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Research Article

Gastroprotective and Anti-*Helicobacter Pylori* Potentials of *Pistacia atlantica* Gum Essential Oil Using Experimental Rat Models

Mona Khoramjouy[a], Afsoon Feizi[b], Adel Qaderi[c], Delnia Bahari[c], Somayeh Khezrian[c], Babak Gholamine[d], Farzad Kobarfard[e], Veria Naseri[c*], Mehrdad Faizi[f,g*]

[a] *Phytochemistry Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*
[b] *Department of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.*
[c] *Department of Research and Development, Jiran Darou Company, Sanandaj, Iran.*
[d] *Department of Pharmacology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*
[e] *Department of Medicinal Chemistry, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*
[f] *Department of Pharmacology and Toxicology, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*
[g] *Pharmaceutical Sciences Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

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Abstract

Gastric ulcers are one of the disorders that have a substantial effect on people's lives, and many treatment options come with side effects. This study was conducted to explore the protective and therapeutic properties of the essential oil of the *Pistacia atlantica* subspecies *kurdica* gum on gastric ulcers and gastropathy in rats and its acute oral toxicity and chemical analysis. The animals were administered the essential oil at different doses (12.5, 25, 50, and 100 mg/kg of body weight orally for 21 days) before receiving 85% ethanol. The stomachs were then removed for macroscopic and microscopic examination. Then, we used the *Helicobacter pylori*-induced rat model of gastropathy. The oral administration of the essential oil at doses of 12.5, 25, 50, and 100 mg/kg of body weight showed strong dose-dependent protection against stomach ulcers caused by ethanol, Additionally, the histological examination shows that the essential oil can prevent ethanol-caused stomach ulcers. Administration of the essential oil at a dose of 100 mg/kg for 21 days may have antibacterial effects on *H. pylori*. The findings showed that the essential oil of *Pistacia atlantica* gum, which contains a high quantity of alpha-pinene (>90%), can be beneficial in treating and preventing peptic ulcers in rat models caused by ethanol and *H. pylori.*

Keywords: Peptic ulcer; *Pistacia atlantica* subspecies *kurdica*, Ethanol; *H. pylori*

1. Introduction

A frequent gastrointestinal disorder and distress that affects 4 million people a year worldwide is peptic or gastric ulcer. It happens when the biological equilibrium between harmful and defensive substances in the gastrointestinal tract is disrupted. Antibiotics against *Helicobacter pylori*, H_2 receptor antagonists, proton pump inhibitors and other medications are used to

*** Corresponding Authors**:
Mehrdad Faizi, Department of Pharmacology and Toxicology, School of Pharmacy, Shahid Beheshti University of Medical Sciences, 2660 Vali-e-Asr Ave., P.O. Box: 14155-6153, Tehran 19919-53381, Iran. E-mail: m.faizi@sbmu.ac.ir.
Veria Naseri, Department of Research and Development, Jiran Darou Company, Sanandaj, Iran. E-mail: werianasseri@gmail.com.

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control and treat peptic ulcers. These medications may interact with a wide range of different medications and have undesired effects. Widespread studies were conducted on natural remedies to discover novel alternative treatments with fewer side effects and more appropriate advantages for controlling diseases.

Pistacia atlantica Desf, is an evergreen plant originating on the plateaus of Iran and North Africa. It is also known as the "Baneh" or "Wild Pistachio" tree. This plant, which is local to Iran and succeeds in the Uramanat region of the Kurdistan area, was used for centuries as a remedy for gastrointestinal problems, wound healing, antiseptics, appetizers, expectorants, astringents, emetics, and diuretics [1, 2]. Recent studies reported that this plant has significant antioxidant, antibacterial, antifungal, antidiabetic, antitumor, and anticholinesterase activities. The *Pistacia* genus, part of the Anacardiaceae family, includes 15 species. *Pistacia atlantica* has four sub-species: *atlantica, mutica, kurdica, and cabulica*. The *kurdica* subspecies of *Pistacia atlantica* is the main source of lesser-known gum. The resin from this plant is used in medicine, and several studies have shown that it has strong antibacterial effects [3, 4]. Earlier studies showed that the main active part of the essential oil of *Pistacia atlantica* subspecies *kurdica* gum is a molecule called α-pinene, a monoterpene type [4, 5]. Alpha pinene has demonstrated Antibacterial, insecticidal, and anticancer effects and is utilized as a solvent and preservative in pharmaceutical products [6, 7].

This research assesses the protective and therapeutic benefits of the essential oil from the *Pistacia atlantica* subspecies *kurdica* by examining its effects on ethanol-induced gastric ulcers and *H. pylori*-induced gastropathy in rats, as well as investigating its acute oral toxicity.

2. Materials and Methods

2.1. Animals

This study utilized male healthy Wistar rats (8-12 weeks old, 200-250 g body weight) following ethical principles and under the supervision of the "Committee on Animal Experiments" associated with Shahid Beheshti University of Medical Sciences with the ethics code of IR.SBMU.PHARMACY.REC.1401.040. The rats were exposed to a 12-hour light/dark cycle consisting of 12 hours of dark (night) and 12 hours of light (day). They were provided free admission to water and food while maintaining an environmental temperature range of 22 ± 2 °C and a humidity level of around 45-50 %. Each rat was used for a single experiment, ensuring no animal was used more than once. Before the experiment, the rats experienced a food deprivation period of 24 hours but had unlimited access to water until 2 hours before the test.

2.2. Preparation and analysis of essential oil

The Jiran Darou Company, Sanandaj, Iran, prepared the essential oil of *Pistascia atlantica* subspecies *kurdica* gum. During the initial month of summer, the gum was harvested from the trees in Iran's Kurdistan area. The gum underwent hydro distillation (5 hours), obtaining an essential oil at 20% yield from the fresh weight of the gum. The essential oil was preserved at -20 °C before evaluation. Analysis of the essential oil was conducted using a gas chromatograph (GC, Varian 3700, Shimadzu C-R3A) with a fusion-silica capillary column (25 m × 0.25 mm i.d., 0.25 µm film thickness) and a flame ionization detector, as described by Sharifi and Hazell [4].

2.3. Ethanol-induced mucosal ulcer:

This experiment randomly divided animals into seven groups, each comprising six rats. These groups included a control group administered with corn oil as a vehicle, a positive control group treated with ranitidine 50 mg/kg, a sham group of normal animals, and four groups treated with various doses (12.5, 25, 50, and 100 mg/kg) of the essential oil of *Pistacia atlantica* subspecies *kurdica* gum. The rats were orally administered the compounds one hour prior to receiving 85% ethanol (1 ml/200 g). All the animals received oral 85% ethanol except the sham group, which received distilled water. After two hours, the rats were anesthetized, and their stomachs were removed. The stomachs were examined macroscopically after being cleaned with ice-cold normal saline. Subsequently, for histological analysis, the samples were submerged in 10% formalin [8-10].

2.4. Measurement of ulcer index and protection rate

A macroscopic analysis was directed to assess the existence of lesions and severity on the stomach surface. Initially, photographs of the surface of the stomach were obtained with a digital camera and subsequently processed using Image J software. The measurement of lesions was quantified as the Ulcer Index (UI) in millimeters, along with the percentage of ulcer inhibition, indicating the level of protection provided. The UI was determined by adding up the lengths of each lesion, with every five petechiae considered equivalent to a 1-millimeter ulcer. Lesions between 1 and 2 millimeters were multiplied by a factor of 2, and those between 2 and 4 millimeters were multiplied by a factor of 3. Similarly, those between 4 and 6 millimeters were multiplied by a factor of 4. Lesions greater than 6 millimeters were multiplied by a factor of 5 [11]. The UI and protection rate were ultimately calculated using specific formulas:

Ulcer Index = Σ (length of each lesion x respective multiplication factor)

Protection rate (%) = [(Control UI - Test UI) / Control UI] ×100

2.5. Microscopic evaluation of Ethanol-induced gastric ulcer

The stomach tissue samples were initially preserved and fixed in a solution of 10% formalin. Subsequently, the samples were subjected to dehydration using various alcohol concentrations, followed by clearing with xylene and embedding in paraffin blocks to conduct a microscopic assessment. Sections of 5 microns in thickness were created using a microtome. The samples were then subjected to the common histological staining method involving Hematoxylin and Eosin. Finally, the histopathological changes were evaluated [11].

2.6. Helicobacter pylori-induced gastropathy

The *Helicobacter pylori* strain (Atcc 43504) used in this experiment was obtained from the Pasteur Institute, Tehran, Iran. The rats were given a 1 mL feed (oral gavage) containing *H. pylori* at a concentration of 10^{8-10} CFU/mL. The rats were separated into four groups: a control group with a single *H. pylori* infection; an *H. pylori* infection treated with essential oil (100 mg/kg); an *H. pylori* infection treated with amoxicillin 50 mg/kg + clarithromycin 25 mg/kg + omeprazole 20 mg/kg (positive control), and a normal control group (sham group). Each group consisted of 6 rats. The rats in the experimental groups were administered an oral dose (1 mL) of *H. pylori* at a concentration of 10^{8-10} CFU/mL, administered six times over three days (every 12 hours). The rats in the control group and *H. pylori* group were given 1 mL of saline through oral administration [12-15]. For the whole 21-day period, this intragastric administration was performed once daily. After 21 days, the rats were sacrificed, and each rat's stomach was dissected alongside the greater curvature towards the duodenum. The stomach was preserved in a paraffin-embedded solution comprising 10% formalin, embedded in paraffin, and sliced into five µm thick sections using a microtome. These sections were then subjected to additional analysis. Staining techniques including H&E and Giemsa were employed to assess any histological abnormalities [16, 17]. **Table 1** shows the evaluation and scoring of gastropathy in the stomach sections.

Table 1. The microscopic evaluation score in H&E staining**.**

	Score 1	**Score 2**	**Score 3**
Depth of the erosion	Mucosal depth of up to 1/3	Mucosal depth of up to 1/3	Total mucosa
Hemorrhage	Focal	Mild	Severe
Inflammation	Light	Mild	Severe
Apoptosis	Light	Mild	Severe

2.7. Acute oral toxicity

Acute toxicity refers to an unintended effect that occurs immediately after the administration of a substance within 24 hours. Studies on acute toxicity provide important information, such as the mortality rate associated with the use of a specific substance. The primary parameter for assessing acute toxicity is the LD_{50} value, which represents the lethal dose of a substance. Various methods are available for determining the lethal dose of a compound, with preference given to those that minimize animal usage. In this study, the Lorke method was utilized to investigate acute toxicity. This method consists of two phases. During the first phase, different doses of the target substance were orally administered as a single dose to each group of animals (10, 100, and 1000 mg/kg). After that, the animals were observed for 24 hours, and any fatalities resulting from compound administration were recorded. The second phase involved administering different doses of the target substance as a single oral dose to each animal (1600, 2900, and 5000 mg/kg). Again, the animals were monitored for 24 hours, and mortalities were reported. From these result, the LD_{50} value was calculated [18]. Adult female Wistar rats, aged 8 to 12 weeks, weighing between 200 and 250 grams, were utilized.

The animals underwent a fasting period lasting one night before the substance was orally administered. In this research, each animal received a single oral dose of the compound containing the essential oil derived from the *Pistacia atlantica* subspecies *kurdica* gum.

2.8. Statistical analysis

The microscopic images of the samples were evaluated using the Image J software for data analysis in an academic context. ANOVA (one-way analysis of variance) and Tukey's post hoc test were applied to examine the differences between the groups. A significance level of $P<0.05$ was considered statistically significant. The data are reported as mean + SEM (standard error of the mean). The GraphPad Prism software was employed for data analysis.

3. Results and Discussion

3.1. Chemical analysis of essential oil

The composition of the *Pistacia atlantica* subspecies *kurdica* gum essential oil presented in **table 2**. The main active compound of essential oil was α-pinene (92.29%).

Table 2. The composition of essential oil of *Pistacia atlantica* subspecies *kurdica* gum**.**

Compounds	Percent of total
α-Pinene	92.29
Camphene	1.06
Sabinene	0.16
β-Pinene	3.20
Δ3-Carene	0.23
Limonene	0.25
Verbenol	1.15
Other	1.66

3.2. Gastroprotective of Pistacia atlantica on Ethanol-induced ulcer

The gastroprotective properties of the essential oil derived from *Pistacia atlantica* subspecies *kurdica* gum were evaluated. According to the macroscopic images, oral administration of several doses of the essential oil, including 12.5, 25, 50, and 100 mg/kg, significantly inhibited ethanol-induced gastric ulcers in the rat experimental model in a dose-dependent mode compared to the control group (**Figure 1**).

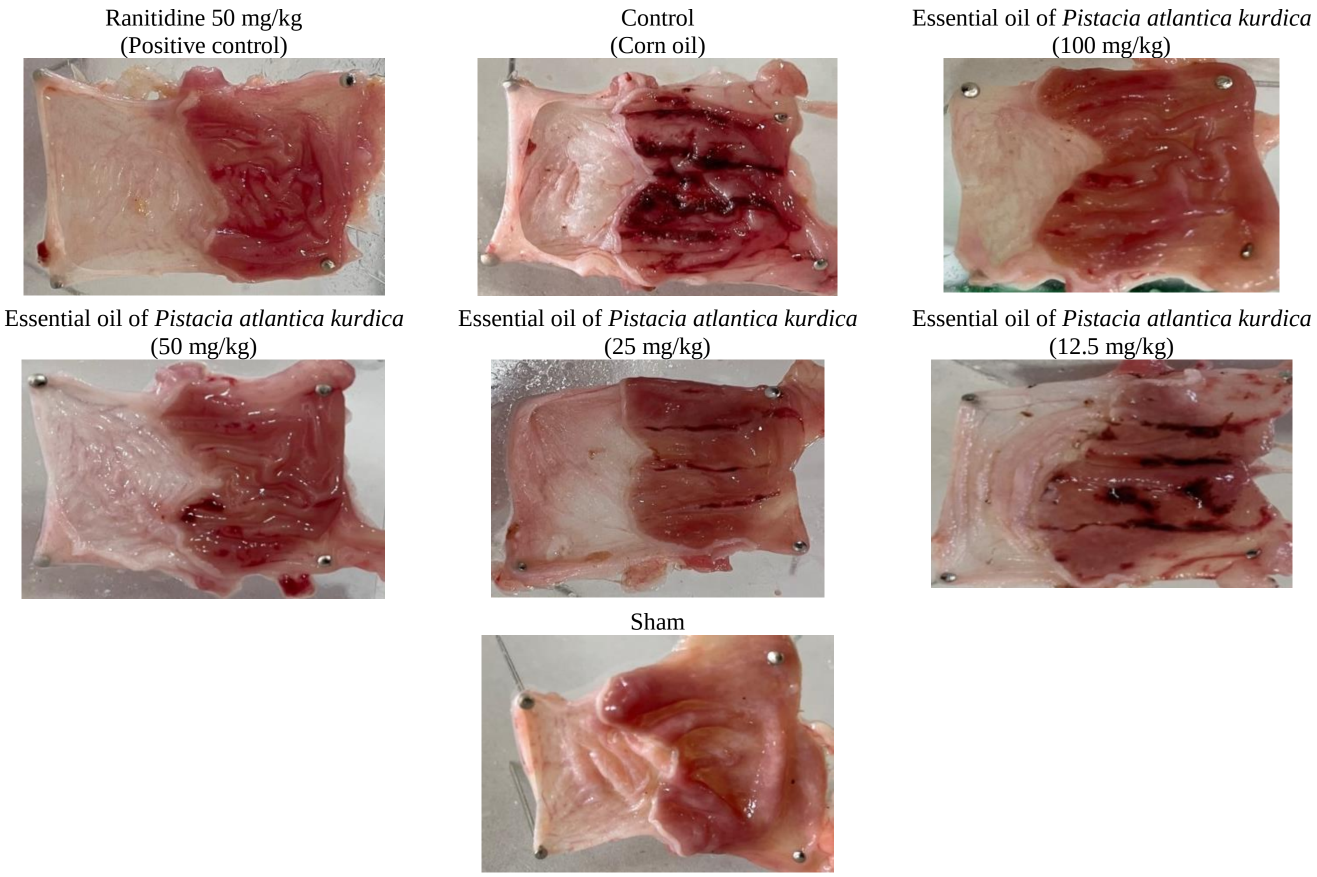

Figure 1. The macroscopic images of stomachs after oral administration of Corn oil (Control), ranitidine 50 mg/kg (Positive control), and various doses of the essential oil of *Pistacia atlantica* subspecies *kurdica* gum (12.5, 25, 50, and 100 mg/kg). A digital camera recorded these images.

Furthermore, the results indicated that the administration of all different doses of the essential oil (12.5, 25, 50, and 100 mg/kg) caused a significant reduction in the ulcer index (P<0.01, P<0.0001, P<0.0001, and P<0.0001, respectively) and a significant increase in protection rate (P<0.05, P<0.0001, P<0.0001, and P<0.0001, respectively) compared to the control group (**Figures 2** and **3**). Additionally, Ranitidine administered at a dosage of 50 mg/kg demonstrates a significant decrease in ulcer index (P<0.0001) and an increase in protection rate (P<0.0001).

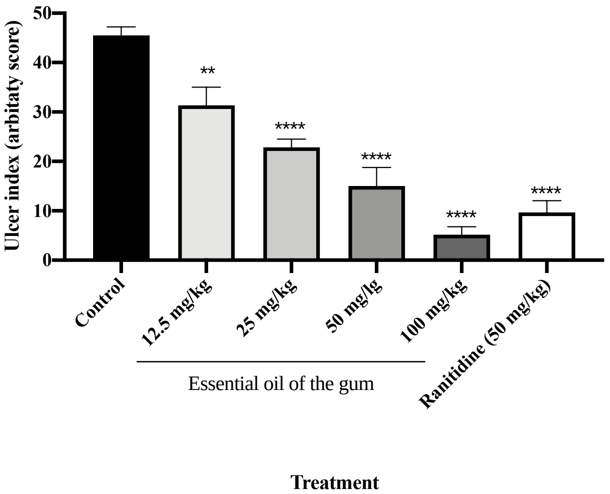

Figure 2. Effects of oral administration of the essential oil of *Pistacia atlantica* subspecies *kurdica* gum on the formation of gastric lesions measured as Ulcer Index (UI). Animals received 12.5, 25, 50, and 100 mg/kg/day essential oil (oral gavage) for 14 days. The positive control group (50 mg/kg of ranitidine), while the control group received corn oil (vehicle). **P < 0.01, ****P < 0.0001 compared with the control group. The results were analyzed by one-way ANOVA followed by Tukey's post-hoc test. Data are presented as mean + SEM (n = 6).

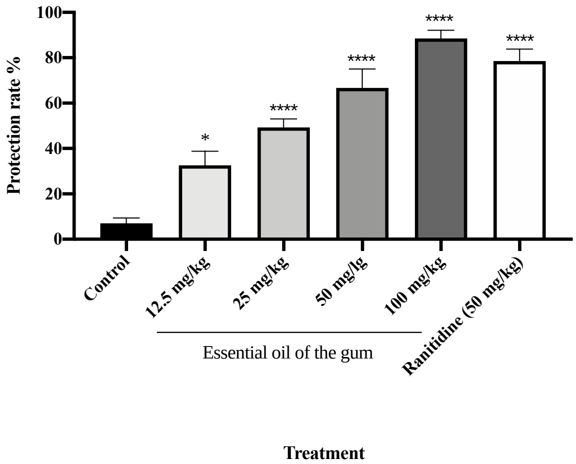

Figure 3. The effects of oral administration of the essential oil of Pistacia atlantica subspecies kurdica gum on inhibiting gastric lesions were measured as the Protection Rate. Animals received 12.5, 25, 50, and 100 mg/kg/day essential oil (oral gavage) for 14 days. The positive control group (50 mg/kg of ranitidine), while the control received corn oil (vehicle). *P < 0.05, ****P < 0.0001 compared with the control group. The results were analyzed by one-way ANOVA followed by Tukey's post-hoc test. Data are described as mean + SEM (n = 6).

3.3. Histopathological evaluation of gastric tissue in Ethanol-induced gastric ulcer

As shown in **Figure 4**, based on the histopathological analysis of the Sham group, the stomach appeared entirely healthy with no signs of bleeding, edema, or any observed wounds.

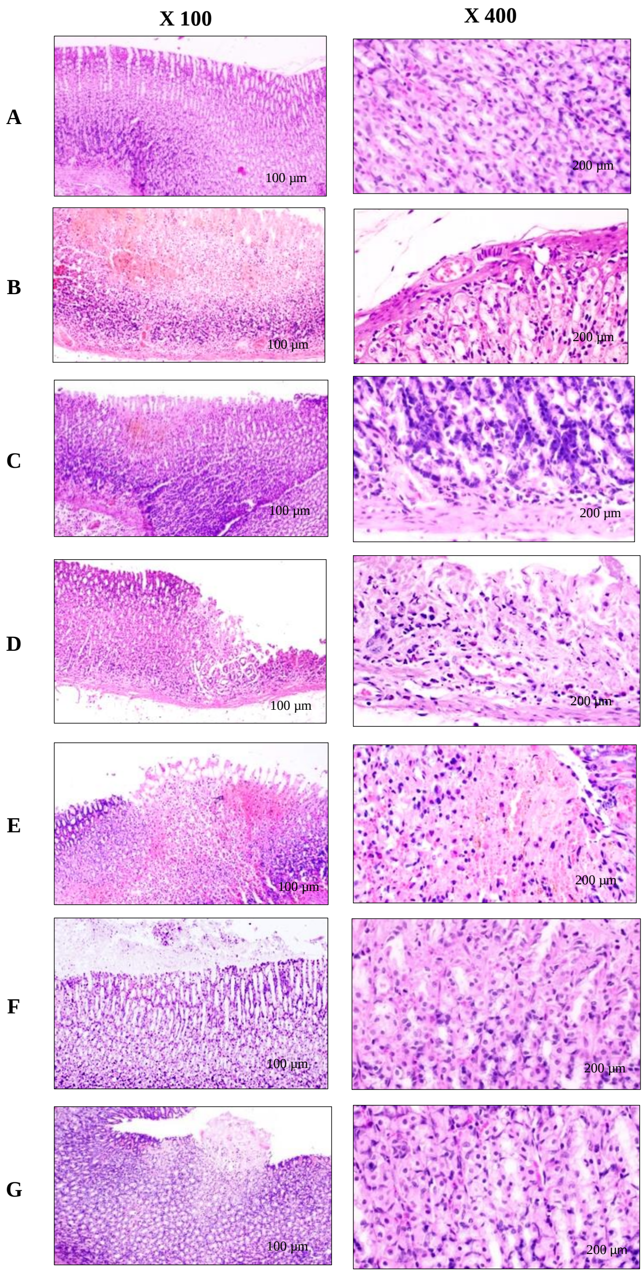

Figure 4. Microscopic images of gastric tissue in ethanol-induced gastric ulcer, stained with Hematoxylin and Eosin methods (First line x100 and Second line x400). First row: Sham group; Second row: control group (ethanol-induced gastric ulcer with no treatment); Third row: *Pistacia atlantica* subspecies *kurdica* (ethanol-induced gastric ulcer treated with 12.5 mg/kg of essential oil); Forth row: *Pistacia atlantica* subspecies *kurdica* (ethanol-induced gastric ulcer treated with 25 mg/kg of essential oil); Fifth row: *Pistacia atlantica* subspecies *kurdica* (ethanol-induced gastric ulcer treated with 50 mg/kg of essential oil); sixth row: *Pistacia atlantica* subspecies *kurdica* (ethanol-induced gastric ulcer treated with 100 mg/kg of essential oil); seventh row: Ranitidine group (ethanol-induced gastric ulcer treated with ranitidine 50 mg/kg).

Conversely, in the control group (mice with gastric ulcers induced by ethanol), the following pathological changes were noted: multiple areas of hyperemia within the mucosa, deep mucosal hemorrhaging, extensive mucosal necrosis, and hemorrhage, mucosal erosion (wounding of the mucosal surface) leading to the destruction of epithelial tissue, degeneration of parietal or partial cells, and severe ulcers (deep wounds) with a loss of blood vessels. Additionally, the mucosa showed hyperemia and significant edema, along with the infiltration of neutrophils.

Upon examining the group that received the essential oil at doses of 12.5 mg/kg, there was evidence of submucosal edema, hemorrhage, mucosal lesions, necrosis, and a substantial infiltration of neutrophils. The group received 25 mg/kg of essential oil and exhibited submucosal edema, neutrophil infiltration, mild mucosal necrosis, mucosal hyperemia, and superficial necrotic foci. In the case of the group received 50 mg/kg doses of the essential oil, there were non-hemorrhagic superficial mucosal lesions, superficial mucosal necrosis, a reduction in submucosal edema, surface wounds, and a decrease in neutrophils. Furthermore, the histopathological examination of the group that received 100 mg/kg of essential oil revealed limited foci of mucosal lesions, a relatively normal capillary structure, and superficial mucosal bleeding.

Lastly, the group treated with ranitidine showed multifocal mucosal ulcers, mild mucosal bleeding, and moderate infiltration of neutrophils (**Figure 4**).

3.4. *Helicobacter pylori-induced gastropathy*

The factors for histological characterization included the depth of tissue erosion and the presence of bleeding (hemorrhage), inflammation, and apoptosis in H&E staining. Table 1 lists the criteria for microscopic examination employed in this study. The stomachs of the sham group received a score of 0. Positive control (amoxicillin 50 mg/kg + clarithromycin 25 mg/kg + omeprazole 20 mg/kg) reduced gastric mucosal damage compared to control (*H. pylori* only). Considering the microscopic scores of ulcer induction in the *H. pylori* model, a reduction in the depth of erosion, hemorrhage, and inflammation scores was observed for the essential oil 100 mg/kg group compared with the control group ($P<0.01$, $P<0.05$, and $P<0.05$, respectively; **Figure 5**). The microscopic images of both H&E and Giemsa staining are shown in **Figure 6**. In Giemsa staining, the *H. pylori* group (B) was initiated to have high positive (+++) reactivity (red arrow), which was stronger than the *Pistacia atlantica* subspecies *kurdica* (treated with 100 mg/kg of essential oil) and positive control groups (+ and +, respectively; C and D). However, in the sham group, there was no evidence of *H. pylori*.

3.5. *Acute oral toxicity*

Oral dose of 10, 100, 1000, 1600, 2900, and 5000 mg/kg of the essential oil was used in two phases to test its acute oral toxicity. Since no clinical indicators of toxicity were discovered in all doses, the essential oil was determined to be non-toxic and practically non-hazardous, and LD_{50} was calculated at > 5000 mg/kg. According to ethnobotanical research, *Pistacia* species are important for human nutrition. *Pistacia atlantica*, a member of the *Anacardiaceae* family, is usually used in traditional Iranian medicine to treat various disorders, including pain, dyspepsia, and peptic ulcer. *Cabulica*, *kurdica*, *atlantica*, and *mutica* are the four subspecies or variants of *Pistacia atlantica* that have been identified. *Pistacia atlantica* and its subspecies have a wide range of traditional uses, which have been supported by pharmacological studies [19, 20]. *Pistacia atlantica* subspecies *kurdica* has the highest antioxidant content. The extract's highest antioxidant activity level could be attributed to a greater total phenolic content [21].

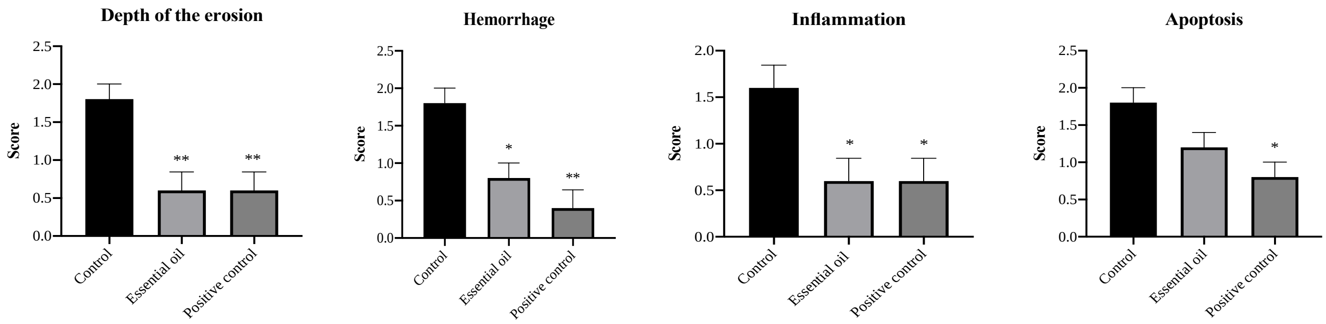

Figure 5. Microscopic scores of oral administrations of essential oil of *Pistacia atlantica* subspecies *kurdica* at a dose of 100 mg/kg for 21 days in the level of wound depth, bleeding, and inflammation caused by *Helicobacter pylori*. *$P < 0.05$, **$P < 0.01$ compared with the control group. The positive control group received amoxicillin 50 mg/kg + clarithromycin 25 mg/kg + omeprazole 20 mg/kg. The results were analyzed by one-way ANOVA followed by Tukey's post-hoc test. Data are described as mean + SEM.

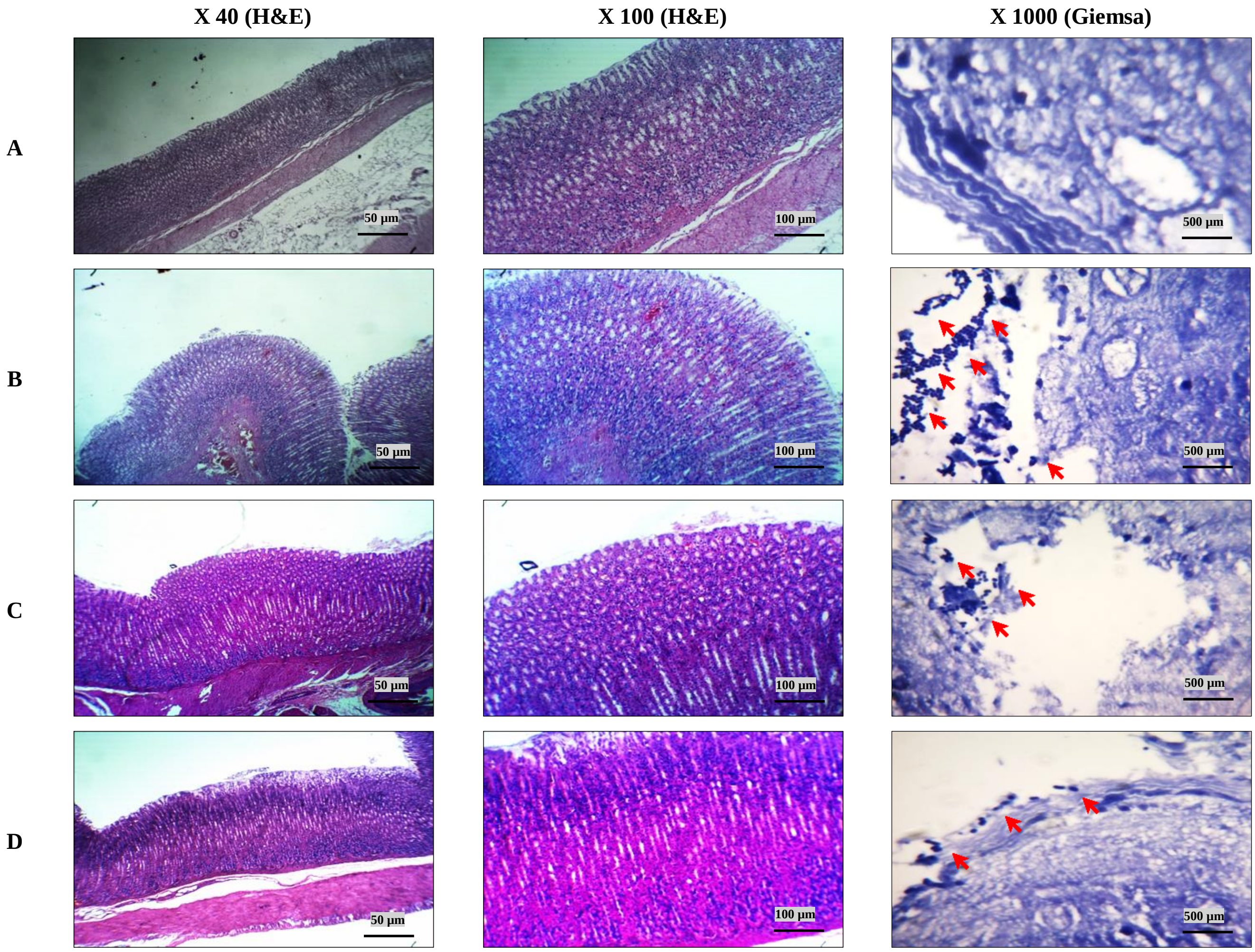

Figure 6. Microscopic images of *H. pylori*-induced gastropathy by H&E and Giemsa staining method 21 days after treatments. A: Sham group. B: control group (*H. pylori*-induced gastropathy with no treatment). C: *Pistacia atlantica* subspecies *kurdica* (*H. pylori*-induced gastropathy treated with 100 mg/kg of essential oil); D: Positive control group (*H. pylori*-induced gastropathy treated with amoxicillin 50 mg/kg + clarithromycin 25 mg/kg + omeprazole 20 mg/kg). The red arrows indicate the presence of bacteria.

The findings of this research show that the essential oil of *Pistacia atlantica* subspecies *kurdica* gum has protective and antibacterial properties against rat models of gastric ulcers. Oral administration of the essential oil at different doses of 12.5, 25, 50, and 100 mg/kg showed significant dose-dependent protection against ethanol-induced gastric ulcers compared to the control group. In all groups receiving different doses of the essential oil compared to the control group, there was a significant decrease in the Ulcer Index and an increase in protection rate against ethanol-induced gastric ulcers. Additionally, the histopathological examination suggests that essential oil can protect against ethanol-induced gastric ulcers. Overall, compared to the control group and similar to the ranitidine-treated group, the mucosal lesions in the groups receiving different doses of the essential oil (12.5, 25, 50, and 100 mg/kg) were much slighter, less wide-ranging, and less severe. Notably, the group that received a dose of 100 mg/kg of the essential oil showed the highest gastroprotective effects.

Additionally, a histopathological examination confirms that the essential oil can prevent ethanol-induced gastric ulcers.

A high-risk factor for the improvement of gastritis, peptic ulcers, and stomach cancer is an *H. pylori* infection. Given the possibility of degeneration, the current method of *H. pylori* suppression is awkward and also resistance to current antibiotic treatments have been shown. Given that one of the most widespread infections in the world is *H. pylori*, the other aim of this study was to determine the efficacy of *Pistacia atlantica* subspecies *kurdica* essential oil in the rat model of gastropathy induced by *H. pylori*.

According to the scores in the study of gastropathy by *H. pylori*, the depth of erosion, hemorrhage, and inflammation were significantly reduced in the group obtaining the essential oil at a dose of 100 mg/kg, compared with the control group. Additionally, as a control, the *H. pylori* group displayed a high positive reaction (+++) in the microscopic images of Giemsa staining, which was stronger than that of the essential oil group at a dose of 100 mg/kg and positive control. These results recommend that the essential oil of *Pistacia atlantica* subspecies *kurdica* gum may have antibacterial effects on *H. pylori* when administered at 100 mg/kg for 21 days.

According to the toxicological investigation, the single oral administration of the essential oil at a 5000 mg/kg dosage proved non-toxic. It did not produce any symptoms of toxicity in rats [22]. However, it is important to assume human trials to determine its toxicity in humans.

The previous study supported the use of *Pistacia atlantica* oleoresin in traditional and folk medicine as a nutritional supplement and supplemental treatment for controlling gastric ulcers. In veterinary research, the essential oil of *Pistacia atlantica* subspecies *kurdica* gum as a food supplement may have the ability to alter the rumen microbial community and progress ruminal fermentation in sheep [5].

In a previous study, the hydro distillation method and a GC-MS analysis were used to extract the essential oil of *Pistacia atlantica* subspecies *kurdica* gum, and 95 different chemicals were discovered. The most important and abundant of them were α-pinene and bornyl acetate. In previous studies, antibacterial efficacy of the essential oil against *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Streptococcus faecalis*, *Bacillus cereus*, *Staphylococcus aureus*, and *Candida albicans* was also investigated [23, 24]. Monoterpene (93.5%) and sesquiterpene hydrocarbons (5.45%) made up the majority of the total detected components of essential oil [25]. The essential oil of *Pistacia atlantica* subspecies *kurdica* gum is one of the best essential oils to use as an additive in the food industry to improve food safety and lower the risk of food contamination and as an antioxidant agent in the medical and pharmaceutical sectors. The *Pistacia atlantica kurdica* extract inhibits *Porphyromonas gingivalis* growth and has bactericidal effects. It also promotes rat epidermal wound healing [26]. Also, this extract may be assumed as a potential anti-mycotoxin agent against *Aspergillus parasiticus* in pharmaceuticals or manufacturing farming [27].

α-pinene may be responsible for the essential oil's gastroprotective and anti-Helicobacter pylori effects. The oral gum of *Pistacia atlantica kurdica* and its volatile oil has been shown in several studies to have anti-inflammatory properties in experimentally produced colitis [4]. According to the clinical trial findings, taking 1g of powdered *P. atlantica* subspecies *kurdica* gum twice a day for two weeks dramatically reduces the presence of *H. pylori*. It improves dyspeptic symptoms when compared to placebo [28]. The essential oil of *Pistacia lentiscus*, a naturally occurring source of bioactive compounds, has a significant antibacterial action against many strains of *H. pylori*, including resistant ones [29]. The essential oil of *Pistacia atlantica* Desf. oleoresin proved effective despite metronidazole-resistant *H. pylori*, and the MIC ranged from 275 to 1100 µg/mL. α-Pinene may be the causative component [3]. Ethnopharmacological studies have demonstrated the anti-ulcerogenic effects of *Styrax liquidus*, a local ethnobotanical treatment utilized in Turkey. Through GC-MS analysis of the *Styrax liquidus* (Turkish sweetgum), substantial components like α-pinene were discovered [30]. A medicinal herb called *Myrtus communis* is utilized in traditional medicine worldwide. This herb's major biologically active components, including α-Pinene, limonene, polyphenols, myrtucommulone, and myrtenyl acetate, were extracted in high quantities. This plant has been traditionally utilized to treat peptic ulcers, diarrhea, and inflammation [31].

4. Conclusion

The results of this study prove that the essential oil of *Pistacia atlantica* subspecies *kurdica* gum, which has a high level of α-pinene, is effective in treating and preventing peptic ulcers induced by both ethanol and *H. pylori* in rat models. The treatment of gastric ulcers is extremely expensive in developing nations. As a result, there is an increasing request for more cost-effective antiulcer medications with fewer undesired effects. In this regard, natural products such as the essential oil of *Pistacia atlantica* subspecies *kurdica* gum provide great outlooks for protecting and managing gastric ulcers.

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production date 27/07/1401 was supplied by *Jiran Darou* Company with registration number 11121 and national number 14007504594, which is on a knowledge-based path and commercialization has been placed.

Conflict of interest

The authors declare to have no conflict of interest.

Data availability

The dataset used and/or analyzed in the current study is available upon request.

Athors Orcid numbers:

Mona Khoramjouy: 0000-0002-4607-5353
Babak Gholamine: 0000-0002-7494-988X
Farzad Kobarfard: 0000-0001-6679-3275
Veria Naseri: 0000-0001-7043-1250
Mehrdad Faizi: 0000-0002-6896-838X

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Using artificial intelligence chatbots

There was no use of artificial intelligence in the making of this article.

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