Antiulcer Activity of *Ceratophyllum Submersum* Linn.: Pharmacological Evaluation and Mechanistic Insights

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ABSTRACT

Background: Peptic ulcer disease (PUD) remains a significant global health issue, often requiring long-term treatment with conventional drugs that may have adverse effects. This study investigates the antiulcer potential of *Ceratophyllum submersum* Linn., a submerged aquatic plant, using established in vivo models of gastric ulceration to explore its efficacy, biochemical impact and underlying mechanisms.

Methods: Methanol derived and aqueous extracts of *Ceratophyllum submersum* were assessed for their antiulcer action in Wistar rats employing pylorus ligation and ethanol-induced ulcer models. The study measured gastric volume, pH, free and total acidity, mucus content and ulcer index. Histopathological analysis was performed to assess tissue integrity and inflammatory responses.

Results: In the pylorus ligation model, the methanol derived extract at dose of 500 mg/kg (MECS500) considerably reduced gastric volume to 7.914 ± 0.450 ($p < 0.01$) related to the control (10.746 ± 0.482). The pH increased to 3.696 ± 0.149 ($p < 0.01$) versus 2.742 ± 0.158 in the control. Free acidity decreased to 24.72 ± 1.276 ($p < 0.01$) and total acidity to 51.44 ± 2.877 ($p < 0.01$). The ulcer index was notably reduced to 2.318 ± 0.393 ($p < 0.01$) from 5.837 ± 0.455 and mucus content increased to 0.205 ± 0.008 ($p < 0.01$). In the ethanol-induced model, MECS500 reduced the ulcer index to 1.083 ± 0.282 ($p < 0.01$) compared to 2.950 ± 0.340 in the control and increased mucus content to 0.310 ± 0.018 ($p < 0.01$). Histopathological analysis corroborated these findings, showing significant mucosal preservation and reduced inflammation in treated groups.

Conclusion: *Ceratophyllum submersum* exhibits significant antiulcer activity, particularly the methanolic extract at 500 mg/kg, as evidenced by reductions in gastric volume, acidity and ulcer indices and increased pH and mucus content. These findings highlight the potential of *Ceratophyllum submersum* as a natural therapeutic for peptic ulcer disease, warranting further investigation into its active compounds and clinical application.

KEYWORDS: Antiulcer activity, *Ceratophyllum submersum* Linn., Peptic ulcer disease, Gastric ulceration, Pylorus ligation, Ethanol-induced ulcer, Gastroprotective effects, Natural therapeutics and Phytotherapy

INTRODUCTION

Peptic ulcers are a significant health concern globally, affecting millions of individuals each year.[1] It is characterized by lesions in the mucosal covering of the digestive or the duodenum, peptic ulcers arise due to a disproportion among destructive factors like acid and pepsin and defensive mechanisms such as mucus secretion and bicarbonate production.[2] While peptic ulcer disease can occur in both sexes and across various age groups, its prevalence is notably high in populations exposed to risk factors such as infection, long drugs usage, extreme alcohol drinking, smoking and strain.[3]

Conventional treatments for peptic ulcers primarily focus on reducing gastric acidity and eradicating *H. pylori*, proton pumps inhibitors (PPIs), H_2 antagonists and antibiotics form the cornerstone of contemporary ulcer management.[4] Despite their efficacy, these treatments are not without drawbacks. Prolonged use of PPIs and H_2-receptor antagonists has been associated with adverse effects, kidney disease and augmented danger of gastric infections.[5] Additionally, the rise of antibiotic-resistant *H. pylori* strains poses a significant challenge to successful eradication and necessitates the exploration of alternative therapeutic options.[6]

Given these limitations, there is a growing interest in natural products and traditional medicines as potential sources of new antiulcer agents.[7] Numerous plant-derived compounds have been reported to possess gastroprotective properties, offering a dual advantage of efficacy and reduced side effects.[8] These natural remedies often work through multiple mechanisms, such as enhancing mucus production, increasing bicarbonate secretion, and providing antioxidant protection, thereby addressing various aspects of ulcer pathogenesis.[9]

Ceratophyllum submersum Linn. universally known as hornwort, is an underwater aquatic plant widely distributed in freshwater ecosystems across Europe, Asia and North America. Historically, it has been employed in old medication for management of various ailments, including gastrointestinal conditions.[10]

Preliminary phytochemical screenings of *Ceratophyllum submersum* have revealed a rich profile of biologically active compounds such as flavonoids, tannins, saponins and alkaloids.[11] These phytochemicals are identified for their diverse pharmacological actions, counting antioxidant, anti-inflammatory and antimicrobial effects, which may contribute to their therapeutic potential in gastrointestinal health.[12-13]
The gastroprotective potential of *Ceratophyllum submersum* is attributed to its multifaceted mechanisms of action. Flavonoids and tannins present in the plant are known to enhance mucosal defense by stimulating mucus secretion and providing a barrier against the corrosive action of gastric acid and pepsin.[14] Additionally, these compounds exhibit significant antioxidant properties, which can mitigate oxidative stress-a crucial factor in the pathogenesis of gastric ulcers. The anti-inflammatory action of saponins and alkaloids further contributes to ulcer healing by reducing inflammation and promoting tissue regeneration.[15]
The primary objective of this study was to evaluate the antiulcer activity of *Ceratophyllum submersum* Linn. using established in vivo models. We specifically aimed to assess the efficacy of *Ceratophyllum submersum* in mitigating gastric lesions induced by ethanol and pylorus ligation, while also analyzing biochemical parameters related to ulcer formation such as gastric volume, pH and mucus content. Furthermore, we sought to elucidate the potential mechanisms underlying the gastroprotective effects of the plant extract through phytochemical analysis and histopathological examination. By addressing these objectives, this study provided a comprehensive understanding of the antiulcer potential of *Ceratophyllum submersum*, contributing to the development of novel, natural therapeutics for peptic ulcer disease.
The relevance and significance of this research lay in its exploration of *Ceratophyllum submersum* as a source of antiulcer agents, aligning with the growing demand for natural products in modern medicine. Our findings could pave the way for the integration of this plant into therapeutic regimens, offering a safer and potentially more effective alternative to conventional antiulcer drugs. Additionally, understanding the underlying mechanisms of its gastroprotective action enhanced our knowledge of natural product pharmacology and supported the rational use of traditional medicines in clinical practice.

MATERIALS AND METHODS

The plant material used in the study was *Ceratophyllum submersum*, which was obtained from its natural environment and verified by a botanist. The plant material was carefully cleaned, dried in the shade and subsequently pulverised into an extremely fine powder. The powdered substance was extracted using methanol as in a Soxhlet device. In addition, another part of the crushed plant substance was soaked in purified water over a three-day period with occasional stirring and the resultant aqueous extract was further filtered to eliminate any insoluble residue. The methanolic & aqueous extracts were then condensed under low pressure using a rotating evaporator and the solid extracts were stored in tightly sealed, light-resistant borosilicate glass containers to maintain their stability and effectiveness.
The animal study involved the use of perfectly normal adult Wistar rats, with a weight range of 150-200g. The rats were kept in a controlled laboratory environment with a temperature of 25 ± 1°C, a humidity level ranging from 55 to 60% and a 12-hour cycle of light and darkness. The participants were given a regular pellet diet and had unrestricted access to water. The experimental protocols followed the standards set by the Institutional Animal Ethics Committee (IAEC) and ethical approval was obtained before starting the investigation.

Pharmacological Evaluation

Pylorus Ligation-Induced Ulcer Model

The effectiveness of various extracts in ulcer treatment was assessed using several models, including the pylorus ligation-induced ulcer model. This investigation involved six distinct cohorts of rats, each comprising six subjects. The treatments administered were as follows: Group I, designated as the Normal Control, was given 10 ml/kg of distilled water orally. Group II received an oral administration of Omeprazole at 20 mg. Group III was treated with the Methanolic Extract of *Ceratophyllum submersum* Linn. at 250 mg, administered orally. Group IV received a higher oral dose of the Methanolic Extract of *Ceratophyllum submersum* Linn. at 500 mg. Group V was given the Aqueous Extract of *Ceratophyllum submersum* Linn. at 250 mg, administered orally. Lastly, Group VI was administered the Aqueous Extract of *Ceratophyllum submersum* Linn. at 500 mg, orally. All doses calculated as / kg of body weight of animals.
Before starting the experiment, the rats had a fasting time frame of 24 hours. Following a 1-hour procedure, the animals were anaesthetized with ether and then submitted to pylorus ligation by securely tying off the posterior portion of the pylorus. A surgical incision was made posterior to the xiphoid process to get access to the gastrointestinal tract. The pylorus region of the stomach was then raised and secured using the Shay et al. method. Measures were implemented to avoid any traction or stress on the pylorus or any damage to the blood vessels. Afterwards, the abdominal lining was closed using intermittent sutures. After the surgical surgery, the animals were isolated in individual housing units and deprived of water. The rats were euthanized following a 6-hour period of receiving pylorus ligation. The abdominal cavity was cut open and the upper part of the gastrointestinal tract was tied off and removed. The gastric content was collected and subsequently submitted to centrifugation. The volume and pH of the stomach content as well as its mucus content, free acidity and total acidity were measured. Additionally, a histological investigation was performed. The stomach was incised along the greater curvature, rinsed with a normal saline solution to remove gastric contents and blood clots and

examined with a 10x magnifying lens to assess the ulcers. The ulcers were assessed using rigorous criteria and the ulcer index was determined by calculating an average ulcer score for each rat. The percentage of ulcer inhibition was calculated using the provided formula:

$$\% \text{ inhibition of ulceration} = \frac{(\text{Ulcer index}_{\text{control group}} - \text{Ulcer index}_{\text{test group}})}{\text{Ulcer index}_{\text{control group}}} \times 100$$

This experiment provided insights into the anti-ulcer properties of the extracts under investigation.[16-19]

Ethanol-Induced Ulcer Model

This study involved six groups, with each group consisting of six individuals. The purpose of the study was to assess the effectiveness of different drugs in treating ulcers. Group I, acting as the Disease Control, was administered an oral dose of 1 ml of ethanol. Group II received the conventional drug Omeprazole at an oral dose of 20 mg, along with 1 ml of ethanol administered orally. Group III was administered the methanolic Extract of *Ceratophyllum submersum* Linn. orally at a dosage of 250 mg, in addition to 1 ml of ethanol. Group IV received an oral dose of 500 mg of Methanolic Extract of *Ceratophyllum submersum* Linn., along with 1 ml of ethanol. Group V received an oral dose of 250 mg of the Aqueous Extract of *Ceratophyllum submersum* Linn., along with 1 ml of ethanol. Group VI was administered the Aqueous Extract of *Ceratophyllum submersum* Linn. orally at a dose of 500 mg, in addition to 1 ml of ethanol. All doses calculated as / kg of body weight of animals.

Prior to the trial, the rats had a 24-hour period of fasting. After receiving their assigned doses for an hour, each group were orally administered 1 ml of 100% ethanol. Following a further hour, the animals subsequently euthanized and the stomachs were surgically extracted and incised along the larger curvature to examine for ulcers. The ulcers were assessed according to established requirements and both, the index of ulceration and the percent of ulcer inhibition were computed. In addition, a histological study was conducted. The aim of this study was to assess the efficacy of the extracts in reducing ethanol-induced ulcers, therefore offering significant insights into their anti-ulcer capabilities.[20]

RESULTS AND DISCUSSION

Results of Pylorus Ligation-Induced gastric Ulceration

Table 1. Effect of *Ceratophyllum submersum* on Pyloric Ligated Rat Model

Parameters	Control	Standard	MECS250	MECS500	AECS250	AECS500
Gastric Volume (ml)	10.746 ± 0.482	6.000 ± 0.450**	9.325 ± 0.414	7.914 ± 0.450**	9.550 ± 0.646	8.444 ± 0.487*
pH	2.742 ± 0.158	4.088 ± 0.194**	2.717 ± 0.217	3.696 ± 0.149**	2.696 ± 0.168	3.686 ± 0.176**
Free Acidity (mEq/l/100g)	44.01 ± 1.950	23.01 ± 1.820**	39.66 ± 0.788	24.72 ± 1.276**	39.36 ± 1.835	29.61 ± 1.781**
Total Acidity (mEq/l/100g)	74.48 ± 7.002	47.29 ± 5.325**	72.19 ± 2.192	51.44 ± 2.877**	76.51 ± 5.364	52.39 ± 2.533**
Ulcer Index	5.837 ± 0.455	1.461 ± 0.246**	3.433 ± 0.255**	2.318 ± 0.393**	3.788 ± 0.317**	3.358 ± 0.393**
Mucus Content	0.114 ± 0.005	0.267 ± 0.011**	0.176 ± 0.002**	0.205 ± 0.008**	0.163 ± 0.005**	0.186 ± 0.004**
Percentage Inhibition	-	74.97	41.18	60.28	35.10	42.47

The data is displayed as the mean ± standard error of the mean (SEM), using a sample size of 6 in every group. * p-values below 0.05 were deemed statistically significant and ** p-values below 0.01 were taken to be highly statistically significant in comparison to the control group. The comparisons were conducted using a one-way analysis of variance (ANOVA) complemented by Dunnett's test.

The gastric volume, measured at 10.746 ± 0.482 in the control group, significantly decreased across all treatment groups, indicating a potential efficacy in reducing gastric volume. Notably, MECS250 and AECS250 showed relatively higher gastric volumes compared to their higher dose counterparts, suggesting a dose-dependent effect on gastric volume reduction.

In terms of pH levels, the standard treatment notably increased the pH to 4.088 ± 0.194 compared to the control's pH of 2.742 ± 0.158, indicating reduced gastric acidity. Similar trends were observed with MECS500 and AECS500, suggesting a potential dose-dependent effect on pH elevation. Free acidity exhibited substantial reductions in all treatment groups compared to the control, with MECS500 and AECS500 displaying

considerable decreases. This indicates the efficacy of these treatments in reducing excess acid production within the stomach.

Total acidity followed a similar pattern, with significant decreases observed with MECS500 and AECS500groups compared to the control. The standard treatment showed the lowest levels, reaffirming its effectiveness in reducing overall gastric acidity.

Ulcer index, a crucial measure of ulcer formation, was significantly lower in all treatment groups compared to the control. The standard treatment exhibited the lowest index, suggesting its superior efficacy in inhibiting ulcer development. Mucus content increased in all treatment groups compared to the control, indicating enhancements in the protective mucus layer in the stomach. This augmentation may contribute to the observed reduction in ulcer formation across the treatment groups. The standard treatment demonstrated the highest percentage inhibition of ulcer formation at 74.97%, followed by MECS500 and AECS500. This highlights the superior efficacy of the standard treatment in inhibiting ulcer development compared to the other treatment groups.

Overall, the findings underscore the significant gastroprotective effects of the treatments with MECS250, MECS500, AECS250 and AECS500 all exhibiting promising results in reducing gastric acidity, inhibiting ulcer formation and enhancing mucus secretion. However, the standard treatment consistently displayed the most pronounced effects across all parameters measured, indicating its superior efficacy. These results suggest the potential therapeutic value of the treatments, particularly the standard treatment, in mitigating gastric ulcer formation. Further research is warranted to elucidate their mechanisms of action and long-term safety profiles for potential clinical applications. The analysis of the provided data reveals important insights into the effects of different treatments on gastric parameters. Comparing various treatments with the control and standard groups, several key observations emerge. Firstly, treatments MECS250, MECS500, AECS250, and AECS500 generally lead to a decrease in gastric volume, indicating potential inhibition of gastric secretion. Secondly, while the standard treatment demonstrates the highest pH levels, suggesting effective reduction of gastric acidity, treatments MECS250 and AECS250 also exhibit moderate effects in this regard. Thirdly, both free acidity and total acidity are notably reduced in the standard group, indicating its therapeutic potential in lowering gastric acidity. Moreover, the standard treatment shows significant efficacy in reducing ulcer formation, as evidenced by the lower ulcer index and higher percentage inhibition compared to all other groups. Interestingly, among the alternative treatments, MECS500 and AECS500 demonstrate promising effects in inhibiting ulcer formation and maintaining gastric health. However, further research is warranted to validate these findings and elucidate the underlying mechanisms, thereby facilitating the development of effective therapeutic strategies for gastric disorders.

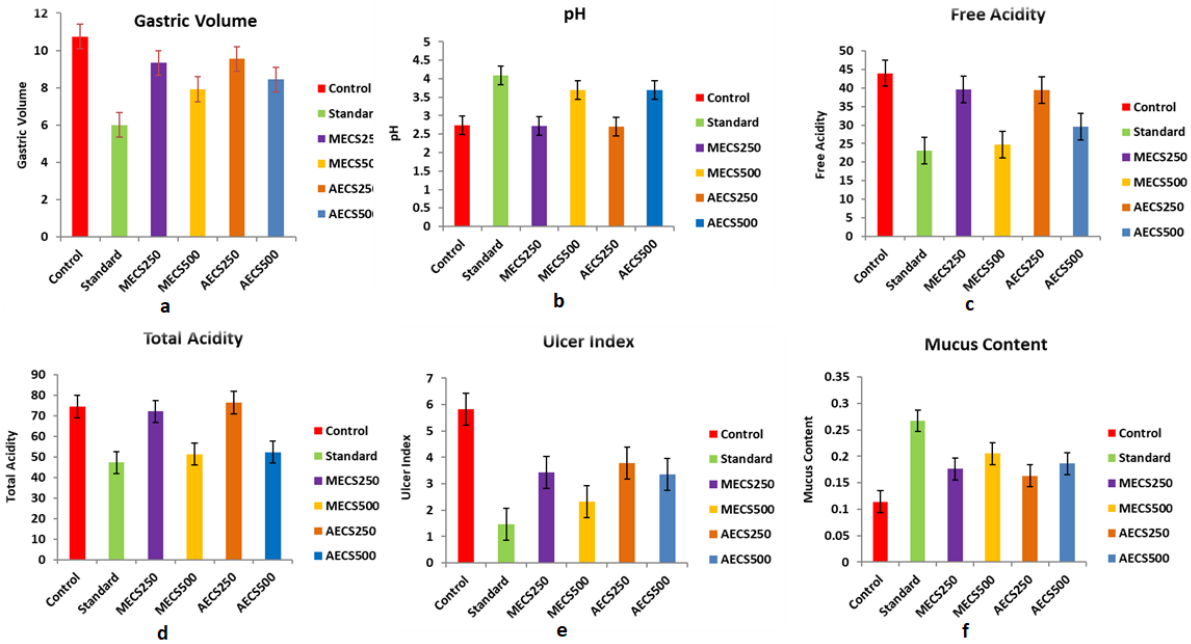

Figure 1. Effect of *Ceratophyllum submersum* on (a) Gastric Volume (b) pH (c) Free Acidity (d) Total Acidity (e) Ulcer Index (f) Mucus Content in Pylorus Ligated Rat Model.

Results of Histopathological Studies of Pylorus Ligated Gastric Ulceration

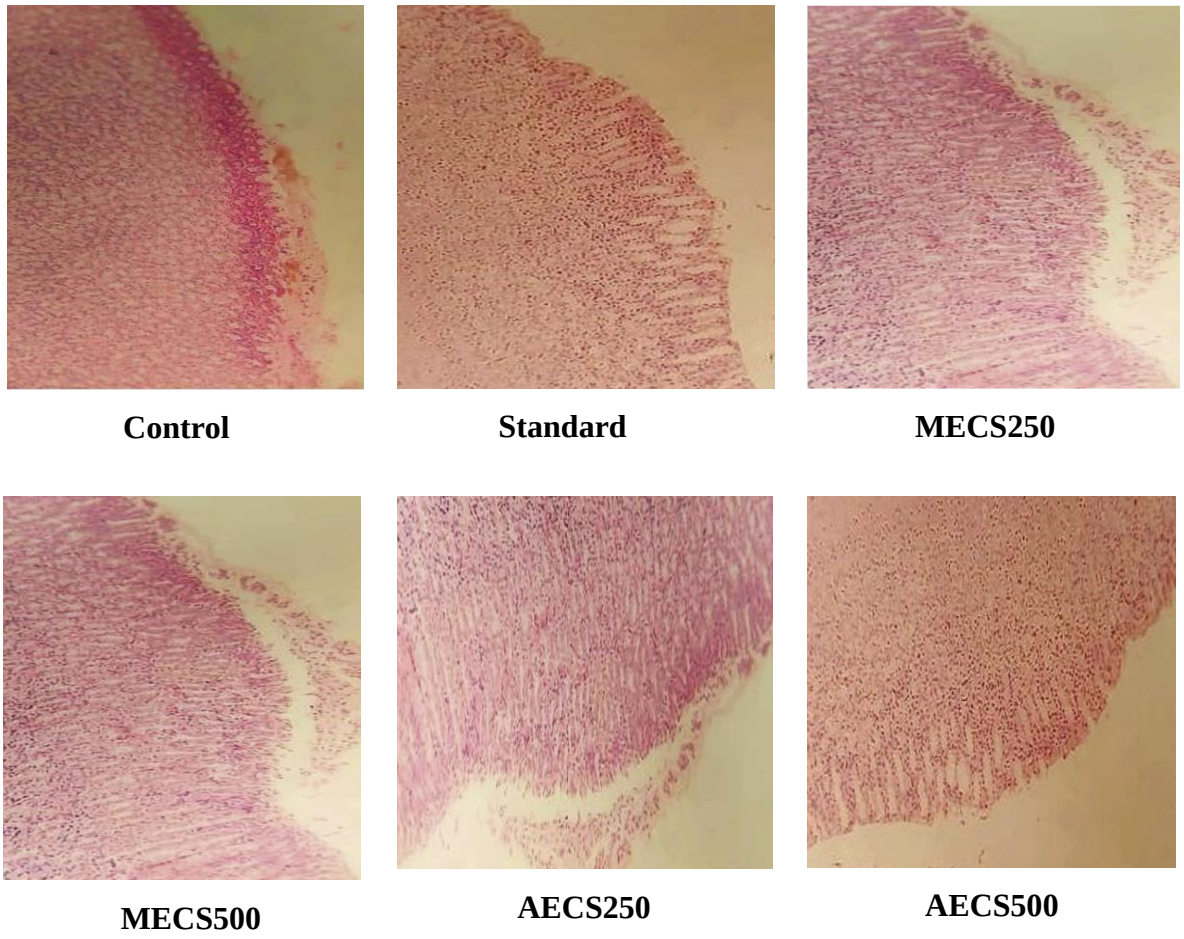

Figure 2. Histopathological Studies of Pylorus Ligation-Induced Ulcer Model

Histopathological results for the pylorus ligation-induced ulcer model typically involve examining tissue samples from the stomach to assess the extent of ulceration, inflammation and tissue damage. In the presented results, the histopathological findings are organized by treatment groups, each providing insights into the effects of different interventions on gastric tissue. The normal control group (Group I) serves as a baseline reference, demonstrating healthy gastric mucosa without any signs of ulceration or inflammation. The tissue appears intact, indicating no damage to the gastric mucosa. The standard treatment group (Group II) receiving Omeprazole demonstrates a protective effect, with preservation of gastric mucosa and minimal signs of ulceration. Negligible inflammatory cell infiltration further supports the efficacy of Omeprazole in preventing ulcer formation. In the MECS (250) treatment group (Group III), mild mucosal damage is observed along with minimal inflammatory cell infiltration in the submucosal layer. This suggests a slight effect on gastric tissue integrity compared to the normal control. The MECS (500) treatment group (Group IV) exhibits partial preservation of gastric mucosa, although moderate inflammatory cell infiltration in the submucosal layer indicates some degree of tissue damage and inflammation. Similarly, in the AECS (250) treatment group (Group V), mild to moderate mucosal damage with evidence of ulceration is noted, accompanied by inflammatory cell infiltration in the submucosal layer. In the AECS (500) treatment group (Group VI), significant mucosal damage with widespread ulceration is observed, along with marked inflammatory cell infiltration in the submucosal layer. This suggests a more pronounced effect on gastric tissue integrity compared to the other treatment groups.

Overall, the histopathological examination provides valuable insights into the effects of treatments on gastric tissue integrity and inflammatory response. These findings aid in evaluating the potential therapeutic benefits of the tested extracts and highlight the protective effects of Omeprazole in preventing ulcer formation.

Results of Ethanol Induced Ulcer Model

Ulcer index and % inhibition of ulcer:

Table 2. Effect of *Ceratophyllum submersum* on Ethanol Induced Ulcer Model

Parameters	Negative Control	Standard	MECS250	MECS500	AECS250	AECS500
Ulcer Index	2.950 ± 0.340	0.982 ± 0.329**	1.965 ± 0.498	1.083 ± 0.282**	1.921 ± 0.448	1.180 ± 0.265**
Mucus Content	0.166 ± 0.004	0.357 ± 0.015**	0.203 ± 0.012	0.310 ± 0.018**	0.189 ± 0.007	0.299 ± 0.015**
Percentage Inhibition	-	66.71	33	63.28	34.88	60

The data is displayed as the mean ± standard error of the mean (SEM), using a sample size of 6 in every group. ** p-values below 0.01 were taken to be highly statistically significant in comparison to the control group. The comparisons were conducted using a one-way analysis of variance (ANOVA) complemented by Dunnett's test.

The table presents data on the effect of *Ceratophyllum submersum* (CS) on an ethanol-induced ulcer model, examining various parameters such as ulcer index, mucus content and percentage inhibition. Analyzing the results reveals significant findings regarding the potential therapeutic efficacy of CS extracts in mitigating ethanol-induced gastric damage.

Firstly, the ulcer index, which measures the extent of ulcer formation, demonstrates a notable reduction in groups treated with CS extracts compared to the negative control. This indicates that CS extracts possess protective properties against ethanol-induced ulcers, as evidenced by lower ulcer indices in treatment groups. Additionally, the standard treatment group exhibits the most substantial reduction in ulcer index, affirming the effectiveness of established treatments in mitigating ulcer formation. Secondly, mucus content, essential for gastric mucosal protection, shows a marked increase in groups treated with CS extracts. The elevated levels of mucus content suggest that CS extracts stimulate mucus secretion, thereby enhancing the protective barrier of the stomach lining against gastric acid damage. This finding underscores the potential of CS extracts to promote gastric mucosal integrity and mitigate ulcer development. Furthermore, the percentage inhibition data reveal the extent to which CS extracts inhibit ulcer formation compared to the negative control. The results indicate varying degrees of inhibition across different treatment groups, with the standard treatment and certain CS extract treatments demonstrating higher efficacy in inhibiting ulcer formation. This highlights the potential of CS extracts, particularly at specific doses, to effectively prevent ethanol-induced ulcer development.

In conclusion, the data from the study support the notion that *Ceratophyllum submersum* extracts possess significant gastroprotective properties against ethanol-induced ulcers. The observed reductions in ulcer index, increase in mucus content and percentage inhibition suggest that CS extracts have promising therapeutic potential in the management of gastric disorders. However, further research is warranted to elucidate the underlying mechanisms of action, identify active compounds and optimize treatment protocols for maximal efficacy and safety in clinical settings.

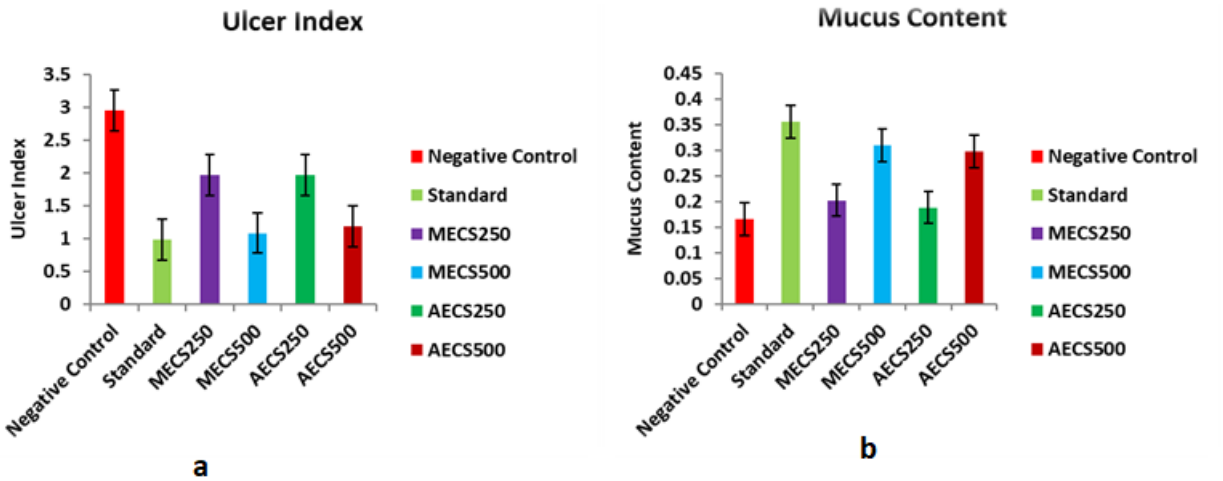

Figure 3. Effect of *Ceratophyllum submersum* on (a) Ulcer Index (b) Mucus Content in Ethanol Induced Ulcer Model

Ulcer index values represent the severity of ulcers observed in the stomach after the administration of ethanol. Lower values indicate fewer and less severe ulcers.

% Inhibition of ulcer values indicate the percentage reduction in ulcer severity compared to the disease control group (Group I). Higher values indicate greater efficacy in preventing ulcer formation.

Results of Histopathological Studies of Ethanol Induced Ulcer Model

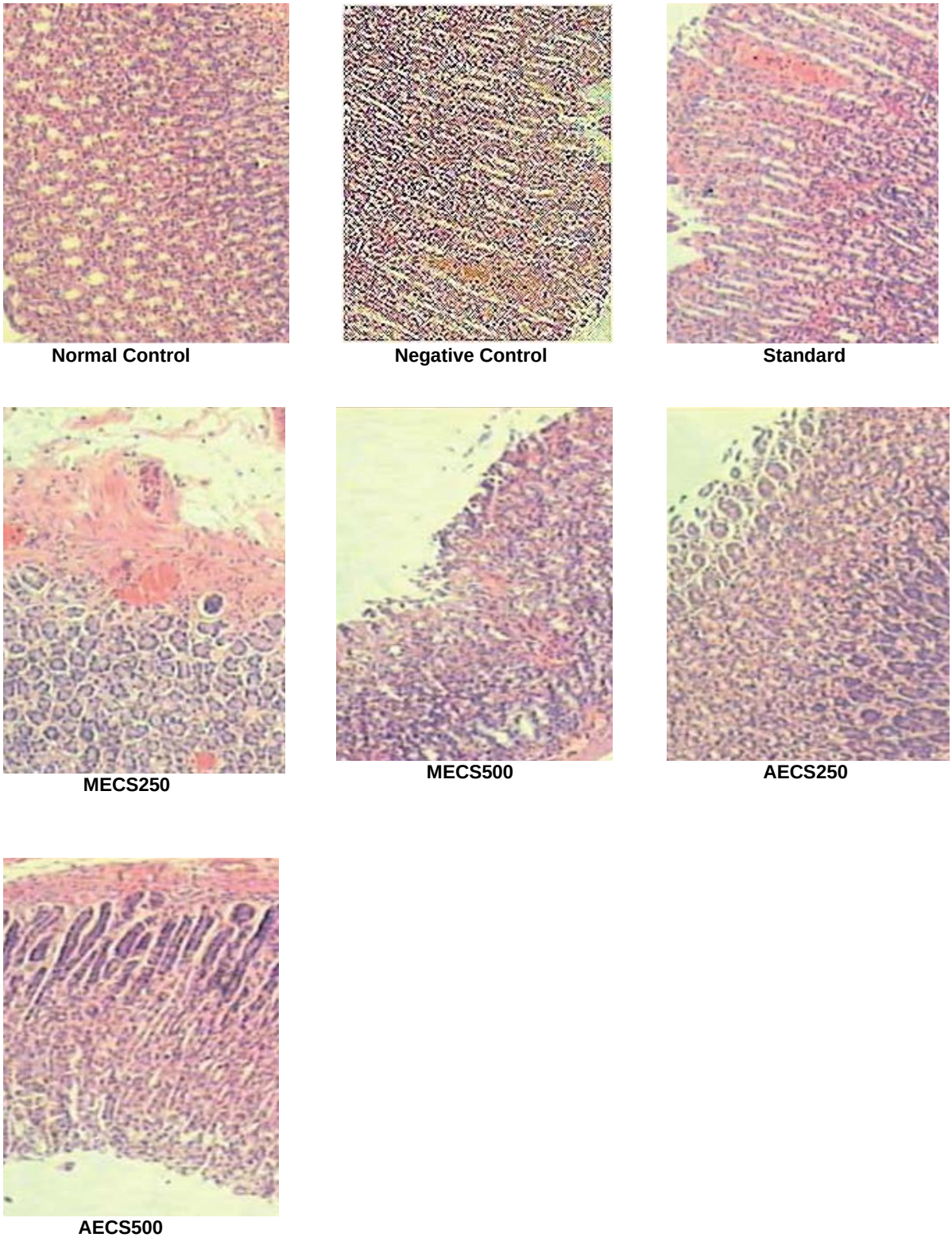

Figure 4: Histopathological Studies of Ethanol-Induced Ulcer Model

The histopathological results outline the effects of various treatments on gastric tissue integrity in the context of ethanol-induced ulceration. The normal control group (Group I) serves as a baseline reference, showing

intact gastric mucosa without any signs of ulceration or inflammation, indicative of healthy tissue. Conversely, the disease control group (Group II) exhibits severe mucosal damage characterized by extensive ulceration, prominent inflammatory cell infiltration in the submucosal layer and evident hemorrhagic areas and tissue necrosis, indicating significant damage due to ethanol-induced ulceration. The standard treatment group (Group III) receiving Omeprazole demonstrates a protective effect against ethanol-induced ulcers, with minimal signs of ulceration and inflammation. Gastric mucosa preservation is notable and inflammatory cell infiltration is minimal, indicating the effectiveness of Omeprazole in preventing ulcer formation. Treatment groups receiving MECS and AECS at different doses (Groups IV-VII) demonstrate varying degrees of protection against ethanol-induced ulcers. While higher doses generally provide better efficacy in preserving gastric tissue integrity, moderate to severe mucosal damage with ulceration is still evident in some areas. Inflammatory cell infiltration varies across these groups, ranging from mild to severe, with limited preservation of gastric mucosa observed in certain instances.

Overall, the histopathological interpretation highlights the severity of ethanol-induced ulceration in the disease control group and the varying degrees of protection offered by different treatments. It underscores the importance of evaluating treatment efficacy in preserving gastric tissue integrity and reducing inflammation in the context of ulcer management.

DISCUSSION

Human ulcers may be induced by a variety of reasons including stress, extended utilization of anti-inflammatory medications and excessive alcohol intake. The precise etiology of the majority of ulcers remains elusive, however it is hypothesized to arise from a dysregulation between forces that inflict damage onto the gastric mucosa and the body's capacity to safeguard it.[21]

Through laboratory experiments utilizing pylorus ligation-induced ulcer models, it was revealed that extracts derived from *Ceratophyllum submersum* effectively decreased the release of stomach acid. This finding highlights the potential of these extracts in mitigating the development of ulcers. Moreover, these extracts shown encouraging outcomes in safeguarding against mucosal harm caused by aspirin, a NSAID anti-inflammatory medicine recognized for its ability to elevate the likelihood of ulcers by impeding prostaglandin production.[22]

Ethanol, often found in alcoholic drinks, is recognized as a contributing factor in the development of ulcers due to its ability to impair the stomach lining's protective systems. Like NSAIDs, ethanol disrupts the production of prostaglandins, which impairs the stomach's capacity to preserve the integrity of its protective lining. Prostaglandins have a vital role in encouraging the release of protective chemicals such as bicarbonate and mucus. They also regulate the flow of blood in the mucosal lining and promote the turnover and repair of cells. Therefore, the suppression of prostaglandin production by ethanol raises the likelihood of mucosal harm and the development of ulcers. Studies demonstrate that both methanolic and aqueous extracts of *Ceratophyllum submersum* effectively reduce damage to the mucous membrane in ethanol-induced ulcer models. This suggests that both extracts have the potential to function as preventive agents against alcohol-induced stomach ulcers.[23]

Various plant sources with elevated tannin levels have been recognized for their anti-ulcerogenic properties. Flavonoids, in addition to tannins, are recognized as natural compounds that have inherent gastroprotective effects. Several approaches have been suggested to elucidate their physiological impacts, such as elevating prostaglandin levels in the mucosa, suppressing histamine release from mast cells, reducing acid generation, and preventing the proliferation of *H. pylori*. Various plant species containing abundant saponins have demonstrated anti-ulcer properties in various experimental ulcer types. Theorists propose that saponins offer protection by activating the defensive processes of the mucosa membrane and controlling the secretion and synthesis of stomach acid. The potential gastroprotective effects of *Ceratophyllum submersum* can be linked to the concurrent existence of saponins, the tannins and flavonoids.[24]

CONCLUSION

Ceratophyllum submersum Linn., an aquatic plant, has gained considerable interest in recent years for its alleged therapeutic benefits. This extensive pharmacological evaluation sought to clarify the therapeutic efficacy of extracts from *Ceratophyllum submersum* in the treatment of gastrointestinal diseases. The plant extracts were subjected to qualitative phytochemical screening, which confirmed the existence of many bioactive components. This finding paves the way for further research into the pharmacodynamic properties of these compounds. *Ceratophyllum submersum* extracts shown potential effectiveness in experimental models for antiulcer tests. These results indicate the need for additional investigation into the mechanisms and therapeutic applications of these extracts.

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