levels, whereas onion extract has had no effect on TX concentration.⁴⁰ There is convincing evidence that TX is ulcerogenic⁴¹ and that TXA synthase inhibitors protect against the development of gastric erosions in certain animals.^{42,43} Thus, in this study, a possible mechanism of inhibition of gastric ulcers by garlic could be its ability to inhibit TX formation. Garlic and onion contain the organosulfur compound alkylcysteine and sulfoxides such as S-propenylcysteine sulfoxide (major component), S-propylcysteine sulfoxide, and S-methylcysteine sulfoxide, and in addition propionaldehyde and dipropyl disulfide.^{44,45} Sparnins et al^{46,47} and Sumiyoshi and Wargovich⁴⁸ studied the effects of oral administration of these compounds on GST activity and found that GST activity increased in all the tissues. Thus, another possible mechanism of the protective effects of garlic and onion on the gastric mucosa is their actions on increasing the GST levels, which is known to increase prostaglandin synthesis and thus cytoprotection.

Because humans often consume garlic and onion in a cooked form, their efficacy as herbs in the prevention of cardiovascular disease and gastric ulcers may be doubtful. Boiled garlic and onion have been shown to have significantly reduced biologic activity.⁴⁰ It was found that boiled garlic and onion showed a reduced effect on platelet aggregation as compared with raw garlic and onion.⁴⁰ Because of these findings, it was decided also to see whether there are any changes in their activities when boiled NS, garlic, or onion are used on ethanol-induced gastric ulcers. We found that, indeed, the effects of garlic and onion on ulcer index were reduced but not completely abolished. Boiling had no effect on the protective effect of NS on gastric ulcer. One can speculate that active ingredients in NS are different from those in garlic and onion, judging from the lack of a reduced effect of boiled NS's protective effect on gastric ulcers. As far as we are aware, no comparative studies have previously been done of the effects of boiled NS, onion, and garlic on ulcer formation. The reduction of the activities when herbal products are cooked is probably due to the alteration of the chemistry of the active ingredients.

Conclusion

From the results of the study we can conclude that NS, onion, and garlic have a protective effect on acidified ethanol-induced gastric ulcer and gastric acid secretion. Thus, NS, onion, and garlic are beneficial in the prevention of ulcer formation and reduction in acid secretion.

Disclosure

The authors report no conflicts of interest in this work.

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