https://doi.org/10.48047/AFJBS.6.14.2024.9049-9063

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Protective Effect of *Myrtus Communis* Against Ethanol-Induced Gastric Ulcer in Rats

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Volume 6, Issue 14, Aug 2024

Received: 15 June 2024

Accepted: 25 July 2024

Published: 15 Aug 2024

doi: 10.48047/AFJBS.6.14.2024.9049-9063

Summary

Myrtus communis subsp.is a plant which is traditionally used for the treatment of ulcer and diarrhea in Algeria. The aim of the study is to evaluate the antiulcer activity of aqueous extract of *Myrtus communis subsp* (AEMc). Fasted rats treated with 96% ethanol (0.5 mL) to induce gastric ulcer, were pretreated orally with AEMc extract from leaves at different doses (400 and 600 mg/kg body weight (BW) and Omeprazole (20 mg/kg) and distilled water were used as a positive and negative control respectively. The results showed that the pre-treatment with AEMc decreased significantly the ethanol gastric ulcer index value and preserved the integrity of the gastric mucosa by preventing the mucosal ulceration caused by ethanol. The AEMc prevented alcohol-induced decrease in stomach antioxidant enzyme activities such as catalase, and superoxide dismutase. Total reduced glutathione and malondialdehyde tissue contents were also reversed in AEMc-pretreated rats when compared with the negative control group.

Key Words: *Myrtus communis subsp*, Gastric ulcer, *Oxidative stress.*

INTRODUCTION

Gastric ulcer is an imbalance between damaging factors within the lumen and mechanisms within the gastro- duodenal mucosa **(Laine, 2008)**. For numerous decades gastric ulcer was linked as a lesion of the gastric mucous wall, and it was the most frequent cause of surgery, with high morbidity and mortality rates **(Alimi *et al*., 2010; Yuan, 2006)**. The factual cause of gastric ulcer is Helicobacter pylori (H. pylori) and the use ofnon-steroidanti-inflammatory medicines **(O'Malley, 2003)**. In addition to these well linked causes, inordinate ingestion of ethanol (EtOH) can be a major cause of gastric ulcer **(Guslandi, 1987)**, by adding the mucosal permeability and releasing vasoactive products, leading to vascular damage and

cell necrosis **(Melchiorri *et al*., 1997)**. Because of unwelcome side goods of current specifics and lack of proper control of the complaint that leads to patient dissatisfaction, further attention has been paid to indispensable curatives. Myrtle (*Myrtus communis* L., Myrtaceae) is a extensively honored factory in traditional drug, belonging to the Myrtaceae family, which comprises 100 rubrics and 3000 species of evergreen shrubs or small trees that can reach up to 5 measures in height **(Sumbul *et al*., 2011)**. The factory is native to Southern Europe, North Africa, and Western Asia and is also set up in other regions similar as South America, northwestern Himalaya, and Australia **(Males *et al*., 2006; Nassar *et al*., 2010)**.

Different parts of the myrtle plant, such as its berries, branches, leaves, and fruits, have long been used as a traditional remedy. The leaves' astringent, tonic, and antiseptic properties make them effective in healing wounds and treating disorders of the digestive and urinary systems. The oil derived from myrtle is antiseptic and anti-catarrhal, making it useful for chest ailments. In the past, fruit decoctions were used to bathe newborns with reddened skin, while decoctions of leaves and fruits were used for washing sores. The leaves' decoction is still used in some countries for vaginal lavage, enemas, and to treat respiratory diseases **(Akin *et al*., 2012).**

In general, this plant has been traditionally used for various ailments including diarrhea, peptic ulcers, hemorrhoids, inflammation, bleeding, headache, palpitation, leucorrhoea, urethritis, epistaxis, conjunctivitis, excessive perspiration, pulmonary and skin diseases **(Gauthier and Gourai, 1989; Evans, 2002).**

Myrtle herb has been found to contain numerous components, among which polyphenols, myrtucommulone (MC), semimyrtucommulone (S-MC), 1,8-cineole, α-pinene, myrtenyl acetate, limonene, linalool, and α-terpinolene have been identified as the major bioactive compounds **(Ghazal,2014).**

To our knowledge, no data have been reported concerning the ability of *Myrtus communis* to counteract gastric ulcer development. We investigated the effect of the aqueous extract of *Myrtus communis* (AEMc) on ethanol-induced gastric ulcer in rats.

MATERIALS AND METHODS

Plant Material and Preparation of Extract

In February 2022, *Myrtus Communis* was collected from the Nador region in Guelma, Algeria. The leaves were carefully cleaned, dried, and kept away from light. They were then crushed using a traditional metal mortar and an electric mixer, resulting in powders that will be utilized for animal treatment at a later time.

To mimic traditional preparations, the vegetal powder was mixed with hot water. Specifically, 300g of each vegetal powder was combined with 2000 ml of distilled water in a crystallizer. The mixture was stirred for approximately 1 hour until it reached boiling point. Once cooled, the mixture was filtered using filter paper. The resulting filtrate was then concentrated through rotavapor and freeze-dried.

Animals

Male Wistar rats, weighing 150-170 g, were procured from the Laboratory Animal Center at the University of Guelma (Algeria). These rats were given free access to standard diet and water, while being kept in controlled conditions of temperature (22 ± 2 C), relative humidity (65 ± 5%), and a 12-hour light/dark cycle. To prevent coprophagia, the rats were housed in cages that had raised floors made of wide mesh. Before the start of the experiment, all animals underwent a 24-hour fasting period. Ethical

approval for the animal experimentation was obtained from the Laboratory of Applied Biochemistry, Faculty of Nature and Life Sciences, Ferhat Abbas University of Setif 1, Algeria (Nr ECA/001/22)

Administration and Dose Selection

A total of 30 rats were used in this study and divided into five groups, each consisting of six rats. The rats were treated with different substances using gavage, as described below:

1. Control group: received 0.5 mL of distilled water, followed by another 0.5 mL of distilled water after 1 hour.
2. EtOH-treated group: received 0.5 mL of distilled water, followed by 0.5 mL of 96% (v/v) EtOH solution after 1 hour.
3. AEMc + EtOH-treated groups: received AEMc at doses of 400 mg/kg and 600 mg/kg, respectively. One hour later, they received 0.5 mL of 96% EtOH.
4. Omeprazole + EtOH-treated group: received Omeprazole at a dose of 20 mg/kg, followed by 0.5 mL of 96% EtOH one hour later.

One hour after the administration of either EtOH or distilled water, the animals were sacrificed by decapitation. The pyloric canal was ligated, and the resulting gastric juice was collected, centrifuged, and its volume and pH were measured.

Estimation of Gastric Wall Mucus

The stomach of each rat was removed and opened along the great curvature. The gastric wall mucus was gently scraped with a glass slide and weighed.

Determination of the Ulcer Index and the Protection Index

Using Image J software, the area of the mucosal lesion was measured in square millimeters (mm2). The Ulcer Index (UI %) was calculated for each rat by determining the mean lesion area (mm2). The percentage of inhibition (PI %), as described by Nguelefack et al. (2008), was also calculated using the formula provided below:

PI % = (UI EtOH - UI Treated)/ UI EtOH x 100

Where UI EtOH is the ulcer index of rats treated with ethanol and UI Treated is the ulcer index of rats pre-treated with AEMc or Omeprazole.

Biochemical Analysis

After conducting macroscopic analyses, the stomach tissues weighing 0.4g each were ground and homogenized in 4 mL of Tris buffer saline solution (pH 7.4) while being kept on ice, using an ultra-Turrax homogenizer. They were then centrifuged at 4°C (6000 g/10 min), and the supernatants were collected for the biochemical assay. The activity of SOD was determined using the method described by Misra and Fridovich (1972), while CAT was measured through the method of Aebi (1984). The MDA was quantified using the method of Buege and Aust (1978).

Histological Analysis

The stomach samples taken from each rat were fixed in 10% buffered formalin and then embedded in paraffin. The paraffin blocks were cut into sections with a thickness of 5 μm and stained with hematoxylin and eosin (H&E) following standard procedures for histological evaluation (Laine and Weinstein, 1988).

Statistical Analysis

The statistical analysis was conducted by employing a one-way ANOVA followed by a Tukey post hoc test using Graph Pad Prism 10. Statistical significance was considered at $p < 0.05$ to determine differences between treatments. The results are presented as mean ± standard error of the mean (SEM).

RESULTS

Effect of AEMc on Various Gastric Physicochemical and Morphological Parameters in Ethanol-Induced Gastric Ulcer

Compared to the control group, rats treated with EtOH showed a significant increase in gastric juice volume (GJV) (4.84 ± 2.2 vs 1.14 ± 1.13 mL; $p < 0.001$), which resulted in an increase in stomach volume (Figure. 1a-b). Omeprazole, which was used as a reference molecule, significantly reduced the expansion of gastric juice and stomach volume induced by EtOH, with a rate of 72.72 % (1.32 ± 1.10 mL vs 4.84 ± 2.2 mL for the EtOH group; $p < 0.001$) (Table 1) (Figure. 1e). It is noteworthy that the stomach changes induced by alcohol intoxication were significantly and dose-dependently reduced by AEMc (Figure. 1c-d).

The administration of 400 and 600 mg/kg of AEMc resulted in a reduction of 43.59% ($p < 0.01$) and 59.09% ($p < 0.001$), respectively, in comparison to the EtOH group (2.73 ± 0.77 and 1.98 ± 3.25, respectively for 400 and 600 mg AEMc/kg), which had a gastric volume of 4.84 ± 2.20 mL. In contrast, the gastric juice pH was significantly lower in EtOH-treated rats (2.78 ± 1.22) than in the control group (5.13 ± 1.32) ($p < 0.001$) (Table 1). Notably, AEMc pretreatment dose-dependently increased the gastric juice pH in EtOH-treated rats (6.15 ± 2.61 ($p < 0.01$) and 8.74 ± 1.76 ($p < 0.001$), respectively, with 400 and 600 mg AEMc/kg) compared to the EtOH group (pH 1.78 ± 0.22) (Table 1). At a high AEMc dose of 600 mg/kg, the pH values were similar to those of Omeprazole (9.65 ± 0.21 vs 8.74 ± 1.76, $p > 0.05$) (Table 1). In the same way, the administration of EtOH resulted in a significant reduction of gastric mucus secretion by 50.53% ($p < 0.001$). However, the administration of AEMc resulted in a dose-dependent increase in the weight of the gastric mucus (SMW) from 61.83 ± 6.74 mg in the EtOH group to 156.5 ± 4.33 ($p < 0.001$) and 191.00 ± 6.18 ($p < 0.0001$), respectively, for 400 and 600 mg AEMc/kg (Table 1).

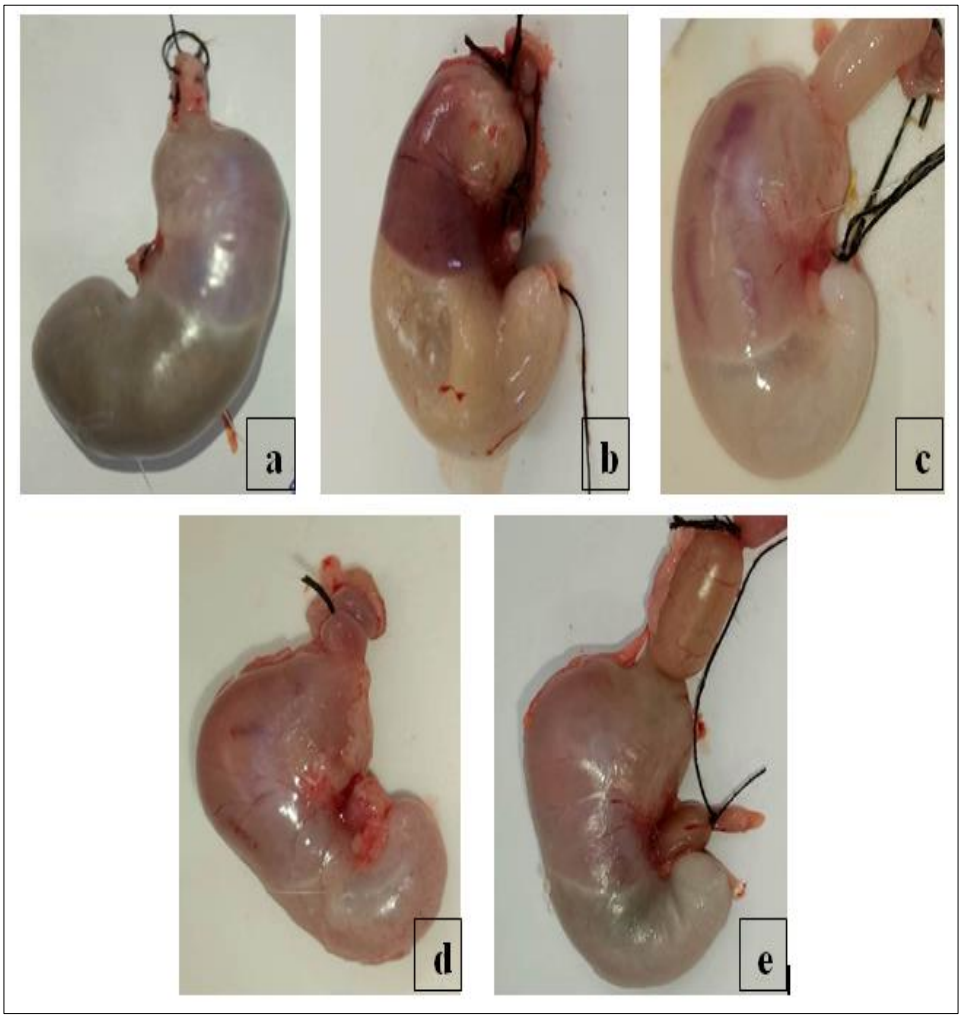


Figure 1. Effect of AEMc and Omperazole on stomach volume of EtOH-administered rats. (*a) Control group, normal stomach volume; (b) EtOH group shows a swelling of the stomach with deep color, and accumulation of gastric juice; (c) (d) and AEMc (400 and 600 mg/kg) treated rats showing protection of the basal volume of the stomach against ethanol action in a dose-dependent manner, maintaining the stomach gastric juice in a normal level ; (e) Omperazole (20 mg/kg) shows a high protection towards EtOH-induced gastric hypertrophy similar to that of AEMc 600 mg/kg.*

Table 1: Effect of AEMc on various gastric physicochemical parameters in gastric EtOH-induced ulcer.

Groups	Treatments		
	GJ V (ml)	pH	SMW (mg)

Control (Distilled water)	1.14 ± 1.13	5.13 ± 1.32	125.00 ± 3.17
EtOH (96%)	4.84 ± 2.20 ###	2.78 ± 1.22###	61.83 ± 6.14###
AEMc (400 mg/kg) + EtOH	2.73 ± 0.77**	6.15 ± 2.61**	156.50 ± 4.33***
AEMc (600 mg/kg) + EtOH	1.98 ± 3.25***	8.74 ± 1.76***	191.00 ± 6.18****
Omeprazole (20 mg/kg) + EtOH	1.32 ± 1.10***	9.65 ± 0.21****	139.60 ± 7.14***

EtOH = ethanol; GJV = gastric juice volume; SMW = mucus weight; AEMc = aqueous extract of Myrtus communis. Values are expressed as mean ± SEM for six animals in each group compared with one way ANOVA followed by Tukey's test. Ethanol solution (96%) was administered at 0.5 mL/rat. AEMc (400 and 600 mg/kg) and Omeprazole (20 mg/kg) were administred one hour before EtOH treatment. $^{\#}P < 0.05$; $^{\#\#}P < 0.01$; $^{\#\#\#}P < 0.001$ compared to control group. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$ compared to ethanol group.

Effect of AEMc on the Gastric Macroscopic Damage Induced by Ethanol and on Ulcer and Protection Indexes

According to Figure 2A, no visible macroscopic lesions were present in the control group. However, intragastric administration of EtOH resulted in significant macroscopic changes in the mucosal layer, such as linear hemorrhages and ulceration craters, leading to a marked increase in the percentage of ulcer index (UI) (Table 2) (Figure. 2B). Although the administration of Omeprazole (20 mg/kg) resulted in only a few areas of hyperemia (Figure 2E), it attenuated the changes induced by EtOH. In contrast, pretreatment with AEMc reduced the extent of gastric damage in a dose-dependent manner (Figure. 2C/D) and decreased the percentage of UI from 64.3% ± 2.33 in the EtOH-treated group to 19.1% ± 4.02 ($p < 0.001$) and 8.03% ± 1.68 ($p < 0.0001$) with 400 and 600 mg AEMc/kg, respectively (Table 2). In comparison, Omeprazole reduced the UI to 3.94% ± 8.90 ($p < 0.0001$) (Table 2).

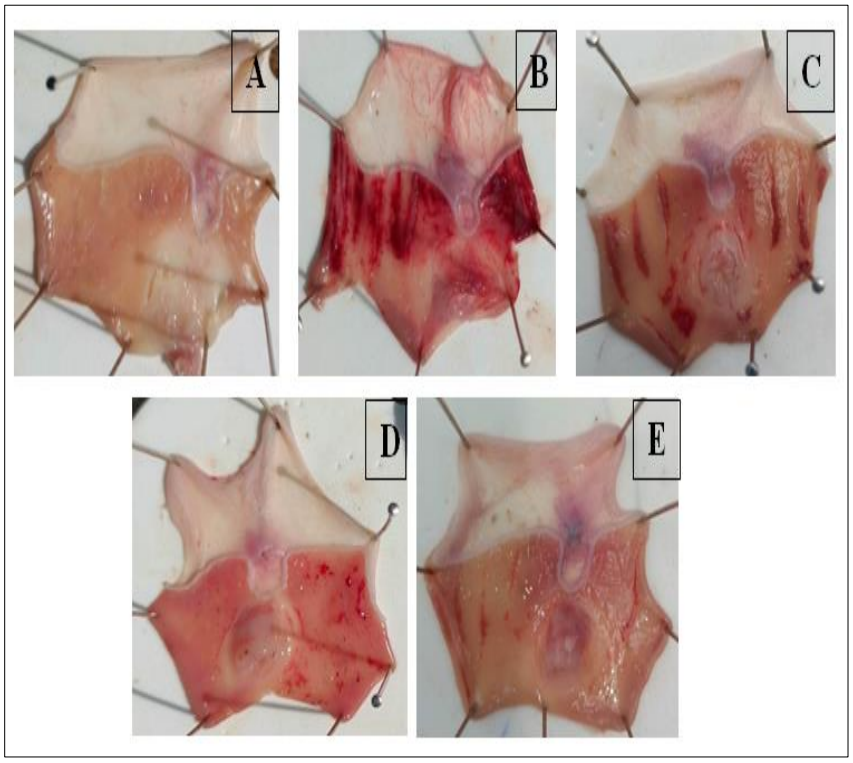


Figure. 2. Gastroprotective effects of Omeprazole and AEMc on ethanol-induced ulcer in rats. *Illustrative pictures of stomach: (A) Control; (B) 96% EtOH; (C) AEMc at 400 mg/kg + 96% ethanol; (D) AEMc of at 600 mg/kg + 96% ethanol; (E) Positive control rats received a single dose of Omeprazole (20 mg/kg). All drugs were administered orally. AEMc: Aqueous extract of Myrtus communis; EtOH: ethanol.*

Table 2. Effect of AEMc on Ulcer index (UI) and Protection index (PI) in gastric EtOH-induced ulcer.

Groups	Treatments	
	UI (%)	PI (%)
Control (Distilled water)	00 ± 00	
EtOH (96%)	64,3 ± 2.33$^{###}$	
AEMc (400 mg/kg) + EtOH	19,1 ± 4.02***	70, 3 ± 3.34
AEMc (600 mg/kg) + EtOH	8,03 ± 1.68****	87,51 ± 2.44
Omeprazole (20 mg/kg) + EtOH	3,94 ± 2.33****	93,87 ± 5.75

EtOH = ethanol; AEMc: Aqueous extract of Myrtus communis; UI = ulcer index; PI = protection index. Values are expressed as mean ± SEM for six animals in each group compared with one way ANOVA followed by Tukey's test. Ethanol solution (96%) was administered at 0.5 mL/rat. AEMc (400 and 600 mg/kg) and Omeprazole (20 mg/kg) were administred one hour before EtOH treatment.

Effect of AEMC on Ethanol-Induced Histopathological Gastric Injury

Animals that were pre-treated with AEMc displayed a significant reduction in EtOH-induced gastric histopathological changes, which was dependent on the dosage administered. Rats that received 400 mg/kg AEMc alongside EtOH had minimal swelling, inflammation, and inflammatory cell count, (Figure. 3C). In rats receiving 600 mg/kg AEMc, a dose-dependent protection was observed in the gastric mucosa, (Figure. 3D). The highest dose of AEMc provided a more pronounced protective effect compared to that of Omeprazole, (Figure. 3E).

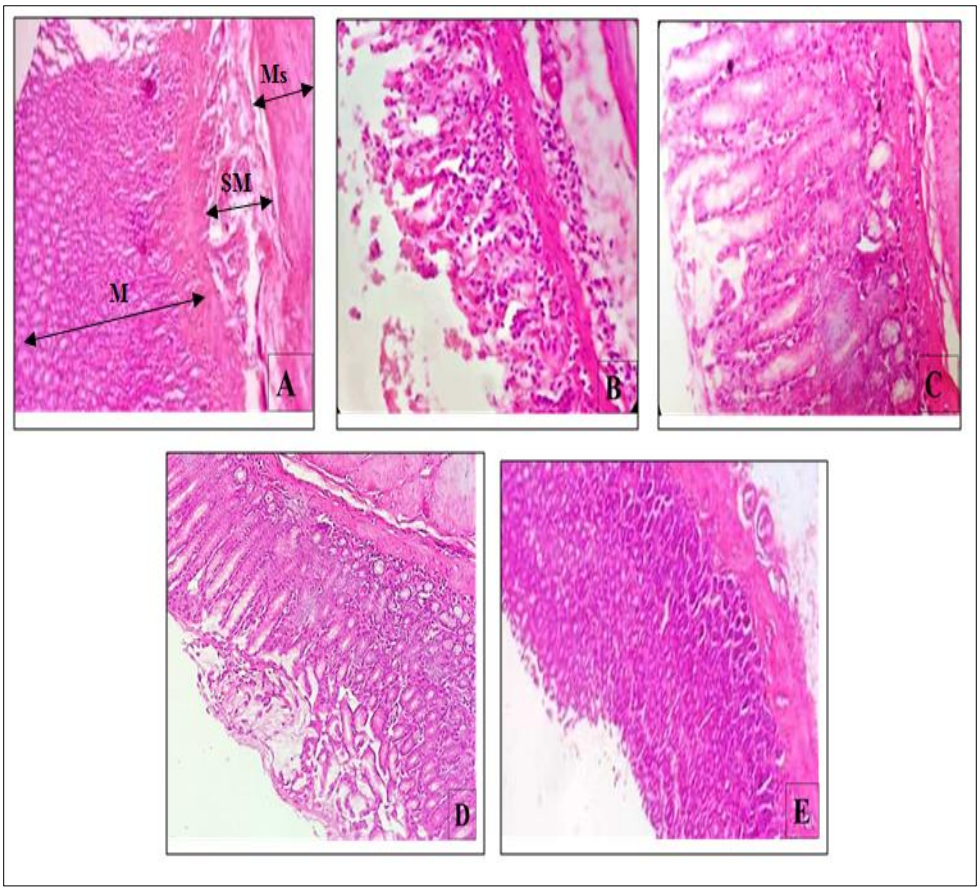


Figure. 3. Histological analysis of stomachs. (A) Control; (B) 96% EtOH: *Note the mucosa cell necrosis with appearance of pyknotic nuclei, inflammatory neutrophil infiltration and hyperemia; (C) AEMc at 400 mg/kg + 96% ethanol: Note the attenuation of necrosis features but the persistence of vacuolization and inflammatory cell infiltration; (D) AEMc at 600 mg/kg + 96% EtOH; (E) Positive control rats received a single dose of Omperazole (20 mg/kg). All drugs were administered orally. M = Mucosa; SM = Sub Mucosa; Ms = Musculosa;. Magnification: A, B, C, D and E (x100).*

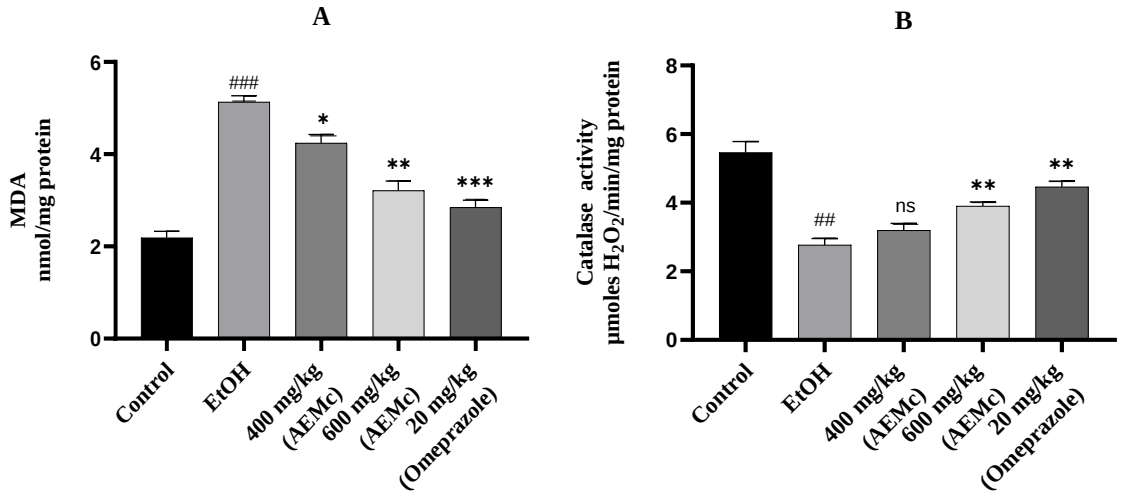
Effect of AEMc on Ethanol-Induced Gastric Oxidative Damage

The group exposed to EtOH showed significant oxidative changes, including an increase in lipid peroxidation, as evidenced by the elevated levels of MDA compared to the control group (5.13 ± 0.12 MDA nmol/mg protein vs 2.18 ± 0.13 ($p < 0.001$), (Figure. 4A). Interestingly, pretreatment with AEMc provided a significant and dose-dependent protective effect against lipid peroxidation in the gastric

mucosa. At 400 and 600 mg/kg AEMc doses, MDA levels were 4.24 ± 0.18 ($p < 0.05$) and 3.21 ± 0.20 ($p < 0.01$) nmol/mg protein, respectively. With the higher dose of AEMc (600 mg/kg), MDA levels were maintained at a comparable value to that of the Omeprazole group (2.84 ± 0.15 vs. 2.18 ± 0.13 for the control group ($p > 0.05$)), (Figure. 3A).

The basal activity of gastric CAT was measured at 5.46 ± 0.32 µmoles H_2O_2/min/mg protein and showed a 49.45% decrease in rats treated with EtOH (measured at 2.76 ± 0.19 µmoles H_2O_2/min/mg protein) ($p < 0.01$) (Figure. 4B). Animals that received pre-treatment with AEMc exhibited a dose-dependent restoration in CAT activity, with CAT activities of 3.19 ± 0.20 and 3.90 ± 0.12 µmoles H_2O_2/min/mg protein ($p < 0.01$) for 400 and 600 mg/kg AEMc, respectively, compared to 2.76 ± 0.19 µmoles H_2O_2/min/mg protein for the EtOH group. Omeprazole restored CAT activity to a level comparable to that of the AEMc (600 mg) group, with a measured activity of 4.46 ± 0.16 for Omeprazole compared to 3.90 ± 0.12 ($p > 0.05$) for AEMc (Figure. 4B).

Similarly, treatment with EtOH resulted in a significant reduction in SOD activity from 3.44 ± 0.18 to 1.75 ± 0.23 UI/min/mg protein ($p < 0.01$). However, pre-treatment with AEMc inhibited this decrease in SOD activity. The most significant inhibition was observed with a dose of 600 mg AEMc/kg, where SOD activity was maintained at a level of 2.59 ± 0.08 UI/min/mg protein, comparable to that of the Omeprazole group (2.97 ± 0.07 UI/min/mg protein), whereas SOD activity was only 1.75 ± 0.23 UI/min/mg protein for the EtOH group ($p < 0.01$). (Figure. 4C).



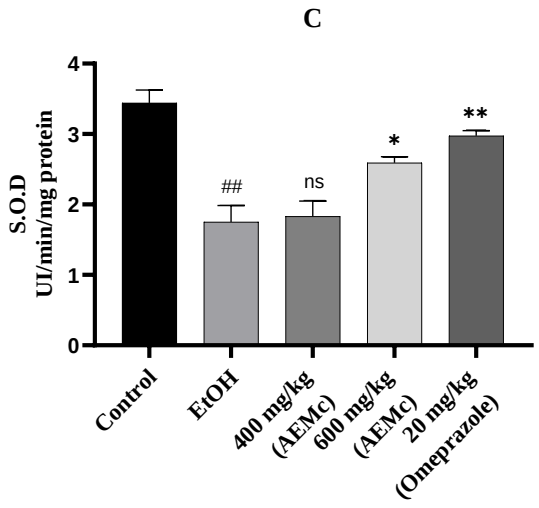


Figure. 4. Effect of aqueous extract of *Myrtus communis* and Omeprazole treatments on lipid peroxidation. (A), *catalase (B), superoxide dismutase(C), EtOH = ethanol; AEMc = aqueous extract Myrtus communis (400 and 600 mg/kg). All drugs were administered by oral way. Values are expressed as mean ± SEM for six animals in each group compared with one way ANOVA followed by Tukey's test. $^{\#}P < 0.05$; $^{\#\#}P < 0.01$; $^{\#\#\#}P < 0.001$ compared to control group. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$ compared to ethanol group.*

DISCUSSION

The main objective of this study was to assess the anti-ulcer properties of *Myrtus communis* by utilizing an experimental gastric ulcer model induced by ethanol, and to explore the underlying mechanisms of its anti-ulcer activity.

Drinking alcohol can cause sudden bleeding and erosion in the stomach lining, and consuming too much can lead to gastritis which is identified by swelling of the stomach lining, bleeding underneath the lining, shedding of cells, and infiltration of inflammatory cells (Guslandi, 1987 ; Ko et al, 2014).

The generation of inflammatory substances is a crucial factor in the development of mucosal lesions. Additionally, the blockage of gastric blood flow and damage to microvessels play a role in the process of hemorrhage and tissue necrosis (Li et al., 2014). The infiltration of neutrophils also contributes to injury and inflammation by accumulating and releasing substances that damage tissues, including the gastric mucosal lining (Kobayashi, Ohta, & Yoshino, 2001). Neutrophil infiltration in the gastric mucosa is involved in the formation of sudden gastric mucosal lesions (Nishida, Ohta, & Ishiguro, 1999). In rats treated with ethanol, microscopic evidence confirmed neutrophil infiltration in the gastric mucosa, and pre-treatment with AEMc resulted in noticeable inhibition of this infiltration, suggesting that AEMc may have gastroprotective properties. Similar anti-inflammatory effects were observed with Ficus indica roots and flowers (Alimi et al., 2010) and Rosmarinus officinalis leaf extracts (Amaral et al., 2013).

The interaction of ROS with various molecules, including proteins, DNA, and lipids, may lead to significant cellular damage and promote lipid peroxidation, resulting in erosion of epithelial cells, expansion of the inter-glandular area, and localized inflammation. This process can contribute to the formation of hemorrhagic gastric ulcers, which may occur due to excessive production of acidic gastric juice (Hamauzu et al , 2008; Li et al , 2008). AEMc treatment may lead to a notable increase in gastric pH by inhibiting hydrochloric acid secretion.

It is worth noting that AEMc demonstrated antioxidant properties, as indicated by decreased MDA level in gastric tissue and increased activity of antioxidant enzymes such as CAT, SOD, and GPx. Additionally, AEMc exhibited protective effects against alcohol-induced lipid peroxidation. These findings are consistent with previous studies conducted by Ben Barka et al. (2017) and Kandhasamy et al. (2013) that used root extracts of *Rhus tripartite* and *Acacia ferruginea* respectively.

Numerous research studies have shown that the essential oil derived and extract from *M. communis* exhibits anti-inflammatory characteristics in animal models. These studies were conducted by Rossi et al. (2009), Hosseinzadeh et al. (2011), Maxia et al. (2011), and Amira et al. (2012).

In their study, Hosseinzadeh et al. (2011) examined the ability of aqueous and ethanolic extracts from the aerial parts of *M. communis* L. to counteract inflammation using xylene-induced ear oedema and cotton pellet tests. The results demonstrated that the extracts had a noteworthy impact on acute inflammation, and this effect was seen to be dependent on the dose of the aqueous extract. The ethanolic extract (0.05 g/kg) and the aqueous extracts (0.005, 0.015, and 0.03 g/kg) displayed anti-inflammatory properties against chronic inflammation. The extracts also showed a significant reduction in cotton pellet-induced granuloma, indicating that the activity may have occurred during the proliferative phase of inflammation.

According to Maxia et al. (2011), the topical application of *M. communis* essential oil led to a notable reduction in both ear oedema and cotton pellet-induced granuloma.

In *vitro* studies have indicated that the ethanolic extract of myrtle possesses anti-inflammatory and antiproliferative properties, which could be useful in treating acne lesions. Fiorini-Puybaret et al. (2011) evaluated the extract's anti-inflammatory activity by measuring the production of 6-keto-prostaglandin F1 and [^{3}H]-arachidonic acid metabolites in keratinocytes that were stimulated for inflammation. They discovered that the extract significantly reduced the production of all metabolites from the cyclooxygenase ($p<0.0001$) and lipoxygenase ($p<0.001$) pathways. Moreover, the extracts inhibited keratinocyte proliferation by 27% and 76% at 1 and 3 μg/mL, respectively ($p<0.001$), as determined by the BrdU incorporation assay in HaCat keratinocytes.

The anti-inflammatory effects of *M. communis in vivo* models of inflammation were explored by Rossi et al. (2009). Intraperitoneal administration of MC (0.5, 1.5, and 4.5 mg/kg) resulted in a dose-dependent reduction in mouse carrageenan-induced paw oedema. Furthermore, MC (4.5 mg/kg i.p. 30 min before and after carrageenan) demonstrated anti-inflammatory effects in the pleurisy model. Particularly, 4 hours after carrageenan injection in the pleurisy model, MC exhibited potent and promising anti-inflammatory effects, as indicated by various inflammation assays, including histological analysis, myeloperoxidase activity, immunohistochemical localization study, cytokine, leukotrienes and prostaglandins measurement, lung peroxidation, and immunostaining methods.

Feißt et al. (2005) found that MC and S-MC, present in the leaves of *M. communis*, have potent antiinflammatory effects. They inhibit the biosynthesis of eicosanoids by directly inhibiting

cyclooxygenase-1 and 5-lipoxygenase in vitro and in vivo. They also prevent the mobilization of calcium in polymorphonuclear leukocytes, mediated by G protein signaling pathways, and suppress the formation of reactive oxygen species and the release of elastase, which are relevant for the initiation and maintenance of inflammatory processes. On the other hand, Koeberle et al. (2009) suggested that MC inhibits cell-free mPGES-1-mediated conversion of PGH2 to PGE2 in a concentration-dependent manner without significantly inhibiting COX enzymes. Moreover, the herb's antiinflammatory properties involve suppression of serum IL-6 and TNF-alpha and consequent reduction of leukocyte migration to the damaged tissue, as reported by Rossi et al. (2009) and Maxia et al. (2011). The selective inhibition of PGE2 formation through interference with microsomal PGE2 synthase (mPGES)-1 may have advantages in treating PGE2-associated diseases like inflammation, fever, and pain, compared with general suppression of all prostaglandin biosynthesis caused by inhibiting COX-1 and 2 (Koeberle et al., 2009). The findings suggest that myrtle has the potential to serve as an alternative therapeutic agent for chronic inflammation, without causing the typical side effects associated with Coxibs and non-steroidal anti-inflammatory drugs (NSAIDs), as per Gerbeth et al. (2012).

CONCLUSION

In conclusion, the results of the present study amply demonstrated that *M. communis* pre-treatment was able to exert protective effects in the ethanol-induced gastric ulcer model. *M. communis* administration significantly increased CAT, SOD activities and decreased MDA level in gastric tissue. The experimental findings render *M. communis* as a promising chemical constituent for the treatment of gastric ulcer. Moreover, the elucidation of the underlying mechanisms of action also helps put the traditional use for gastrointestinal diseases on a solid scientific footing.

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