FUDMA Journal of Sciences (FJS)
ISSN online: 2616-1370
ISSN print: 2645 - 2944
Vol. 10 No. 6, March, 2026, pp 88 – 94
DOI: https://doi.org/10.33003/fjs-2026-1006-4360

GASTROPROTECTIVE AND REPARATIVE EFFECTS OF *Alstonia boonei* AGAINST ASPIRIN-INDUCED GASTROENTEROPATHY IN RAT'S MODEL

Ogeyemhe Blessing Emosho and *Odigie Efosa Bolaji

Department of Medical Laboratory Science, School of Basic Medical Science, University of Benin, P.M.B. 1154, Benin City, Nigeria

*Corresponding authors' email: bolaji.odigie@uniben.edu
ORCID IDs: https//orcid.org/0000-0002-1233-0491

ABSTRACT

Nonsteroidal anti-inflammatory drugs such as aspirin are widely used but are limited by their potential to induce gastrointestinal injury through oxidative stress, inflammation, and epithelial disruption. This study investigated the protective effects of *Alstonia boonei* against aspirin-induced gastroenteropathy by evaluating body and organ weights, oxidative stress markers, gross gastric lesions, and histopathological changes in the eosophagus, stomach, and duodenum. Rats administered aspirin exhibited reduced weight gain (154.67 ± 18.28 g to 146.67 ± 14.68 g), increased gastric and duodenal organ weights, elevated malondialdehyde levels, depletion of glutathione, and a markedly increased gastric lesion index. These changes were accompanied by severe mucosal alterations, including inflammatory infiltration, glandular distortion, villous disruption, and early erosive damage. Administration of *A. boonei* alone produced no adverse effects and maintained normal physiological and histological profiles, confirming its safety. Co-treatment with *A. boonei* resulted in progressive, dose-dependent protection against aspirin-induced injury. Improvements included restoration of weight gain, reduction of organ weight abnormalities, attenuation of oxidative stress, and significant decreases in gross gastric lesions. Histologically, the extract preserved epithelial integrity, reduced inflammatory cell infiltration, and supported normal glandular and villous architecture, with the most pronounced recovery observed at 1500–2000 mg/kg. At these doses, mucosal features approached those of the control group, indicating near-complete structural and biochemical restoration. Overall, the findings demonstrate that *A. boonei* confers substantial gastroprotective effects through antioxidant and anti-inflammatory mechanisms that stabilize gastrointestinal tissues and counteract aspirin-mediated injury. The extract shows promise as a natural therapeutic agent for mitigating NSAID-induced gastrointestinal damage and warrants further investigation.

Keywords: *Alstonia boonei*, Aspirin-induced gastroenteropathy, Gastroprotection, Mucosal injury, NSAID gastropathy, Gastric mucosa

INTRODUCTION

The gastrointestinal tract plays a vital role in nutrient assimilation, mucosal immunity, and maintenance of epithelial barrier integrity, making it highly responsive but also vulnerable to chemical and pharmacological injury. Gastric mucosa is continually exposed to mechanical friction, digestive enzymes, acid, and oxidative metabolites, yet it maintains structural stability through a combination of mucus secretion, bicarbonate buffering, epithelial restitution, angiogenesis, and prostaglandin mediated cytoprotection (Bhattacharyya et al., 2014). Disruption of these endogenous defense mechanisms predisposes the stomach to erosions, ulceration, inflammation, and haemorrhage, which are major manifestations of gastrointestinal toxicity and are strongly influenced by oxidative and inflammatory pathways (Bhattacharyya et al., 2014; Chandimali et al., 2025).

Aspirin remains one of the most widely used nonsteroidal anti-inflammatory drugs for analgesic, antipyretic, and cardioprotective purposes. Despite its clinical value, aspirin is well recognized as a leading cause of gastric mucosal injury. Inhibition of cyclooxygenase 1 reduces prostaglandin synthesis, resulting in compromised mucus and bicarbonate secretion, impaired mucosal blood flow, and weakened epithelial repair (Lavie et al., 2017). In addition, aspirin exerts direct topical irritation due to its acidic nature and lipid solubility, allowing it to penetrate epithelial cells where it induces mitochondrial dysfunction, oxidative stress, and intracellular acidosis. These events culminate in epithelial apoptosis, vascular leakage, and mucosal ulceration in both experimental and clinical models of aspirin induced gastrointestinal toxicity (Lavie et al., 2017; Iwamoto et al., 2013; Tawfik et al., 2025). Recent work further emphasizes that disturbances in inflammatory cascades, oxidative imbalance, and microbiota related factors are central to the pathogenesis of nonsteroidal anti-inflammatory drug associated mucosal injury throughout the upper gastrointestinal tract (Bindu et al., 2020; Hijos-Mallada et al., 2022; Zhou et al., 2025).

Medicinal plants have gained increasing attention for their potential to counteract gastrointestinal injury through antioxidant, anti inflammatory, cytoprotective, and mucosal restorative properties. *A. boonei* is a widely used African medicinal plant rich in flavonoids, alkaloids, phenolic acids, and triterpenoids. These phytochemicals exhibit radical scavenging activity, membrane stabilizing effects, and anti-inflammatory actions that support cellular defense under toxic stress (Oyebode et al., 2019; Olanlokun et al., 2021). Evidence from toxicological and pharmacological studies demonstrates that extracts of *A. boonei* and related medicinal plants can modulate oxidative pathways, preserve epithelial or organ integrity, and attenuate tissue damage in models of drug induced toxicity, including ulcerative colitis and systemic oxidative disorders (Adjouzem et al., 2020; Uroko et al., 2020; Chen et al., 2025; Park et al., 2019). Recent reviews of gastroprotective plants further highlight the relevance of polyphenol rich African and North African species in the prevention and mitigation of peptic ulcers and mucosal injury (Cherrada et al., 2024; Martins-Gomes et al., 2024).

Although extensive work has addressed the toxicities associated with aspirin and the protective effects of various medicinal plants, there remains limited information on the gastroprotective and reparative potential of *A. boonei* in aspirin induced gastrointestinal toxicity. Considering the global burden of nonsteroidal anti-inflammatory drug related gastric and duodenal complications and the need for safer plant-based interventions, investigating this medicinal plant in a validated gastric injury model is scientifically warranted (Wallace, 2012; Takeuchi, 2012; Sohail et al., 2023). The present study evaluates the gastroprotective and restorative effects of *A. boonei* in aspirin induced gastrointestinal toxicity in rats, integrating oxidative stress indices, gross gastric parameters, and histopathological assessment of the oesophagus, stomach, and duodenum to elucidate the plant's capacity to preserve mucosal integrity and promote epithelial repair.

MATERIALS AND METHODS

Study Setting

The study was conducted in a controlled animal research laboratory within the Department of Anatomy, University of Benin, Nigeria where environmental parameters including temperature, humidity, light exposure, and ventilation were maintained within physiological limits for rodent experimentation. All procedures followed internationally recognized ethical guidelines for experimental animal use and were aligned with the recommendations of the Organisation for Economic Co operation and Development regarding humane handling, monitoring, and reduction of animal stress during toxicological testing (OECD, 2022). These ethical standards are consistent with contemporary expectations for biomedical research involving medicinal plant extracts and gastrointestinal injury models (Mugale et al., 2024).

Plant Collection and Extract Preparation

Fresh leaves of *A. boonei* were sourced locally and authenticated by a qualified botanist (voucher number UBH-A591). The leaves were rinsed to remove contaminants, air dried at room temperature to preserve phytochemical quality, and milled into a fine powder. The powdered sample was macerated in ethanol for seventy-two hours with intermittent agitation. Filtrates were concentrated at low temperature using a rotary evaporator to obtain a crude extract rich in alkaloids, flavonoids, and phenolic compounds. This method corresponds with established extraction protocols used in evaluating antioxidant and anti-inflammatory potentials of *A. boonei* and other medicinal plants (Oyebode et al., 2019; Uroko et al., 2020; Adjouzem et al., 2020; Mollica et al., 2022). Extracts were stored in airtight containers under refrigeration until administration.

Preparation of Aspirin Solution

Pharmaceutical grade aspirin tablets were procured from an approved supplier. A fresh solution was prepared daily by dissolving the tablets in distilled water to achieve a dose of 10 mg/kg body weight. This dose is commonly employed in experimental models to induce gastric and upper intestinal mucosal injury through prostaglandin inhibition, oxidative stress, and epithelial barrier disruption while avoiding excessive systemic toxicity (Lavie et al., 2017; Bjarnason et al., 2018; Matsui et al., 2011). The model reflects the clinical pattern of nonsteroidal anti-inflammatory drug related gastropathy and enteropathy described in mechanistic and clinical studies (Wallace, 2012; Hladkykh & Chyzh, 2021).

Acute Toxicity Study (LD_{50} Determination)

A preliminary acute toxicity evaluation was conducted prior to the main experiment to determine the safety margin of the *A. boonei* extract. The study followed the OECD Up and Down Procedure for acute oral toxicity testing, which involves stepwise dose administration and observation of animals for behavioral changes, toxicity signs, or mortality for up to seventy-two hours (OECD, 2022). No mortality or visible signs of distress were recorded at the administered doses. Animals remained active and demonstrated normal feeding and grooming behavior. These findings indicate that the extract possesses a wide safety margin and is suitable for oral administration in repeated dose studies. Similar observations regarding the high oral safety and tolerability of medicinal plant extracts have been reported in recent preclinical safety evaluations (Mugale et al., 2024; Chen et al., 2025).

Experimental Animals and Grouping

Thirty adult albino rats weighing between 130 g and 180 g were used for the study. Animals were housed in polypropylene cages under a twelve-hour light and dark cycle and were provided free access to standard rat feed and water. A two-week acclimatization period was observed to minimize physiological variability and ensure stabilization before treatment, in accordance with recommended standards for preclinical toxicity and gastroprotective research (OECD, 2022; Mugale et al., 2024).

Animals were randomly assigned into six groups of five rats each.

Group I served as the untreated control.

Group II received aspirin at 10 mg/kg.

Group III received *A. boonei* extract at 1000 mg/kg.

Group IV received aspirin followed by 1000 mg/kg of *A. boonei*.

Group V received aspirin followed by 1500 mg/kg of *A. boonei*.

Group VI received aspirin followed by 2000 mg/kg of *A. boonei*.

Extract doses were selected based on findings from the acute toxicity study and earlier reports demonstrating biological effectiveness and safety of *A. boonei* at moderate to high concentrations in rodent models (Olanlokun et al., 2021; Adjouzem et al., 2020; Mugale et al., 2024). All treatments were administered orally once daily for fourteen days using calibrated gavage equipment.

Assessment of Gastric Parameters and Biochemical Markers

At the end of the treatment period, the rats were fasted overnight and then sacrificed humanely. The oesophagus, stomach, and duodenum were carefully excised and opened longitudinally for gross evaluation. Each segment was rinsed with physiological saline to remove luminal contents and to allow clear visualization of mucosal surfaces. Macroscopic assessment included examination of mucosal coloration, continuity of the epithelial lining, presence of hemorrhagic streaks, erosions, ulcerative spots, edema, and loss of mucosal folds. These parameters are well established indicators of upper gastrointestinal injury after nonsteroidal anti inflammatory drug exposure and correspond to classical patterns of aspirin induced mucosal damage (Lavie et al., 2017; Wallace, 2012; Matsui et al., 2011).

For biochemical evaluation, representative portions of gastric and duodenal tissues were homogenized in ice cold buffer and centrifuged to obtain supernatants for oxidative stress assays. Although the oesophagus is structurally distinct and less

commonly used for such assays, its tissues were retained for histological assessment. The biochemical markers assessed in homogenates included malondialdehyde and reduced glutathione, which serve as sensitive indicators of lipid peroxidation and antioxidant capacity in gastrointestinal mucosa. Alterations in these indices reflect redox imbalance and mucosal vulnerability, which are central features of nonsteroidal anti-inflammatory drug induced gastrointestinal injury and inflammatory mucosal disease (Bhattacharyya et al., 2014; Muro et al., 2024). This combined macroscopic and biochemical assessment allowed a comprehensive evaluation of mucosal integrity, oxidative stress status, and upper gastrointestinal vulnerability across the oesophagus, stomach, and duodenum, providing an integrated framework for interpreting the gastroprotective role of *A. boonei*.

Histopathological Examination

Sections of the oesophagus, stomach, and duodenum were harvested immediately after sacrifice and fixed in ten percent neutral buffered formalin to preserve cellular and mucosal architecture. Tissues were processed through routine dehydration, clearing, and paraffin embedding. Serial sections of approximately five micrometres were obtained using a rotary microtome and stained with hematoxylin and eosin. Microscopic examination included assessment of epithelial continuity, thickness and integrity of mucosal layers, glandular morphology, submucosal vascular congestion, inflammatory cell infiltration, edema, ulcer formation, and evidence of hemorrhagic or erosive lesions. This comprehensive histological approach aligns with established standards for evaluating gastrointestinal toxicity and is widely applied in characterizing the structural consequences of nonsteroidal anti-inflammatory drug induced mucosal injury and the protective effects of plant derived agents (Matsui et al., 2011; Wallace, 2012; Hladkykh & Chyzh, 2021; Park et al., 2019).

Statistical Analysis

Data were presented as mean plus or minus standard deviation. Statistical comparisons were performed using one way analysis of variance followed by appropriate post hoc tests to determine intergroup differences. A p-value of less than 0.05 was considered statistically significant. This analytical method is widely used in evaluating the effects of plant derived agents on drug induced tissue injury and in linking biochemical changes with histopathological outcomes in toxicology research (Carr & Pirmohamed, 2018; Chen et al., 2025).

RESULTS AND DISCUSSION

The pattern of body weight and organ weight changes observed in this study provides the first indication of the physiological impact of aspirin and the modulatory potential of *A. boonei*. Animals in the control group demonstrated steady weight gain, which reflects normal feeding and gastrointestinal comfort. In contrast, the aspirin treated group showed a reduction in weight gain as shown in Table 1. This pattern is consistent with earlier reports that aspirin induced gastrointestinal irritation disrupts appetite, digestion, and nutrient absorption due to prostaglandin inhibition and mucosal dysfunction (Lavie et al., 2017; Wallace, 2012; Matsui et al., 2011). The reduced appetite and discomfort associated with mucosal erosion and inflammation have been implicated in similar weight suppression patterns in animal models of NSAID injury (Iwamoto et al., 2013).

Co administration of *A. boonei* with aspirin produced a gradual improvement in final body weight across increasing extract doses. This improvement aligns with the ability of antioxidant rich plants to enhance feeding comfort and restore gastrointestinal function in models of mucosal injury (Cherrada et al., 2024; Martins Gomes et al., 2024). The extract only group showed the highest weight gain, demonstrating that *A. boonei* is well tolerated and nontoxic at 1000 mg/kg, which supports earlier safety studies on the plant (Uroko et al., 2020; Adjouzem et al., 2020; Oyebode et al., 2019).

Organ weight changes further illustrate the influence of aspirin and the protective effects of the extract. Table 1 shows that stomach and duodenum weights increased significantly in the aspirin group. This increase is a recognized manifestation of edema, inflammatory infiltration, and mucosal congestion which occur when prostaglandin depletion and oxidative stress compromise mucosal integrity (Bjarnason et al., 2018; Wallace, 2013). When *A. boonei* was co-administered, organ weights shifted toward normal values in a dose dependent manner, suggesting attenuation of inflammation and edema. Similar responses have been documented for other phenolic rich extracts that stabilize epithelial membranes and limit fluid accumulation within inflamed mucosa (Park et al., 2019; Cherrada et al., 2024). The near normalization of stomach and duodenal weights at 1500 mg/kg and 2000 mg/kg indicates progressive restoration of mucosal homeostasis.

The biochemical findings in Table 2 complement the physiological and organ weight changes. Aspirin markedly increased gastric and duodenal malondialdehyde while reducing glutathione levels. This shift reflects intense lipid peroxidation and depletion of antioxidant defenses which are central mechanisms in NSAID induced gastrointestinal toxicity (Bhattacharyya et al., 2014; Bindu et al., 2020). These oxidative changes have been widely reported in aspirin injury models and are closely linked with delayed epithelial repair and increased ulcer susceptibility (Muro et al., 2024; Wallace, 2012). Treatment with *A. boonei* effectively reversed these biochemical alterations with dose dependent reductions in malondialdehyde and restoration of glutathione toward control levels. The improvement reflects strong antioxidant activity of the plant as demonstrated in earlier studies involving its flavonoids, phenolic acids, and terpenoid constituents (Oyebode et al., 2019; Uroko et al., 2020; Olanlokun et al., 2021). The 1500 mg/kg and 2000 mg/kg groups showed the most favorable oxidative profile which provides biochemical evidence for dose dependent mucosal protection.

The trends in the biochemical markers are consistent with the gross gastric lesion scores. Table 2 shows that aspirin produced the highest lesion index with widespread erosions while co-administration of the extract significantly reduced these lesions in a dose dependent pattern. Reduction in lesion index has been described as a hallmark of successful gastroprotection in NSAID injury models and is typically associated with enhanced mucus secretion, improved epithelial renewal, and suppression of inflammatory oxidants (Takeuchi, 2012; Martins Gomes et al., 2024). The marked decline in gastric lesion index at 1500 mg/kg and 2000 mg/kg indicates that these doses of *A. boonei* effectively counteract the damaging effects of aspirin.

The histological findings across Plates 1.1-1.6 integrate the physiological, biochemical, and gross observations into a coherent structural pattern. The control tissues maintain normal esophageal, gastric, and duodenal architecture with intact epithelia and organized mucosal layers as expected for unstressed gastrointestinal tissues. Aspirin induced severe alterations in the stomach and duodenum with dense

inflammatory infiltrates, glandular distortion, goblet cell hyperplasia, villous shortening, and stromal edema. These features match the classical microscopic characteristics of NSAID gastropathy and enteropathy described in previous literature (Matsui et al., 2011; Wallace, 2013; Iwamoto et al., 2013). The duodenum was particularly vulnerable which agrees with reports that the small intestine exhibits significant susceptibility to aspirin mediated mitochondrial injury, bacterial translocation, and oxidative stress (Kakizaki et al., 2025; Bindu et al., 2020).

The extract only group maintained normal histology consistent with its established safety profile. When *A. boonei* was administered alongside aspirin, a clear dose dependent recovery of gastrointestinal structure became evident. At 1000 mg/kg the esophagus was fully protected while the stomach showed mild glandular irregularity and vacuolation. The duodenum still exhibited inflammatory expansion and partial epithelial loss which indicates that this dose provided incomplete protection. Increasing the extract to 1500 mg/kg produced stronger protection with preserved gastric glands and near normal duodenal villi. The esophagus remained comparable to control tissue. These findings are consistent with the partial but improving effects observed in the biochemical markers and organ weights.

The highest dose of 2000 mg/kg provided the most complete protection with preserved villous architecture in the duodenum, intact gastric epithelium, absence of ulceration, and only mild inflammatory cell presence. This response corresponds with the lowest oxidative stress levels and near normalization of organ weights at this dose. The histology therefore confirms that *A. boonei* exerts its protective effects through restoration of epithelial integrity, suppression of inflammatory infiltration, stabilization of mucosal glands, and limitation of oxidative injury. These mechanisms align with those described for plant based gastroprotective agents that enhance cytoprotection, tighten epithelial junctions, reduce leukocyte mediated injury, and promote epithelial turnover (Cherrada et al., 2024; Park et al., 2019; Martins Gomes et al., 2024).

The collective evidence from Tables 1 and 2 and Plates 1.1-1.6 demonstrates a strong dose dependent protective pattern. Low dose *A. boonei* provides partial protection but higher doses progressively restore mucosal structure and function. The highest dose produces near complete reversal of aspirin induced injury. This dose dependent relationship mirrors the pharmacodynamic behavior of antioxidant rich extracts which exhibit greater therapeutic effect with increasing phytochemical availability (Uroko et al., 2020; Oyebode et al., 2019). The coordinated improvements across body weight, organ weight, oxidative stress markers, gastric lesions, and histopathology provide a unified interpretation that *A. boonei* enhances gastrointestinal resilience against aspirin mediated oxidative and inflammatory stress.

CONCLUSION

This study shows that *A. boonei* provides clear, dose dependent protection against aspirin induced gastroenteropathy. Aspirin caused marked physiological, biochemical, and histological disturbances, including impaired weight gain, elevated gastric lesions, increased oxidative stress, and severe mucosal injury. Co-treatment with *A. boonei* progressively reversed these effects, with higher doses producing greater improvement. The extract reduced gastric and duodenal oxidative stress, lowered lesion indices, and preserved mucosal structure by maintaining epithelial continuity, reducing inflammatory infiltration, and supporting normal glandular and villous architecture. The highest doses (1500-2000 mg/kg) offered near complete restoration of gastric and duodenal morphology and improved biochemical profiles. These findings suggest that *A. boonei* possesses significant gastroprotective properties, likely mediated through antioxidant and anti-inflammatory mechanisms, and may serve as a promising therapeutic agent for NSAID induced gastrointestinal injury.

ACKNOWLEDGEMENTS

The authors sincerely thank the technical staff of the Histopathology Unit, Department of Medical Laboratory Science, University of Benin, for their invaluable support in tissue processing, staining, and laboratory assistance. We also acknowledge the Animal Research Facility team for ensuring animal welfare and adherence to ethical standards. Special appreciation is extended to colleagues and mentors whose guidance and insights greatly contributed to this study's success.

REFERENCES

Adjouzem, C. F., Gilbert, A., Mbiantcha, M., Yousseu Nana, W., Matah Marthe Mba, V., Djuichou Nguemnang, S. F., Tsafack, E. G., & Atsamo, A. D. (2020). Effects of Aqueous and Methanolic Extracts of Stem Bark of *Alstonia boonei* De Wild. (Apocynaceae) on Dextran Sodium Sulfate-Induced Ulcerative Colitis in Wistar Rats. *Evidence-based complementary and alternative medicine: eCAM*, *2020*, 4918453. https://doi.org/10.1155/2020/4918453

Bhattacharyya, A., Chattopadhyay, R., Mitra, S., & Crowe, S. E. (2014). Oxidative stress: an essential factor in the pathogenesis of gastrointestinal mucosal diseases. *Physiological reviews*, 94(2), 329–354. https://doi.org/10.1152/physrev.00040.2012

Bindu, S., Mazumder, S., & Bandyopadhyay, U. (2020). Non-steroidal anti-inflammatory drugs (NSAIDs) and organ damage: A current perspective. *Biochemical pharmacology*, *180*, 114147. https://doi.org/10.1016/j.bcp.2020.114147

Bjarnason, I., Scarpignato, C., Holmgren, E., Olszewski, M., Rainsford, K. D., & Lanas, A. (2018). Mechanisms of damage to the gastrointestinal tract from nonsteroidal anti-inflammatory drugs. *Gastroenterology*, *154*(3), 500–514. https://doi.org/10.1053/j.gastro.2017.11.081

Carr, D. F., & Pirmohamed, M. (2018). Biomarkers of adverse drug reactions. *Experimental biology and medicine (Maywood, N.J.)*, *243*(3), 291–299. https://doi.org/10.1177/1535370217733425

Chandimali, N., Bak, S. G., Park, E. H., & Lee, S. J. (2025). Free radicals and their impact on health and antioxidant defenses: A review. *Cell Death Discovery*, 11, 19. https://doi.org/10.1038/s41420-024-02278-8

Chen, Y., Mei, Y. Q., Hou, L., & Li, K. J. (2025). Therapeutic potential of plant-derived natural products against drug-induced liver injury. *Frontiers in pharmacology*, *16*, 1652860. https://doi.org/10.3389/fphar.2025.1652860

Cherrada, N., Chemsa, A. E., Gheraissa, N., Laib, I., Gueboudji, Z., El-Shazly, M., Zaater, A., Abid, A., Sweilam, S. H., Emran, T. B., Nani, S., Benamor, B., Ghemam Amara, D., Atoki, A. V., & Messaoudi, M. (2024). Gastroprotective Efficacy of North African Medicinal Plants: A Review on Their Therapeutic Potential for Peptic Ulcers. *Food science &*

nutrition, *12*(11), 8793–8824. https://doi.org/10.1002/fsn3.4536

Cherrada, N., Chemsa, A. E., Gheraissa, N., Laib, I., Gueboudji, Z., El-Shazly, M., Zaater, A., Abid, A., Sweilam, S. H., Emran, T. B., Nani, S., Benamor, B., Ghemam Amara, D., Atoki, A. V., & Messaoudi, M. (2024). Gastroprotective Efficacy of North African Medicinal Plants: A Review on Their Therapeutic Potential for Peptic Ulcers. *Food science & nutrition*, *12*(11), 8793–8824. https://doi.org/10.1002/fsn3.4536

Hijos-Mallada, G., Sostres, C., & Gomollón, F. (2022). NSAIDs, gastrointestinal toxicity and inflammatory bowel disease. *Gastroenterología y Hepatología (English Edition)*, *45*(3), 215-222. https://doi.org/10.1016/j.gastre.2021.06.002 Hladkykh, F., & Chyzh, M. (2021). Nonsteroidal anti-inflammatory drugs: A modern understanding of the mechanisms of damage to the digestive tract, the shortcomings of pathogenetic drugs and prospects for biological therapy of NSAID-induced esophagogastroenterocolonopathy. *Gastroenterology*, *54*(4), 253–266. https://doi.org/10.22141/2308-2097.54.4.2020.216714

Iwamoto, J., Saito, Y., Honda, A., & Matsuzaki, Y. (2013). Clinical features of gastroduodenal injury associated with long-term low-dose aspirin therapy. *World journal of gastroenterology*, *19*(11), 1673–1682. https://doi.org/10.3748/wjg.v19.i11.1673

Kakizaki, F., Miyazaki, T., Ueda, H., Iwamoto, J., Honda, A., & Ikegami, T. (2025). Small intestinal bacteria accelerate aspirin-induced small intestinal injuries. *Experimental and Molecular Pathology*, *143*, 104984. https://doi.org/10.1016/j.yexmp.2025.104984

Lavie, C., Howden, C. W., Scheiman, J., & Tursi, J. (2017). Upper gastrointestinal toxicity associated with long-term aspirin therapy: Consequences and prevention. *Current Problems in Cardiology*, *42*(5), 146–166. https://doi.org/10.1016/j.cpcardiol.2017.01.006

Martins-Gomes, C., Nunes, F. M., & Silva, A. M. (2024). Natural products as dietary agents for the prevention and mitigation of oxidative damage and inflammation in the intestinal barrier. *Antioxidants*, *13*(1), 65. https://doi.org/10.3390/antiox13010065

Matsui, H., Shimokawa, O., Kaneko, T., Nagano, Y., Rai, K., & Hyodo, I. (2011). The pathophysiology of non-steroidal anti-inflammatory drug (NSAID)-induced mucosal injuries in stomach and small intestine. *Journal of clinical biochemistry and nutrition*, *48*(2), 107–111. https://doi.org/10.3164/jcbn.10-79

Mollica, A., Zengin, G., Sinan, K. I., Marletta, M., Pieretti, S., Stefanucci, A., Etienne, O. K., Jekő, J., Cziáky, Z., Bahadori, M. B., Picot-Allain, C., & Mahomoodally, M. F. (2022). A Study on Chemical Characterization and Biological Abilities of *Alstonia boonei* Extracts Obtained by Different Techniques. *Antioxidants (Basel, Switzerland)*, *11*(11), 2171. https://doi.org/10.3390/antiox11112171

Mugale, M. N., Dev, K., More, B. S., Mishra, V. S., Washimkar, K. R., Singh, K., Maurya, R., Rath, S. K., Chattopadhyay, D., & Chattopadhyay, N. (2024). A comprehensive review on preclinical safety and toxicity of medicinal plants. *Clinical Complementary Medicine and Pharmacology*, *4*(1), 100129. https://doi.org/10.1016/j.ccmp.2024.100129

Muro, P., Zhang, L., Li, S., Zhao, Z., Jin, T., Mao, F., & Mao, Z. (2024). The emerging role of oxidative stress in inflammatory bowel disease. *Frontiers in endocrinology*, *15*, 1390351. https://doi.org/10.3389/fendo.2024.1390351

Okorie, N. H., Mbah, C. J., Ugodi, G. W., & Magbo, C. C. (2022). Investigation into the gastro-protective properties of *Alstonia boonei* (de wild) leaves and stem bark. *Tropical Journal of Natural Product Research*, *6*(3), 403–407. https://tjnpr.org/viewarticle.aspx?articleid=2258

Olanlokun, J. O., Olowofolahan, A. O., Bodede, O., Adegbuyi, A. T., Prinsloo, G., Steenkamp, P., & Olorunsogo, O. O. (2021). Anti-Inflammatory Potentials of the n-Hexane Fraction of *Alstonia boonei* Stem Bark in Lipopolysaccharide-Induced Inflammation in Wistar Rats. *Journal of inflammation research*, *14*, 3905–3920. https://doi.org/10.2147/JIR.S304076

Organisation for Economic Co-operation and Development (OECD). (2022, June 30). *Test No. 425: Acute Oral Toxicity: Up-and-Down Procedure*. OECD Guidelines for the Testing of Chemicals, Section 4. https://www.oecd.org/en/publications/2022/06/test-no-425-acute-oral-toxicity-up-and-down-procedure_g1gh2953.html

Oyebode, O. A., Erukainure, O. L., Ibeji, C. U., Koorbanally, N. A., & Islam, M. S. (2019). Phytochemical constituents, antioxidant and antidiabetic activities of different extracts of the leaves, stem and root barks of *Alstonia boonei*: An in vitro and in silico study. *Ethnobotany & Pharmacology*, *166*(4), 444–456. https://doi.org/10.1080/23818107.2019.1624980

Park, J. U., Kang, J. H., Rahman, M. A. A., Hussain, A., Cho, J. S., & Lee, Y. I. (2019). Gastroprotective Effects of Plants Extracts on Gastric Mucosal Injury in Experimental Sprague-Dawley Rats. *BioMed research international*, *2019*, 8759708. https://doi.org/10.1155/2019/8759708

Sohail, R., Mathew, M., Patel, K. K., Reddy, S. A., Haider, Z., Naria, M., Habib, A., Abdin, Z. U., Razzaq Chaudhry, W., & Akbar, A. (2023). Effects of Non-steroidal Anti-inflammatory Drugs (NSAIDs) and Gastroprotective NSAIDs on the Gastrointestinal Tract: A Narrative Review. *Cureus*, *15*(4), e37080. https://doi.org/10.7759/cureus.37080

Takeuchi K. (2012). Pathogenesis of NSAID-induced gastric damage: importance of cyclooxygenase inhibition and gastric hypermotility. *World journal of gastroenterology*, 18(18), 2147-2160. https://doi.org/10.3748/wjg.v18.i18.2147

Tawfik, A. G., Gomez-Lumbreras, A., Del Fiol, G., Kawamoto, K., Trinkley, K. E., Reese, T., Jones, A., & Malone, D. C. (2025). Nonsteroidal anti-inflammatory drugs and risk of gastrointestinal bleeding: A systematic review and meta-analysis. *Clinical Pharmacology & Therapeutics*. Advance online publication. https://doi.org/10.1002/cpt.70054

Tulassay, Z., & Herszényi, L. (2010). Gastric mucosal defense and cytoprotection. *Best practice & research. Clinical*

gastroenterology, *24*(2), 99–108. https://doi.org/10.1016/j.bpg.2010.02.006

Uroko, R., Sangodare, R., Onyeabo, C., Agbafor, A., Uchenna, O., Nwuke, C., & Asadu, C. (2020). Investigation of antioxidant composition and antioxidative activities of ethanol extract of Alstonia boonei. *Nigerian Journal of Pharmaceutical Research*, 16(1), 71-80. https://doi.org/10.4314/njpr.v16i1.8

Wallace J. L. (2013). Mechanisms, prevention and clinical implications of nonsteroidal anti-inflammatory drug-enteropathy. *World journal of gastroenterology*, *19*(12), 1861-1876. https://doi.org/10.3748/wjg.v19.i12.1861

Wallace, J. L. (2012). NSAID gastropathy and enteropathy: Distinct pathogenesis likely necessitates distinct prevention strategies. *British Journal of Pharmacology*, *165*(1), 67–74. https://doi.org/10.1111/j.1476-5381.2011.01509.x

Zhou, J., Li, N., Li, X., Ye, J., Wang, M., & Sun, G. (2025). Review on recent advancements in understanding acetylsalicylic acid-induced gastrointestinal injury: Mechanisms, medication, and dosage refinement. *Naunyn-Schmiedeberg's Archives of Pharmacology*, *398*(11), 3297–3320. https://doi.org/10.1007/s00210-024-03521-w

Table 1: Body Weight and Organ Weights After Treatment with Aspirin and *A. Boonei*

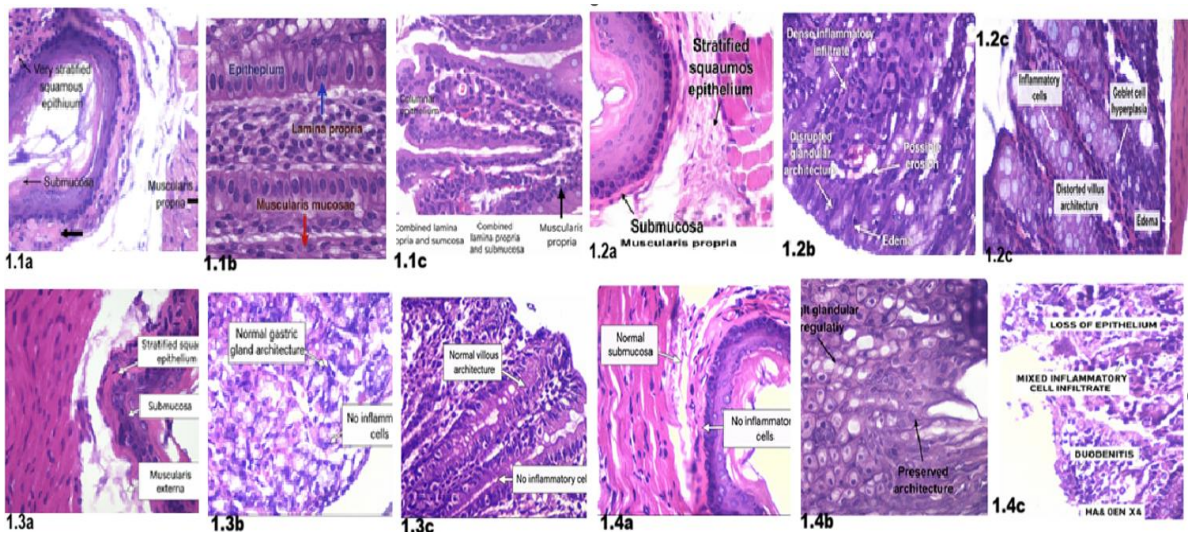
Group	Treatment	Initial Body Weight (g)	Final Body Weight (g)	Oesophagus Weight (g)	Stomach Weight (g)	Duodenum Weight (g)
I	Control	101.67 ± 1.20^{a}	126.00 ± 0.58^{ab}	0.25 ± 0.02^{a}	0.80 ± 0.05^{a}	0.45 ± 0.03^{a}
II	Aspirin 10 mg/kg	154.67 ± 18.28^{b}	146.67 ± 14.68^{bc}	0.30 ± 0.03^{b}	1.05 ± 0.06^{c}	0.60 ± 0.04^{c}
III	*A. boonei* 1000 mg/kg	137.33 ± 12.44^{bc}	154.00 ± 4.93^{c}	0.26 ± 0.02^{ab}	0.82 ± 0.04^{a}	0.48 ± 0.03^{ab}
IV	Aspirin + *A. boonei* 1000 mg/kg	119.33 ± 5.78^{ac}	126.33 ± 5.70^{ab}	0.27 ± 0.02^{ab}	0.88 ± 0.05^{ab}	0.50 ± 0.03^{b}
V	Aspirin + *A. boonei* 1500 mg/kg	135.00 ± 8.00^{bc}	144.00 ± 8.08^{bc}	0.28 ± 0.02^{ab}	0.85 ± 0.04^{ab}	0.49 ± 0.03^{b}
VI	Aspirin + *A. boonei* 2000 mg/kg	106.33 ± 4.41^{ac}	114.33 ± 5.67^{a}	0.29 ± 0.03^{b}	0.90 ± 0.05^{bc}	0.52 ± 0.04^{bc}

Values are mean ± SD (n = 5). Superscripts represent significant differences at $p < 0.05$

Table 2: Effect of *A. Boonei* on Gross Gastric Lesions and Oxidative Stress Markers in Aspirin-Induced Gastroenteropathy

Group	Treatment	Gastric Lesion Index (0–10)	Gastric MDA (nmol/mg protein)	Gastric GSH (µmol/g tissue)	Duodenal MDA (nmol/mg protein)	Duodenal GSH (µmol/g tissue)
I	Control	0.3 ± 0.5^{a}	1.50 ± 0.20^{a}	8.20 ± 0.60^{a}	1.30 ± 0.15^{a}	7.80 ± 0.55^{a}
II	Aspirin 10 mg/kg	7.8 ± 1.0^{c}	4.20 ± 0.35^{c}	3.10 ± 0.40^{c}	3.80 ± 0.30^{c}	3.40 ± 0.45^{c}
III	*A. boonei* 1000 mg/kg	0.5 ± 0.6^{a}	1.60 ± 0.25^{ab}	8.00 ± 0.50^{a}	1.40 ± 0.20^{ab}	7.60 ± 0.50^{a}
IV	Aspirin + *A. boonei* 1000 mg/kg	2.5 ± 0.8^{b}	2.60 ± 0.30^{b}	6.70 ± 0.45^{b}	2.30 ± 0.25^{b}	6.10 ± 0.40^{b}
V	Aspirin + *A. boonei* 1500 mg/kg	1.8 ± 0.6^{b}	2.20 ± 0.28^{b}	7.20 ± 0.55^{ab}	2.00 ± 0.22^{b}	6.80 ± 0.50^{ab}
VI	Aspirin + *A. boonei* 2000 mg/kg	3.0 ± 0.9^{b}	2.90 ± 0.32^{b}	6.20 ± 0.50^{b}	2.50 ± 0.27^{b}	6.00 ± 0.45^{b}

Values are mean ± SD (n = 5). Different superscripts (^{a}, ^{b}, ^{c}) indicate significant differences at $p < 0.05$



Group I - Control (Untreated)
Plates 1.1a-c
Histological sections of the esophagus, stomach, and duodenum from control rats demonstrate completely normal architecture.

i. The esophagus shows an intact stratified squamous epithelium, normal submucosa, and well-organized muscularis externa, with no inflammation or epithelial disruption.
ii. The stomach displays a well-preserved gastric mucosa, consisting of normal columnar epithelial lining, intact lamina propria, and orderly gastric glands without erosion or inflammatory infiltrates.
iii. The duodenum shows slender, uniformly contoured villi, intact epithelial lining, a clear lamina propria, and a well-defined muscularis propria, with no distortion or inflammatory cell accumulation. These features collectively confirm normal baseline histology for all tissues examined.

Group II - Aspirin Only (10 mg/kg)
Plates 1.2a–c: Aspirin administration induces notable pathological alterations, particularly in the stomach and duodenum.

i. The esophagus retains an intact epithelial lining with preserved mucosal layers and no significant erosion, indicating relative resistance to aspirin injury.
ii. The stomach shows marked gastritis, characterized by dense inflammatory infiltrates (neutrophils and lymphocytes), distortion of glandular architecture, stromal edema, and focal early mucosal erosion, hallmarks of aspirin-induced gastric injury.
iii. The duodenum demonstrates pronounced duodenitis, with marked inflammatory infiltrates in the lamina propria, goblet cell hyperplasia, villous distortion, and stromal edema. Overall, aspirin at this dose causes substantial gastrointestinal mucosal damage, most severe in the stomach and duodenum.

Group III - *A. boonei* Extract Only (1000 mg/kg)
Plates 1.3a-c: Rats treated solely with *A. boonei* extract show normal histology across all tissues.

i. The esophagus exhibits intact epithelium and normal submucosal and muscular layers.
ii. The stomach maintains normal gastric architecture, with well-aligned glands and absence of inflammation or epithelial degeneration.
iii. The duodenum shows fully preserved villi and no structural or inflammatory abnormalities. These findings confirm that *A. boonei* at 1000 mg/kg is non-toxic and does not alter normal histoarchitecture.

Group IV - Aspirin + *A. boonei* (1000 mg/kg)
Plates 1.4a-c
Co-administration of aspirin and 1000 mg/kg *A. boonei* demonstrates partial protection.

i. The esophagus shows normal mucosal architecture with no inflammatory changes, indicating effective esophageal protection at this dose.
ii. The stomach exhibits generally preserved mucosal structure with minor deviations such as slight glandular irregularity and moderate epithelial vacuolation, reflecting incomplete but noticeable mitigation of aspirin-induced injury.
iii. The duodenum, however, still shows mild to moderate inflammatory expansion of the lamina propria, near loss of epithelial lining in some areas, and villous distortion, changes progressing toward erosive duodenitis, indicating insufficient protection at this dose. Protection is therefore organ-dependent and incomplete.

Group V - Aspirin + *A. boonei* (1500 mg/kg)
Plates 1.5a–c: Increasing the dose of *A. boonei* to 1500 mg/kg results in improved mucosal protection.

i. The esophagus displays intact epithelium, normal mucosal and muscular layers, and absence of inflammatory infiltrates, comparable to the control group.
ii. The stomach shows largely preserved glandular pattern, with mild epithelial vacuolation and slight irregularity but no ulceration or significant inflammation, suggesting stronger attenuation of aspirin injury.
iii. The duodenum shows preserved villous architecture with intact epithelial lining and normal lamina propria, along with only mild villous distortion, indicating substantial reduction of aspirin-induced changes. At this dose, *A. boonei* provides marked gastrointestinal protection.

Group VI - Aspirin + *A. boonei* (2000 mg/kg)
Plates 1.6a-c: At the highest dose, *A. boonei* demonstrates near-complete protective effects.

i. The esophagus appears entirely normal, with intact stratified squamous epithelium and preserved mucosal architecture, showing no evidence of aspirin-related injury.
ii. The stomach shows preserved glandular organization, mild–moderate lamina propria inflammatory infiltrates, and cytoplasmic vacuolation, but no ulceration, necrosis, or collapse of architecture, indicating substantial protection with only mild residual gastritis.
iii. The duodenum demonstrates preserved villous structure, intact mucosa, mild lamina propria inflammation, and no crypt destruction or ulceration, showing significant mucosal stabilization at this dose. These findings indicate that *A. boonei* at 2000 mg/kg provides the highest degree of protection, with only minimal residual changes.

Overall, Aspirin alone causes significant mucosal injury, especially in the stomach and duodenum.
A. boonei alone is safe and preserves normal histology.
Co-treatment shows a dose-dependent protective effect, with:

i. 1000 mg/kg → partial protection
ii. 1500 mg/kg → moderate to strong protection
iii. 2000 mg/kg → near-complete protection