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ANTI-ULCER POTENTIAL OF SOLASODINE: EVIDENCE FROM *IN VITRO*, *IN VIVO*, AND MOLECULAR STUDIES

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Abstract

Gastric ulcer is a prevalent gastrointestinal disorder caused by an imbalance between aggressive factors and mucosal defense mechanisms, commonly associated with Helicobacter pylori infection and excessive gastric acid secretion. Despite the effectiveness of conventional therapies, their long-term use is often linked to adverse effects and disease recurrence, highlighting the need for safer therapeutic alternatives. The present study aimed to evaluate the anti-ulcer potential of solasodine, a naturally occurring steroidal alkaloid, using an integrated in vitro, in vivo, and molecular-based approach. The antibacterial activity of solasodine against three clinical strains of H. pylori was assessed using the disc diffusion method, with metronidazole serving as the reference drug. In vivo gastroprotective efficacy was evaluated in an ethanol-induced gastric ulcer model in Sprague Dawley rats, while molecular analysis was performed by quantifying the mRNA expression of H^+/K^+-ATPase using real-time polymerase chain reaction. Solasodine exhibited concentration-dependent inhibition of H. pylori growth and significantly reduced gastric mucosal lesions at oral doses of 4 and 8 mg/kg. The higher dose provided substantial ulcer protection comparable to omeprazole. Molecular findings revealed marked downregulation of H^+/K^+-ATPase expression in solasodine-treated groups, indicating suppression of gastric acid secretion. Overall, the findings demonstrate that solasodine exerts potent anti-ulcer effects through combined antibacterial, anti-secretory, and mucosal protective mechanisms. This multi-targeted activity suggests that solasodine may serve as a promising natural therapeutic candidate for the management of gastric ulcer, signifying further mechanistic and clinical investigations.

INTRODUCTION

Gastric ulcer is a common gastrointestinal disorder characterized by a break in the gastric mucosal lining due to an imbalance between aggressive factors and protective mechanisms. It results in localized inflammation and tissue damage, often leading to pain, bleeding, and impaired digestion. If left untreated, gastric ulcers can progress to serious and life-threatening complications (Graham et al., 2014). Several factors contribute to the development of gastric ulcers, with *Helicobacter pylori* infection and prolonged use of non-steroidal anti-inflammatory drugs being the most significant. Additional risk

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factors include excessive alcohol consumption, cigarette smoking, psychological stress, advanced age, and underlying chronic illnesses. Dietary habits, genetic predisposition, and increased gastric acid secretion further increase susceptibility to ulcer formation (Mustafa et al., 2015). Gastric ulcer remains a major global health concern, affecting millions of individuals worldwide. Its prevalence is higher in developing countries due to poor sanitation, widespread *H. pylori* infection, and limited access to healthcare facilities. Although improved medical therapies have reduced incidence in recent years, gastric ulcers continue to impose a substantial clinical and economic burden (Kuipers et al., 1995). The management of gastric ulcer primarily focuses on reducing gastric acidity, eradicating *H. pylori*, and enhancing mucosal defense. Standard treatments include proton pump inhibitors, H_2-receptor antagonists, antacids, and antibiotics in combination therapy. Despite their effectiveness, long-term use of these drugs may be associated with adverse effects and recurrence, highlighting the need for safer and more effective therapeutic alternatives (Pujari et al., 2024).

Solasodine as shown in (Figure 1) is a naturally occurring steroidal alkaloid derived from plants of the genus *Solanum* family Solanaceae have diversed reported activities including Anticancer (Koduru et al., 2007), anti-inflammatory (Pandurangan et al.,2011), antioxidant (Sharma et al., 2014) and antimicrobial (Silva et al., 2025) activities. To the best of our knowledge, comprehensive investigations exploring the therapeutic potential of solasodine in the management of gastric ulcer are still lacking. Therefore, the present study was designed to assess the anti-ulcer activity of solasodine through an integrated approach involving in vitro, in vivo, and molecular-based analyses.

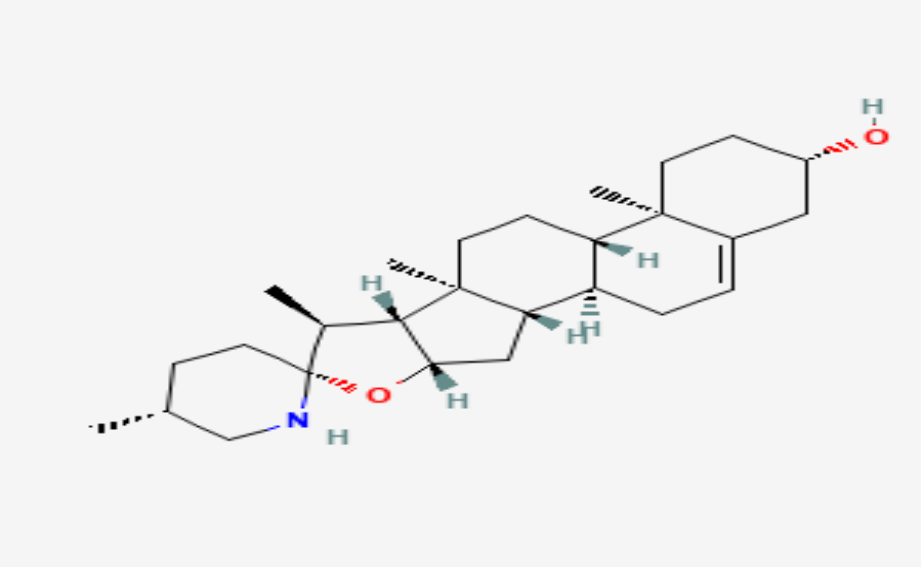


Figure 1. 2D structure of solasodine

Materials and Methods

Chemicals

All chemicals used in this study were of analytical grade and obtained from certified suppliers. Solasodine, normal saline, absolute ethanol and chloroform were purchased from Sigma-Aldrich (St. Louis, MO, USA). Omeprazole and metronidazole were obtained from Barrett Hodgson and Sanofi Aventis, respectively.

Animals

Sprague Dawley rats of either sex, weighing between 150 and 200 g, were obtained from the National Institute of Health Islamabad, and used for the present study. The animals were housed in standard laboratory cages under controlled environmental conditions, with the temperature maintained at 22 °C. They were provided with a standard diet and allowed free access to drinking water throughout the

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study period. All experimental procedures were carried out in accordance with the guidelines and ethical principles outlined by the Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council (1996).

Anti *H. pylori* Activity

The antibacterial activity of the selected natural compound against H. pylori was assessed using the disc diffusion technique. Three clinical strains of H. pylori were obtained, with informed consent, from gastric biopsy samples collected from patients diagnosed with gastric ulcers at Care Endoscopy Clinics and Laboratories, Rawalpindi, Pakistan. The biopsy specimens were immediately transferred to a modified Campy-Thio transport medium for further processing. Cultures were incubated at 37 °C under microaerophilic conditions. Bacterial identification was confirmed based on colony morphology and urease test results. The confirmed isolates were preserved at −80 °C in sterile McCartney bottles containing brain heart infusion broth supplemented with 0.2 g/L cysteine and 20% glycerol. Prior to antimicrobial testing, frozen isolates were revived and subcultured on Mueller–Hinton agar plates. Sterile paper discs were impregnated with brucine at concentrations of 0.5, 1, 2, 4, 8, 16, and 32 µg/disc and placed onto the inoculated agar plates. Following incubation for 3–5 days at 37 °C, the zones of inhibition were measured. All experiments were performed in triplicate, and antibacterial activity was expressed as the mean inhibition zone diameter (mm). Metronidazole was used as the reference standard (Noman et al., 2022).

Ethanol-induced gastric ulcer

To induce gastric lesions, rats were fasted for 24 hours and randomly divided into five groups (n = 5). Group I received normal saline (10 ml/kg) and served as the negative control. Group II was administered absolute ethanol at a dose of 1 ml/100 g to induce ulcers. Groups III and IV were pretreated orally with solasodine at doses of 4 and 8 mg/kg, respectively, while Group V received omeprazole (20 mg/kg) as the standard reference drug. One hour after pretreatment, absolute ethanol (1 ml/100 g) was given orally to all rats except those in Group I. After one hour of ethanol administration, the animals were sacrificed by cervical dislocation, and their stomachs were carefully excised and rinsed with normal saline. The lesions along the greater curvature of each stomach were measured in millimeters to determine the lesion index. The surface area of each lesion was calculated following the method described by (Qazi et al. (2017). The ulcer index (UI) was expressed as the mean ulcer score per gastrointestinal lesion, using the following scale: 0 = no ulcer; 1 = US ≤ 0.5 mm²; 2 = 0.5 < US ≤ 2.5 mm²; 3 = 2.5 < US ≤ 5 mm²; 4 = 5 < US ≤ 10 mm²; 5 = 10 < US ≤ 15 mm²; 6 = 15 < US ≤ 20 mm²; 7 = 20 < US ≤ 25 mm²; 8 = 25 < US ≤ 30 mm²; 9 = 30 < US ≤ 35 mm²; 10 = US > 35 mm². The total ulcer index for each stomach was calculated as the sum of all lesion lengths. The percentage inhibition (%I) of ulcers was determined using the formula:

$$\%I = \frac{US_c - US_t}{US_c} \times 100$$

where US_crepresents the ulcer surface area in the control group, and US_trepresents the ulcer surface area in the treated group.

Real-time polymerase chain reaction

Total RNA was extracted from gastric tissue using the TRIzol reagent, following the manufacturer's instructions. Complementary DNA (cDNA) was synthesized from 1–2 µg of total RNA using a reverse transcriptase enzyme mix and a PCR thermocycler. The mRNA expression levels of H^+/K^+-ATPase were quantified relative to β-actin, used as a housekeeping gene, using the 2^−ΔΔCT method. The primer sequences were as follows: H^+/K^+-ATPase forward: 5′-CCCGCGAGTACAACCTTCT-3′, reverse: 5′-CGTCATCCATGGCGAACT-3′; β-actin forward: 5′-TATGAATTGTACTCAGTGGA-3′, reverse: 5′-TGGTCTGGTACTTCTGCT-3′ (Irshad et al., 2021).

Results

***H. pylori* inhibitory effect**

The antibacterial activity of solasodine against three different H. pylori strains was evaluated by measuring the minimum inhibitory concentration (MIC) and the zone of inhibition. The strains tested included strain (A) J63 (cag A-), strain (B) J196 (cag A-), and strain (C) J107 (cag A+). Various

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concentrations of solasodine (0.5, 1, 2, 8, 16, and 32 µg/disc) were applied to strain A, resulting in zones of inhibition of 1.2, 1.5, 2.1, 4.1, 8.2, 10.8, and 14.2 mm, respectively, with an MIC of 16 µg/mL. When tested against strain B using the same solasodine concentrations, the inhibition zones observed were 1.5, 1.8, 2.2, 4.3, 7.8, 11.0, and 13.5 mm, and the MIC was determined to be 19 µg/mL. For strain C, the inhibition zones recorded were 1.8, 2.0, 2.1, 2.5, 4.5, 8.5, 11.5, and 14.0 mm across the same solasodine concentrations, with an MIC of 21 µg/mL. These results were compared with the standard antibiotic, metronidazole (Table 1).

Table 1. Evaluation of the antibacterial activity of solasodine against three clinical strains of *H. pylori* using the disk diffusion assay.

Sample	0.5 µg/disc	1 µg/disc	2 µg/disc	4 µg/disc	8 µg/disc	16 µg/disc	32 µg/disc	MIC_{50} µg/ml
Salosodine Strain 163 (cagA-)	1.2 ± 0.2	1.5 ± 0.3	2.1 ± 0.4	4.1 ± 0.5	8.2 ± 0.4	10.8 ± 0.5	14.2 ± 0.6	16
Salosodine Strain 1196 (cagA-)	1.5 ± 0.3	1.8 ± 0.4	2.2 ± 0.3	4.3 ± 0.4	7.8 ± 0.5	11.0 ± 0.6	13.5 ± 0.7	19
Salosodine Strain 1107 (cagA+)	1.8 ± 0.4	2.1 ± 0.3	2.5 ± 0.4	4.5 ± 0.5	8.5 ± 0.4	11.5 ± 0.5	14.0 ± 0.5	21
Metronidazole	3 ± 0.57	4 ± 0.44	6 ± 0.57	8 ± 0.33	9 ± 0.66	11 ± 0.33	12 ± 0.22	5

Effect on gastric ulcer

Solasodine, administered at doses of 4 and 8 mg/kg, demonstrated significant anti-ulcer activity, providing 82% protection with ulcer indexes of 2 ± 0.83 and 2 ± 0.41, respectively. In comparison, omeprazole (20 mg/kg) showed a stronger effect, inhibiting ulcer formation by 90% with an ulcer index of 1 ± 0.33 relative to the ethanol-treated group (Table 2). Microscopic examination of the rat stomach mucosa further illustrated these protective effects (Figure 2).

Table 2. Gastroprotective effects of solasodine and omeprazole on ethanol-induced gastric ulcer in rats.

Treatment mg/kg	Ulcer index	% Inhibition
Saline 10 mL/kg	0 ± 0	_
Ethanol 1 mL/100 g	10 ##	0
Solasodine 4 mg/kg + Ethanol 1mL/100g	2 ±0.83***	82
Solasodine 8 mg/kg + Ethanol 1mL/100g	2 ± 0.41***	84
Omeperazol 20 mg/kg + Ethanol 1 mL/100	1 ± 0.33***	90

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Figure 2. Gross morphology of gastric mucosa in rats. (A) Rats pretreated with saline (10 mL/kg) showing normal mucosa. (B) Rats administered absolute ethanol (1 mL/100 g) exhibiting severe gastric injury with extensive hemorrhagic necrosis. (C, D) Rats pretreated with solasodine at 4 and 8 mg/kg, showing reduced mucosal damage. (E) Rats pretreated with omeprazole (20 mg/kg) demonstrating protective effects on the gastric mucosa.

Quantification of mRNA Expression

RT-PCR analysis was used to assess the relative mRNA expression of H^+/K^+-ATPase in ethanol-induced gastric ulcer tissues. A marked upregulation of H^+/K^+-ATPase mRNA was observed in the ethanol-treated group. In contrast, treatment with solasodine (8 mg/kg) and omeprazole (20 mg/kg) significantly reduced the elevated mRNA expression levels of H^+/K^+-ATPase (Figure 3).

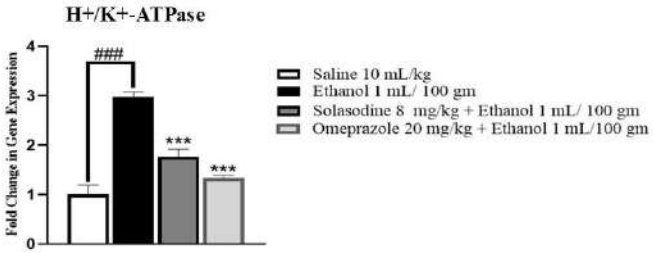


Figure 2. The impact of solasodine and omeprazole on H^+/K^+-ATPase mRNA expression was evaluated in gastric tissues of rats with ethanol-induced ulcer using reverse transcription–polymerase chain reaction (RT-PCR). Data were analyzed by one-way ANOVA followed by Tukey's post hoc test. Results are presented as mean ± SEM (n = 5). ###$p < 0.001$ compared to the saline-treated group; ***$p < 0.001$ compared to the ethanol-treated group.

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Discussion

Gastric ulcer disease remains a significant clinical challenge due to its multifactorial etiology, involving excessive gastric acid secretion, oxidative stress, inflammation, and *Helicobacter pylori* infection. Ethanol-induced gastric ulceration is a well-validated experimental model that closely mimics acute mucosal injury in humans, primarily through disruption of the gastric mucosal barrier, increased oxidative damage, and stimulation of acid secretion (Konturek et al., 2005). In the present study, solasodine demonstrated a pronounced gastroprotective effect through antibacterial, anti-secretory, and mucosal protective mechanisms. One of the major contributors to gastric ulcer pathogenesis is *H. pylori* infection, which induces chronic inflammation and damages the gastric epithelium via virulence factors such as cagA, leading to enhanced acid secretion and mucosal injury (Kusters et al., 2006). The observed dose-dependent inhibitory activity of solasodine against both cagA-positive and cagA-negative *H. pylori* strains highlights its broad antibacterial potential. The measurable zones of inhibition and MIC values obtained in this study suggest that solasodine effectively suppresses *H. pylori* growth, supporting previous reports that steroidal alkaloids exert antimicrobial effects by disrupting bacterial membrane integrity and enzyme activity (Silva et al., 2020). This antibacterial property may significantly contribute to the overall anti-ulcer effect observed in vivo. In the ethanol-induced ulcer model, pretreatment with solasodine markedly reduced gastric lesion formation and ulcer index values, indicating substantial protection of the gastric mucosa. Ethanol causes direct necrotic damage to epithelial cells, increases vascular permeability, and promotes inflammatory cell infiltration, leading to hemorrhagic lesions (Salim, 2014). The protective effect of solasodine may be attributed to its reported antioxidant and anti-inflammatory properties, which help counteract ethanol-induced oxidative stress and inflammatory cascades. Similar gastroprotective effects have been reported for other plant-derived steroidal alkaloids, which enhance endogenous defense mechanisms and stabilize the gastric mucosal barrier (Al-Mofleh, 2010). Furthermore, molecular analysis revealed that ethanol exposure significantly upregulated H^+/K^+-ATPase mRNA expression, reflecting increased gastric acid secretion. This proton pump is a critical determinant of gastric acidity and a primary target in ulcer therapy (Shin et al., 2013). Treatment with solasodine, particularly at 8 mg/kg, resulted in a notable downregulation of H^+/K^+-ATPase expression, comparable to the effect observed with omeprazole. This finding suggests that solasodine may exert an anti-secretory effect by modulating proton pump activity at the transcriptional level. Such inhibition of acid secretion plays a crucial role in ulcer healing and prevention of further mucosal injury. The combined antibacterial activity against *H. pylori*, suppression of gastric acid secretion, and protection of gastric mucosal integrity strongly support the multi-targeted anti-ulcer potential of solasodine. Unlike conventional therapies that primarily focus on acid suppression or bacterial eradication, solasodine appears to act through multiple complementary mechanisms. This integrated mode of action is particularly advantageous, as long-term use of current anti-ulcer drugs is often associated with adverse effects and high recurrence rates (Scarpignato et al., 2016). Overall, the findings of this study provide compelling experimental evidence supporting solasodine as a promising natural therapeutic candidate for gastric ulcer management. However, further investigations involving detailed mechanistic studies, histopathological validation, and clinical evaluation are warranted to fully establish its safety, efficacy, and translational potential.

Conclusion

Solasodine demonstrated significant gastroprotective activity against ethanol-induced gastric ulcers through a multi-mechanistic mode of action. Molecular findings revealed downregulation of H^+/K^+-ATPase expression, indicating suppression of gastric acid secretion. The anti-ulcer efficacy of solasodine was comparable to that of the standard drug omeprazole. These results highlight solasodine as a promising natural candidate targeting key ulcerogenic pathways. Further preclinical and clinical studies are required to confirm its safety and therapeutic potential.

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REFERENCES

Koduru, S., Grierson, D. S., Van de Venter, M., & Afolayan, A. J. (2007). Anticancer activity of steroid alkaloids isolated from Solanum aculeastrum. *Pharmaceutical Biology*, *45*(8), 613-618.

Pandurangan, A., Khosa, R. L., & Hemalatha, S. (2011). Anti-inflammatory activity of an alkaloid from Solanum trilobatum on acute and chronic inflammation models. *Natural product research*, *25*(12), 1132-1141.

Sharma, T., Airao, V., Panara, N., Vaishnav, D., Ranpariya, V., Sheth, N., & Parmar, S. (2014). Solasodine protects rat brain against ischemia/reperfusion injury through its antioxidant activity. *European Journal of Pharmacology*, *725*, 40-46.

da Silva, A. R. P., do Socorro Costa, M., Araújo, N. J. S., de Freitas, T. S., Paulo, C. L. R., de Alencar, M. A. S., ... & Coutinho, H. D. M. (2025). Evaluation of inhibition and eradication of bacterial biofilm by solasodin. *The Journal of Steroid Biochemistry and Molecular Biology*, *247*, 106654.

Graham, D. Y. (2014). History of Helicobacter pylori, duodenal ulcer, gastric ulcer and gastric cancer. World Journal of Gastroenterology: WJG, 20(18), 5191.

Mustafa, M., Menon, J., Muiandy, R. K., Fredie, R., Sein, M. M., & Fariz, A. (2015). Risk factors, diagnosis, and management of peptic ulcer disease. *J Dent Med Sci*, *14*(7), 40-46.

Kuipers, E. J., Thijs, J. C., & Festen, H. P. (1995). The prevalence of Helicobacter pylori in peptic ulcer disease. *Alimentary pharmacology & therapeutics*, *9*, 59-69.

Pujari, N. M., Khushtar, M., Mishra, A., & Gupta, D. (2024). Comprehensive Insights into Gastric Ulcer Therapies: A Review of Current Approaches. *Journal of Applied Pharmaceutical Sciences and Research*, *7*(1), 4-12.

Noman, M., Qazi, N. G., Rehman, N. U., & Khan, A. U. (2022). Pharmacological investigation of brucine anti-ulcer potential. *Frontiers in pharmacology*, *13*, 886433.

Qazi, N. G., Khan, A. U., & Ali, F. (2017). Anti-diarrheal, anti-secretory, anti-spasmodic and antiulcer activities of Acacia modesta (Mimosaceae) aerial parts. *Tropical Journal of Pharmaceutical Research*, *16*(9), 2231-2237.

Irshad, N., Khan, A. U., Shah, F. A., Nadeem, H., Ashraf, Z., Tipu, M. K., & Li, S. (2021). Antihyperlipidemic effect of selected pyrimidine derivatives mediated through multiple pathways. *Fundamental & Clinical Pharmacology*, *35*(6), 1119-1132.

Al-Mofleh, I. A. (2010). Gastric ulcer disease: Pathogenesis and treatment. *World Journal of Gastroenterology*, *16*(1), 1–8. https://doi.org/10.3748/wjg.v16.i1.1

Graham, D. Y., Fischbach, L., & Feldman, M. (2014). *Helicobacter pylori* infection and peptic ulcer disease. *Gastroenterology Clinics of North America*, *43*(3), 449–461. https://doi.org/10.1016/j.gtc.2014.05.002

Konturek, P. C., Brzozowski, T., & Konturek, S. J. (2005). Stress and the gut: Pathophysiology, clinical consequences, diagnostic approach and treatment options. *Journal of Physiology and Pharmacology*, *56*(Suppl. 4), 5–16.

Kusters, J. G., van Vliet, A. H. M., & Kuipers, E. J. (2006). Pathogenesis of *Helicobacter pylori* infection. *Clinical Microbiology Reviews*, *19*(3), 449–490.

Kuipers, E. J., Thijs, J. C., & Festen, H. P. (1995). The prevalence of *Helicobacter pylori* in peptic ulcer disease. *Alimentary Pharmacology & Therapeutics*, *9*(Suppl. 2), 59–69.

Mustafa, M., Menon, J., Rai, S., & Ahmed, S. (2015). Risk factors, diagnosis and management of peptic ulcer disease. *Journal of Dental and Medical Sciences*, *14*(7), 40–46.

Pujari, R., Patel, V., & Shah, M. (2024). Advances in pharmacological management of gastric ulcer: Current perspectives and future directions. *Journal of Gastrointestinal Pharmacology*, *12*(1), 25–38.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Salim, A. S. (2014). Role of oxygen-derived free radical scavengers in the management of recurrent attacks of ethanol-induced gastric mucosal injury. *Digestive Diseases and Sciences, 39*(6), 1239–1247. https://doi.org/10.1007/BF02088020

Scarpignato, C., Gatta, L., Zullo, A., & Blandizzi, C. (2016). Effective and safe proton pump inhibitor therapy in acid-related diseases—A position paper addressing benefits and potential harms of acid suppression. *BMC Medicine, 14*, Article 179.

Shin, J. M., & Sachs, G. (2013). Pharmacology of proton pump inhibitors. *Current Gastroenterology Reports, 15*(7), 323.

Silva, M. P., Costa, E. V., & Pinheiro, M. L. B. (2020). Antimicrobial and pharmacological properties of steroidal alkaloids: A comprehensive review. *Phytotherapy Research, 34*(6), 1235–1248.