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Gastroprotective and Anti-*Helicobacter pylori* Efficacy of a Polyherbal Formulation of *Musa paradisiaca*, *Curcuma longa*, *Brassica oleracea*, and *Zingiber officinale* in Wistar Rats

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ABSTRACT

Unripe plantain (*Musa paradisiaca*), turmeric (*Curcuma longa*), cabbage (*Brassica oleracea*), and ginger (*Zingiber officinale*) are widely used in West African traditional medicine for gastrointestinal ailments, but their combined efficacy against *Helicobacter pylori* and gastric ulcers has not been systematically evaluated. The major aim of this research is to evaluate the *in vivo* gastroprotective and anti-*H. pylori* efficacy of hydroethanolic extracts of these four plants, individually and in combination, using Wistar rat models. Acute toxicity was assessed using Lorke's method (up to 5000 mg/kg). Anti-*H. pylori* efficacy was evaluated in an infection model (seven groups, n=3) with oral treatment for 7 days, measuring gastric bacterial load (log₁₀ CFU) on Days 1, 3, 5, and 7. Gastroprotective activity was assessed in indomethacin-induced ulcer models (prophylactic and curative), with ulcer index, percentage inhibition, and gastric secretory parameters (total acidity, free acidity, pepsin activity) determined. Histopathological analysis of gastric tissues was performed. All extracts were safe up to 5000 mg/kg with no mortality. The combined formulation (U.P+T+C+G) achieved complete *H. pylori* clearance (0.000 log₁₀ CFU) by Day 7, with the fastest reduction (3.380 by Day 3). Ginger and unripe plantain also achieved complete clearance by Day 7. Cabbage showed

incomplete clearance (2.204 log₁₀ CFU at Day 7). In the prophylactic ulcer test, the combined extract achieved the highest inhibition (91.38%), surpassing cimetidine (86.21%). In the curative test, unripe plantain (94.51%) and cabbage (94.59%) showed efficacy comparable to cimetidine (94.61%), while the combination achieved 94.33% with the lowest ulcer index (0.32 ± 0.11). Histopathology revealed near complete mucosal restoration in combined-extract-treated groups. The polyherbal formulation demonstrated significant gastroprotective and anti-*H. pylori* efficacy, with synergistic interactions enhancing both mucosal healing and bacterial clearance. These findings support the traditional use of these plants and warrant further clinical evaluation.

Keywords: *Helicobacter pylori*, gastric ulcer, polyherbal formulation, gastroprotection

1. INTRODUCTION

Helicobacter pylori infection affects approximately 50% of the global population and is the primary cause of chronic gastritis, peptic ulcer disease, and gastric cancer (Hooi *et al.*, 2017; Rawla & Barsouk, 2019). Indomethacin and other non-steroidal anti-inflammatory drugs (NSAIDs) are also major causes of gastric ulceration, primarily through inhibition of prostaglandin synthesis, increased oxidative stress, and impaired mucosal defense (Suleyman *et al.*, 2010; Wallace *et al.*, 2000). The intersection of *H. pylori* infection and NSAID use creates a compounded risk for severe gastrointestinal pathology.

Current management relies on proton pump inhibitors, H₂-receptor antagonists, and antibiotics. However, antibiotic resistance, adverse effects, and recurrence rates necessitate alternative or adjunctive therapies (Thung *et al.*, 2016; Zhou *et al.*, 2023). Plant-based medicines offer promising alternatives due to their multi-target mechanisms, safety, and cultural acceptability.

Unripe plantain (*Musa paradisiaca*) is rich in resistant starch, dietary fiber, tannins, and saponins, with documented anti-ulcerogenic properties (Olorunfemi *et al.*, 2011; Oboh *et al.*, 2014). Turmeric (*Curcuma longa*) contains curcumin, a polyphenol with anti-inflammatory, antioxidant, and anti-*H. pylori* activities (De *et al.*, 2019; Hewlings & Kalman, 2017). Cabbage (*Brassica oleracea*) contains glutamine, S-methylmethionine (vitamin U), and glucosinolate-derived isothiocyanates that promote mucosal healing and inhibit *H. pylori* (Luthra *et al.*, 2015; Fahey *et al.*, 2002). Ginger (*Zingiber officinale*) contains gingerols and shogaols with gastroprotective and antimicrobial effects (Mahady *et al.*, 2003; Ghasemzadeh *et al.*, 2016).

Despite their individual efficacy, the combined therapeutic potential of these four plants against *H. pylori* infection and gastric ulcers has not been systematically investigated *in vivo*. This study aimed to evaluate the acute toxicity, anti-*H. pylori* efficacy, and gastroprotective activity of hydroethanolic extracts of these plants, individually and in combination, using Wistar rat models.

2. MATERIALS AND METHODS

2.1 Plant Collection and Extraction

Unripe fruits of *Musa paradisiaca*, fresh rhizomes of *Zingiber officinale* and *Curcuma longa*, and fresh cabbage (*Brassica oleracea*) were purchased from Eke Awka Market, Anambra State, Nigeria. Authentication was performed by Dr. C. F. Iloka, Department of Botany, Nnamdi Azikiwe University, Awka, with herbarium numbers: *Musa paradisiaca* (NAUTH-07), *Curcuma longa* (NAUTH-021), *Zingiber officinale* (NAUTH-026), and *Brassica oleracea* (NAUTH-034).

Plant materials were washed, sliced, air-dried at ambient temperature for 7 days, and ground to coarse powder. Hydroethanolic extraction (70% ethanol) was performed by soaking 300 g of unripe plantain powder, 200 g each of turmeric, ginger, and cabbage powders in 1000 mL of solvent for 72 h. Extracts were filtered, concentrated using a rotary evaporator at 50°C, and stored at 4°C until use (Oboh *et al.*, 2024).

2.2 Animals

Adult Wistar rats (200–250 g) were obtained from the animal house of the Department of Zoology, Nnamdi Azikiwe University, Awka, Nigeria. Animals were housed under standard conditions with free access to food and water. Ethical approval was obtained from the Animal Ethics Committee of Chukwuemeka Odumegwu Ojukwu University, and animals were handled according to established guidelines (Ogbuagu *et al.*, 2024).

2.3 Acute Toxicity Test

Lorke's method (1983) was used with modifications. In Stage 1, 15 rats were divided into three groups (n=5) receiving 10, 100, and 1000 mg/kg of each extract orally. In Stage 2, 5 rats received 1500, 2500, 3500, and 5000 mg/kg (one per dose). Animals were observed for 24 h for mortality and signs of toxicity. This was performed for each extract and the combined formulation.

2.4 *H. pylori* Infection Model

Twenty-one adult Wistar rats were divided into seven groups (n=3). Animals were fasted for 24 h before inoculation. Groups were inoculated with *H. pylori* 35BH (10⁷ CFU/mL) in phosphate-buffered saline twice over 3 days. Two weeks post-inoculation, groups received oral treatments daily for 7 days:

- Group 1: Distilled water (negative control)
- Group 2: Indomethacin (100 mg/kg, positive control)
- Group 3: Unripe plantain extract (100 mg/kg)
- Group 4: Turmeric extract (100 mg/kg)
- Group 5: Cabbage extract (100 mg/kg)
- Group 6: Ginger extract (100 mg/kg)

- Group 7: Combined extract (25 mg/kg each)

Gastric tissues were harvested on Days 1, 3, 5, and 7 post-treatment for quantification of *H. pylori* colonization ($\log_{10}$ CFU) and histology.

2.5 Indomethacin-Induced Ulcer Models

Prophylactic Model: Twenty-one rats were divided into seven groups (n=3). Groups received treatments as above (with cimetidine 100 mg/kg as positive control) 1 h before ulcer induction with indomethacin (30 mg/kg orally). Animals were sacrificed 8 h post-induction, and ulcer index was determined.

Curative Model: Forty-two rats were divided into seven groups (n=6). Ulcers were induced with indomethacin (30 mg/kg). Eight hours post-induction, two animals per group were sacrificed for baseline ulcer quantification. Remaining animals received treatments as above for 3 days, then two more per group were sacrificed. The remaining animals continued treatment for another 3 days before final ulcer index determination.

2.6 Quantification of Ulceration

Ulcer index was determined as described by Ogbuagu *et al.* (2024). Stomachs were extracted, cleaned, pinned on corkboards, and examined under a microscope with a square-grid eyepiece. Ulcers were scored on a 0–4 scale based on severity. Ulcer index (U.I.) was calculated as:

$$\text{U.I.} = (\text{Ulcerated area} / \text{Total stomach area}) \times 100$$

$$\text{Percentage ulcer inhibition} = [(\text{U.I. control} - \text{U.I. test}) / \text{U.I. control}] \times 100$$

2.7 Gastric Secretory Parameters

Total acidity, free acidity, and pepsin activity were determined in gastric contents as described by Reddy *et al.* (2018). Acidity was expressed in mEq/L, and pepsin activity was determined spectrophotometrically at 610 nm.

2.8 Histopathology

Stomach tissues were fixed in 10% formal saline, dehydrated through graded ethanol, cleared in xylene, embedded in paraffin, sectioned (3–6 μm), and stained with hematoxylin and eosin. Sections were examined under a light microscope (Nikon Eclipse TS100, Japan) with digital camera.

2.9 Statistical Analysis

Results were expressed as mean $\pm$ SEM. Differences between groups were analyzed by one-way ANOVA. $p < 0.05$ was considered significant.

3. RESULTS

3.1 Acute Toxicity

No mortality or signs of toxicity were observed at any dose (up to 5000 mg/kg) for any extract or the combination (Table 1). This indicates a high margin of safety, with LD₅₀ > 5000 mg/kg.

Table 1: Acute Toxicity Evaluation of Botanical Extracts and Their Combination in Experimental Animals

Plant Extract / Treatment	Dose Range (mg/kg Body Weight)	Mortality (Dead / Tested)	Survival Rate (Survivors / Tested)
Unripe Plantain (<i>Musa paradisiaca</i>)	10 – 5000	0/15	15/15
Turmeric (<i>Curcuma longa</i>)	10 – 5000	0/15	15/15
Cabbage (<i>Brassica oleracea</i>)	10 – 5000	0/15	15/15
Ginger (<i>Zingiber officinale</i>)	10 – 5000	0/15	15/15
Synergistic Combination	10 – 5000	0/15	15/15

3.2 Anti-*H. pylori* Efficacy in Vivo

The combined formulation achieved complete bacterial clearance (0.000 log₁₀ CFU) by Day 7, with the most rapid reduction (3.380 by Day 3). Ginger and unripe plantain also achieved complete clearance by Day 7. Turmeric achieved complete clearance by Day 7 but with slower kinetics. Cabbage showed incomplete clearance (2.204 log₁₀ CFU at Day 7) (Table 2).

Table 2: Evaluation of Bacterial Load or Kinetic Reduction Across Treatment Days

Treatment	Day 1	Day 3	Day 5	Day 7
Unripe Plantain	7.477	5.380	2.114	0.000

Ginger	7.556	4.415	2.322	0.000
Turmeric	7.505	5.255	3.204	0.000
Cabbage	7.531	5.447	4.114	2.204
Combination	7.556	3.380	2.079	0.000

3.3 Prophylactic Anti-Ulcer Activity

The combined extract achieved the highest ulcer inhibition (91.38%), surpassing Cimetidine (86.21%). Ginger showed the lowest ulcer index (0.18 ± 0.4) with 81.34% inhibition. Unripe plantain and cabbage showed 88.32% and 79.32% inhibition, respectively. Turmeric showed the least inhibition (63.21%) (Table 3).

Table 3: Prophylactic Anti-Ulcer Effects of Botanical Extracts and Reference Drug

Group	Agent	Ulcer Incidence (%)	Ulcer Index	Inhibition (%)
1	Distilled water	100.00	29.00 ± 1.10	0.00
2	Cimetidine (100 mg/kg)	33.33	0.45 ± 0.41	86.21
3	Unripe Plantain	66.67	0.25 ± 0.05	88.32
4	Turmeric	66.67	0.31 ± 0.01	63.21
5	Cabbage	66.67	0.25 ± 0.05	79.32
6	Ginger	66.67	0.18 ± 0.40	81.34
7	Combination	66.67	0.31 ± 0.02	91.38

3.4 Curative Anti-Ulcer Activity

In the curative model, unripe plantain (94.51%), cabbage (94.59%), and the combination (94.33%) showed efficacy comparable to Cimetidine (94.61%). The combination had the

lowest ulcer index (0.32 ± 0.11). Turmeric showed moderate efficacy (88.96%), while ginger showed 90.31% (Table 4).

Table 4: Curative Anti-Ulcer Effects, Gastric Acidity, and Pepsin Activity of Botanical Extracts and Controls

Treatment	Ulcer Index	% Curative	Total Acidity (mEq/L / 100g)	Free Acidity (mEq/L / 100g)	Pepsin Activity ($\mu\text{mol/min/mL}$)
Normal Control	0.00	0.00	30.25 ± 5.26	10.50 ± 1.00	27.67 ± 1.87
Negative Control	6.42 ± 0.19	0.08 ± 2.99	108.00 ± 9.35	51.28 ± 2.87	49.23 ± 1.86
Positive Control	0.35 ± 0.10	94.61 ± 1.67	32.25 ± 4.03	11.75 ± 2.22	29.40 ± 1.36
Unripe Plantain	0.36 ± 0.10	94.51 ± 1.48	25.75 ± 6.34	17.00 ± 2.83	35.35 ± 2.23
Turmeric	0.71 ± 0.10	88.96 ± 1.64	45.75 ± 11.47	25.00 ± 1.63	36.86 ± 4.73
Cabbage	0.35 ± 0.15	94.59 ± 2.36	39.75 ± 5.56	13.50 ± 1.29	30.50 ± 0.75
Ginger	0.62 ± 0.15	90.31 ± 2.36	30.75 ± 6.13	14.00 ± 1.83	32.70 ± 3.17
Combination	0.32 ± 0.11	94.33 ± 0.21	28.33 ± 0.21	16.02 ± 1.26	29.42 ± 0.21

3.5 Histopathological Findings

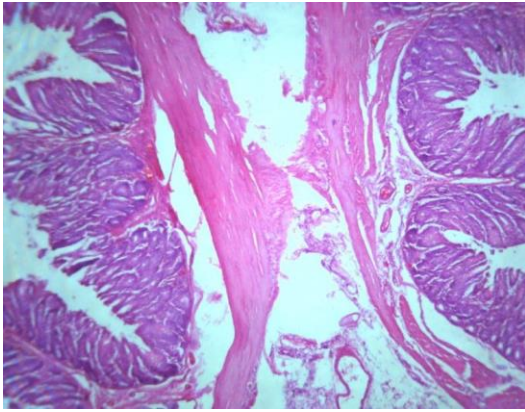


Plate 1 (Normal Control): Normal cytoarchitecture with intact epithelium, organized glands, and no inflammation.

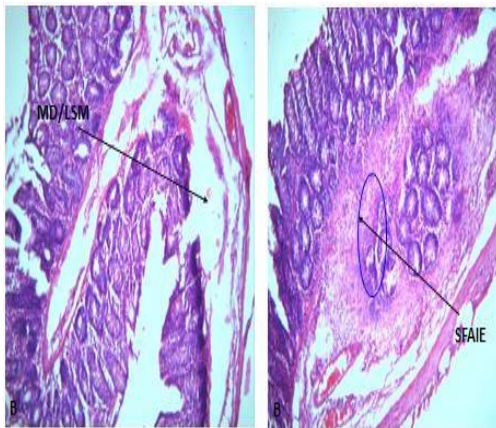


Plate 2 (Indomethacin Control): Severe focal inflammatory exudates, moderate dilation and loss within submucosa.

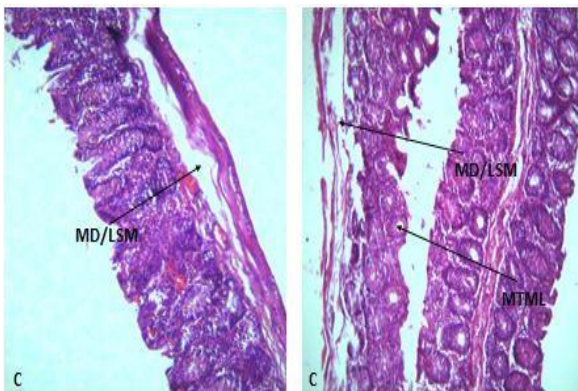


Plate 3 (Unripe Plantain): Mild healing with moderate thinning of mucosa and mild submucosal dilation.

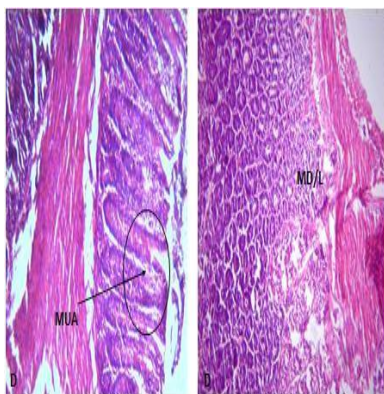


Plate 4 (Turmeric): Moderate healing with mild submucosal dilation and residual ulcerated areas.

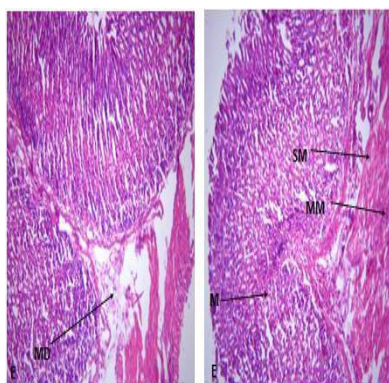


Plate 5(Combination): Near-complete mucosal restoration with normal mucosa, muscularis mucosa, and submucosa.

4. DISCUSSION

This study demonstrates that a polyherbal formulation of unripe plantain, turmeric, cabbage, and ginger extracts possesses significant gastroprotective and anti-*H. pylori* efficacy *in vivo*, with an excellent safety profile.

The acute toxicity results ($LD_{50} > 5000$ mg/kg) classify these extracts as practically non-toxic (OECD, 2001), consistent with previous reports for each plant (Ammon & Wahl, 1991; Ajayi *et al.*, 2021; Oboh *et al.*, 2014; Charron *et al.*, 2019). This supports their safe use in oral therapeutic formulations.

The anti-*H. pylori* efficacy of the combined formulation was remarkable, achieving complete bacterial clearance by Day 7 with the fastest reduction kinetics. This synergy likely arises from complementary mechanisms: gingerols and shogaols from ginger disrupt bacterial membranes and inhibit urease (Mahady *et al.*, 2003; Kim *et al.*, 2008); curcumin from turmeric inhibits NF- κ B signaling and bacterial adhesion (De *et al.*, 2009); isothiocyanates from cabbage induce oxidative stress and inhibit urease (Fahey *et al.*, 2002); and tannins and saponins from unripe plantain enhance mucosal defense and disrupt bacterial membranes (Olorunfemi *et al.*, 2011; Oboh *et al.*, 2014). This multi-target approach is a key advantage of polyherbal formulations over single agents (Wagner & Ulrich-Merzenich, 2009).

Cabbage's incomplete clearance of *H. pylori* despite its gastroprotective effects suggests that its primary role may be mucosal protection rather than direct antimicrobial eradication. This is consistent with its high glutamine and vitamin U content, which promote epithelial repair (Luthra *et al.*, 2015).

In the prophylactic ulcer model, the combined formulation achieved 91.38% inhibition, surpassing cimetidine (86.21%). This suggests that the extracts may act through mechanisms beyond acid suppression, including antioxidant defense, prostaglandin synthesis, and mucosal regeneration. The high efficacy of ginger (81.34%) and unripe plantain (88.32%) as monotherapies is consistent with their documented gastroprotective properties (Hasan *et al.*, 2017; Olorunfemi & Emikpe, 2014).

The curative model confirmed these findings, with unripe plantain, cabbage, and the combination showing efficacy comparable to cimetidine. The significant reductions in total acidity, free acidity, and pepsin activity in treated groups indicate that the extracts modulate gastric secretion, a key factor in ulcer healing. The combination's ability to normalize these parameters to levels comparable to normal control suggests a comprehensive gastroprotective effect.

Histopathological analysis provided tissue-level evidence of healing. The progression from severe inflammation and submucosal loss in indomethacin controls to near-complete mucosal restoration in the combination group mirrors the biochemical and microbiological findings. The synergistic effect is likely due to the combination of anti-inflammatory (curcumin, gingerols), antioxidant (flavonoids, phenolics), and mucosal protective (glutamine, mucilage, saponins) compounds (Toma *et al.*, 2018; Mahmood *et al.*, 2021).

5. CONCLUSION

The polyherbal formulation of *Musa paradisiaca*, *Curcuma longa*, *Brassica oleracea*, and *Zingiber officinale* demonstrated significant gastroprotective and anti-*H. pylori* efficacy in Wistar rats, with synergistic interactions enhancing both bacterial clearance and mucosal healing. The formulation was safe up to 5000 mg/kg and showed efficacy comparable to or exceeding cimetidine in ulcer models. These findings provide a strong preclinical rationale for developing this formulation as a phytotherapeutic intervention for *H. pylori* infection and gastric ulcers. Further studies should focus on clinical trials, formulation development, and mechanistic studies to fully realize its therapeutic potential.

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