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Assessment of Anti-inflammatory and Cyto-protective Action of Jatropha Tanjorensis and Biomarkers on Indomethacin Induced Ulcer in Adult Female Mice

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ABSTRACT

Gastric ulcers are a growing global health burden, particularly in Nigeria. Jatropha tanjorensis, used traditionally in African medicine, has reported anti-inflammatory and antioxidant properties. This study evaluated the anti-inflammatory and cytoprotective effects of Jatropha tanjorensis aqueous leaf extract on indomethacin-induced gastric ulcers in adult female mice. Twenty-five mice were randomly assigned into five groups (n=5): control (distilled water), indomethacin-only (20 mg/kg), low-dose extract (200 mg/kg + 10 mg/kg indomethacin), high-dose extract (400 mg/kg + 20 mg/kg indomethacin), and omeprazole (20 mg/kg + 20 mg/kg indomethacin). Treatments were administered orally for 7 days. Biochemical markers and histopathology were assessed. Interleukin-1β levels were significantly reduced in both extract-treated groups (25.20 ± 1.27 and 26.10 ± 1.41 pg/mL) compared to control (31.60 ± 1.98 pg/mL), indicating anti-inflammatory activity. Malondialdehyde levels showed no significant changes across groups. Superoxide dismutase (SOD) activity was significantly decreased in the indomethacin-only group (13.68 ± 2.14 U/mg protein) compared to control (28.68 ± 3.62 U/mg protein), while extract treatment restored SOD activity (25.65 ± 2.05 and 18.22 ± 0.01 U/mg protein at low and high doses, respectively), demonstrating dose-dependent antioxidant effects. Histopathological examination revealed reduced ulceration and inflammatory infiltration in extract-treated groups compared to indomethacin-only group. The aqueous extract of Jatropha tanjorensis demonstrated significant anti-ulcerogenic and antioxidant properties, suggesting its potential as a therapeutic agent for managing NSAID-induced gastric ulcers.

Keywords: Antioxidant, Cyto-protective, Gastric ulcer, Indomethacin, Jatropha tanjorensis; NSAID-induced ulcer, Omeprazole.

INTRODUCTION

Gastric ulcer disease remains a significant global health challenge, with an alarming increase in its prevalence, particularly in developing countries.[1] These ulcers, often induced by factors such as nonsteroidal anti-inflammatory drugs (NSAIDs), are a major cause of morbidity, affecting millions of people worldwide.[2]

The rising burden of gastric ulcers has sparked increasing interest in identifying effective therapeutic agents, especially those with fewer side effects than conventional treatments.[2] While proton pump inhibitors (PPIs) and histamine (H_2) receptor antagonists are

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commonly used, their long-term effectiveness in preventing NSAID-induced ulcers remains limited, and prolonged use can result in adverse effects, such as gastrointestinal infections and nutrient malabsorption.[3-5] Due to these limitations, there is growing interest in the use of alternative therapies, particularly plant-based remedies, for their potential to protect the gastric mucosa while alleviating inflammation.

One such plant, *Jatropha tanjorensis*, has gained recognition in traditional African medicine for its use in treating various ailments, including ulcer diseases. It is known for its diverse pharmacological properties and has been studied for its anti-inflammatory, analgesic, and antioxidant effects, which may offer promising cytoprotective benefits.[5,6]

Botanically, *Jatropha tanjorensis* belongs to the Plantae kingdom and the Tracheophyta phylum, with a classification within the Magnoliopsida class. It is part of the Malpighiales order, which includes various plants known for their antioxidant and anti-inflammatory properties.[7] *Jatropha tanjorensis* is a member of the Euphorbiaceae family and has been widely utilized in African herbal medicine, either as a standalone treatment or in combination with prescribed drugs.[1] The plant's leaves and other parts contain bioactive compounds, such as flavonoids and alkaloids, which are believed to contribute to its medicinal efficacy.[8] Common names of the plant include "Catholic vegetable," "reverend father vegetable," "blood of Jesus," "chaya leaf," "Jatropha," "miracle leaf," "tree spinach," "God's gift," and "hospital too far."

Currently, NSAID-induced ulcers are a major concern due to their ability to disrupt the gastric mucosal barrier and lead to inflammation and ulceration.[2] Traditional therapeutic strategies focus primarily on reducing gastric acid secretion, but these approaches fail to address the underlying oxidative stress and inflammation that contribute to mucosal damage.[9] There is a need for new, adjunctive therapies that not only mitigate gastric acid secretion but also enhance mucosal protection and repair. This has led to a renewed interest in natural compounds, such as *Jatropha tanjorensis*, which may offer dual benefits by acting as both an anti-inflammatory and antioxidant agent.

The objective of this study was to assess the cytoprotective and anti-inflammatory effects of *Jatropha tanjorensis* against indomethacin-induced ulcers in adult female mice. Through the investigation of its impact on biomarkers of inflammation (such as interleukin-6 and malondialdehyde) and antioxidant activity (such as superoxide dismutase levels), this research aimed to provide valuable insights into the potential of *Jatropha tanjorensis* as a therapeutic agent for managing NSAID-induced gastric ulcers. The findings could contribute to the development of safer, more effective treatments for ulcer diseases, particularly in populations with limited access to conventional medications.

MATERIALS AND METHODS

Collection of plant materials

Fresh leaves of *Jatropha tanjorensis* were collected from the natural habitat in Makurdi, Benue State, Nigeria. Sample of leaves collected were identified in the Department of Biological Sciences Faculty of Science, Rev. Fr. Moses Orshio Adasu University, Benue State and was allocated voucher number BSUM/PSB/026.

A picture of leaves of *Jatropha tanjorensis*

Extraction of plant materials.

This maceration method is a standard technique for aqueous extraction of plant materials as described by Harborne (1998) and widely employed in phytochemical studies. The leaves of *Jatropha tanjorensis* were washed, air-dried, and pulverized using a manual grinder. The powdered plant material (50 g)

was macerated in 500 mL of distilled water at room temperature for 6 hours with occasional stirring to ensure proper extraction. The mixture was then filtered through Whatman No. 1 filter paper, and the filtrate was concentrated to dryness using a water bath set at approximately 40°C to obtain the crude aqueous extract.[10]

Drugs and chemicals

Indomethacin was obtained from a registered Pharmacy with batch number A4-9417 and LD_{50} of 50 mg/kg. Omeprazole manufactured by Nemel Pharmaceuticals Limited with batch number 01C and LD_{50} of 4,000 mg/kg were procured from a registered pharmacy store.

Animal models

A total of twenty-five healthy adult mice were procured from the animal house at the College of Health Sciences, Rev. Fr. Moses Orshio Adasu University, Benue State. They were kept in animal cages and treated in accordance with the Guide for the Care and Use of Laboratory Animals by the National Research Council.[11] They were fed with standard pellet diet and water. The mice were randomly allocated into five groups (n = 5), and the *Jatropha tanjorensis* extract was administered orally for seven days, after fourteen days of acclimatization.

Experimental Design

Twenty-five (n-25) female adult mice weighing between 27-43g were randomly allocated into five (5) groups of 5 mice per group (n = 5). They were allowed 14 days to acclimatize before the commencement of

GROUPS	DOSE ADMINISTRATION	DURATION
GROUP 1	Distilled water and feed	7 Days
GROUP 2	Distilled water and feed	7 Days
	20mg/kg B.W of Indomethacin	
GROUP 3	200mg/kg B.W of *J.tanjorensis*	7 Days
	20mg/kg B.W of Indomethacin	
GROUP 4	400mg/kg B.W of *J.tanjorensis*	7 Days
	20mg/kg B.W of Indomethacin	
GROUP 5	20mg/kg B.W of Omeprazole	7 Days
	20mg/kg B.W of Indomethacin	

B.W-Body weight

At the end of the experiment, all the 25 mice were not fed for 24 hours but were still allowed water. The animals were humanely sacrificed by chloroform anesthesia and blood samples were taken via cardiac puncture using sterile needles and syringes into EDTA containing sample tubes for biochemical analysis. The organ of interest (stomach) were harvested and fixed in 10% formol saline for histological analysis and tissue processing.[12]

Histological study

The stomach tissues of the control and treated mice were fixed in Bouin's fluid for 6 hours before they were transferred into 10% formalin for histological evaluation. They were automatically processed by passing them through different grades of alcohol. The tissues were routinely processed and examined under the light microscope. Photomicrograph of the slides were then taken.

The severity of gastric mucosal injury, was assessed by a pathologist blinded to the treatment groups. The degree of gastric mucosal injury, leukocyte infiltration, and hemorrhage on a scale from 0 (normal) to 4 (severe), was assessed as previously described by Liang et al.[13]

Biochemical Assays

Assay of superoxide dismutase (SOD) activity: Superoxide dismutase activity was measured using stomach tissue homogenate, according to the method of Winterbourn (1975)[14] as modified by Rukmini *et al*. (2004).[15] The principle of the assay was based on the ability of SOD to inhibit the reduction of nitro-blue tetrazolium (NBT). The reaction mixture contained 2.7 ml of 0.067M phosphate buffer, pH 7.8, 0.05 ml of 0.12mM riboflavin, 0.1 ml of 1.5mM NBT, 0.05 ml of 0.01M methionine and 0.1 ml of enzyme samples. Uniform illumination of the tubes was ensured by placing it in an aluminum foil in a box with a 15W fluorescent lamp for 10 minutes. Control without the enzyme source was included. The absorbance was measured at 560nm. One unit of SOD was defined as the amount of enzyme required to inhibit the reduction of NBT by 50% under the specific conditions. Activity of enzyme was expressed as units /mg protein.

Estimation of Lipid Peroxidation (Malondialdehyde):

Lipid peroxidation of stomach tissue homogenate was estimated calorimetrically by thiobarbituric acid reactive substances (TBARS) method of Buege and Aust (1978).[16] A principle component of TBARS is malondialdehyde (MDA), a product of lipid peroxidation. In brief, 0.1 ml of tissue in Tris-HCl buffer, pH 7.5 was treated with 2 ml of (1:1:1 ratio) TBA-TCA-HCl reagent (thiobarbituric acid 0.37%, 0.25 N HCl and 15% TCA) and placed in water bath for 15 min, cooled. The absorbance of clear supernatant was measured against reference blank at 535 nm. Concentration was calculated using the molar absorptivity of malondialdehyde which is 1.56×10^5 M^{-1} cm^{-1} and expressed as nmol/mg protein.

Determination of the of Pro-inflammatory Cytokines (IL-6, and IL-1beta): Stomach tissues were homogenized in phosphate-buffered saline (pH 7.4) at a ratio of 1:10 (w/v) using a tissue homogenizer. The homogenates were then centrifuged at 4,000 × g for 15 minutes at 4°C to remove cellular debris. The resulting clear supernatants were collected and used for cytokine measurements. Pro-inflammatory cytokines (IL-6) and anti-inflammatory cytokines (IL-1beta) were measured using ELISA kits according to the manufacture's guidelines. The cytokines concentration was expressed in pg/ml.

Ethical Clearance

Ethical clearance was obtained from College of Health Sciences Research and Ethic Committee and was assigned number, CREC/UGP/094. The experiment was conducted in accordance with the Guide for the Care and Use of Laboratory Animals by the National Research Council.[11]

Statistical Analysis

The data was subjected to statistical analysis using SPSS version 25.0 manufactured by International Business Machine (IBM). Mean differences between groups was analyzed using one-way analysis of variance (ANOVA) and comparison between the means by Dunnett post hoc test. A p-value less than 0.05 ($p \leq 0.05$) was considered statistically significant.

RESULTS

Table 1: Body Weight Changes Across Experimental Group

GROUP (N)	INITIAL BODY WEIGHT (g)	FINAL BODY WEIGHT (g)	BODY WEIGHT DIFFERENCE (g)
GROUP 1 (Control)	33.40±3.25	31.70±2.81	-1.70±1.35
GROUP 2 (20mg/kg IDC)	34.16±3.67	32.12±2.86	-2.04±0.90
GROUP 3 (LD J.tj + 20mg/kg IDC)	31.52±5.31	30.40±4.84	-1.12±0.67
GROUP 4 (HD J.tj + 20mg/kg IDC)	34.40±4.12	32.27±4.47	-1.42±0.35
GROUP 5 (OPZ + 20mg/kg IDC)	36.02±7.19	33.62±7.35	-2.40±1.91

Values are expressed as MEAN±SD; N = 5

IDC = Indomethacin; J.tj = *Jatropha tanjorensis*; LD = Low Dose; HD = High Dose; OPZ = Omeprazole

Table 1 shows a decrease in mean body weight across groups, but it was not statistically significant.

Table 2: Distribution of Anti-inflammatory Markers: Interleukin-6 & Interleukin-1

GROUP (N)	INTERLEUKIN-6 (pg/ml)	INTERLEUKIN-1 (pg/ml)
GROUP 1 (Control)	25.60±2.12	31.60±1.98^{+}
GROUP 2 (20mg/kg IDC)	25.35±0.35	27.03±0.00
GROUP 3 (LD J.tj + 20mg/kg IDC)	23.35±2.61	25.20±1.27*
GROUP 4 (HD J.tj + 20mg/kg IDC)	27.15±0.06	26.10±1.41*
GROUP 5 (OPZ + 20mg/kg IDC)	24.80±2.12	24.59±3.51*

Values are expressed as MEAN±SD; N = 5
IDC = Indomethacin; J.tj = *Jatropha tanjorensis*; LD = Low Dose; HD = High Dose; OPZ = Omeprazole
^{a}=p < 0.05 compared to Group 1 (Control)
*=p < 0.05 compared to Group 2 (Indomethacin-only)
$^{+}$= p < 0.05 compared to Group 5 (Omeprazole and indomethacin)

Table 2 shows no significant effect on the inteleukin-6 level of mice. With respect to interleukin-1, both indomethacin and the extract of *Jatropha tanjorensis* showed a significant decreasing effect on the anti-inflammatory marker level which implies a decrease in tissue inflammation, as observed in groups 3 – 5 of this research.

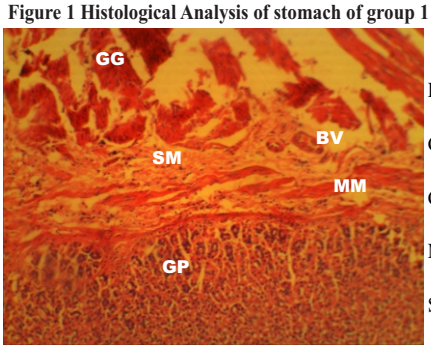
Table 3 Effects of Oxidative Stress Markers: MDA & SOD

GROUP (N)	MDA (nmol/mg pro)	SOD (U/mg pro)
GROUP 1 (Control)	0.70±0.28	28.68±3.62 ^{a}
GROUP 2 (20mg/kg IDC)	1.50±0.84	13.68±2.14*$^{+}$
GROUP 3 (LD J.tj + 20mg/kg IDC)	0.91±0.41	25.65±2.05^{a}
GROUP 4 (HD J.tj + 20mg/kg IDC)	1.05±0.21	18.22±0.01*
GROUP 5 (OPZ + 20mg/kg IDC)	0.90±0.00	22.65±4.87^{a}

Values are expressed as MEAN±SD; N = 5
IDC = Indomethacin; J.tj = *Jatropha tanjorensis*; LD = Low Dose; HD = High Dose; OPZ = Omeprazole
^{a}=p < 0.05 compared to Group 1 (Control)
*=p < 0.05 compared to Group 2 (Indomethacin-only)
$^{+}$= p < 0.05 compared to Group 5 (Omeprazole and indomethacin)

The result in Table 3 shows that the administration of indomethacin alone had a significant decreasing effect on the SOD levels of the mice which implies an increase in oxidative stress as seen in group 2 of this research, while the administration of the extract of *Jatropha tanjorensis* showed a notable protective effect against the rise in oxidative stress as observed in the notable increase in SOD levels from groups 3 – 5 of this research.

Figure 1 Histological Analysis of stomach of group 1 mice (plate 1A and IB)



BV - Blood vessels
GP - Gastric pit
GG - Gastric gland
MM - Muscularis mucosa
SM - Submucosa

Plate 1A- Stomach section of group 1 mice [stain: H&E: X400]

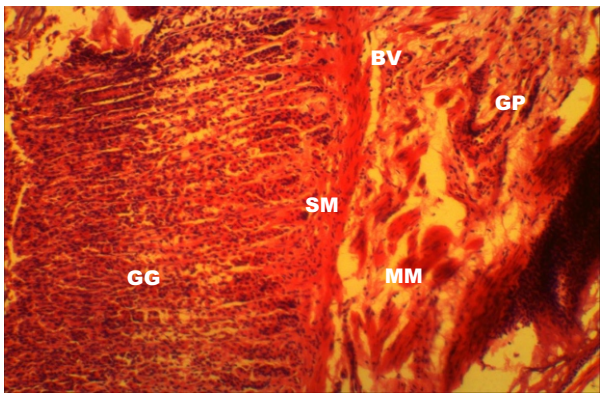
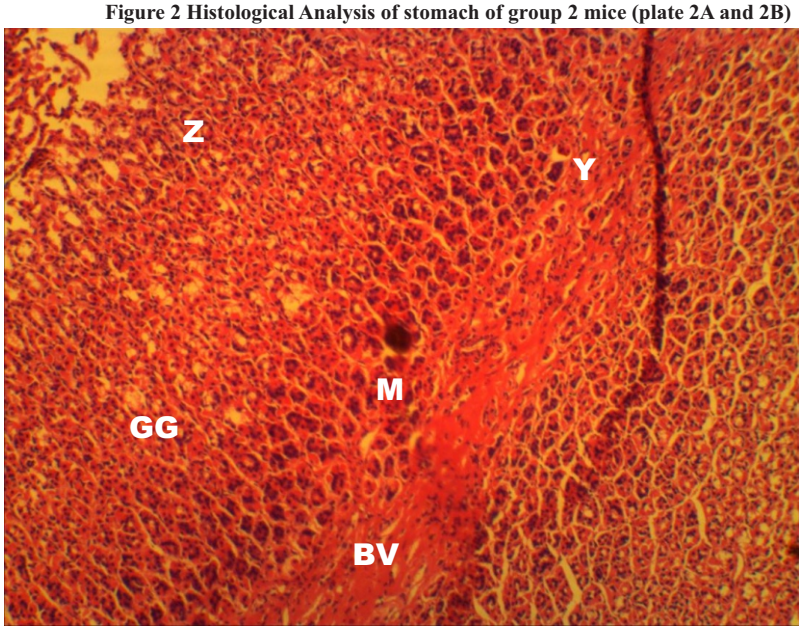


Plate 1B: Stomach section of group 1 mice [stain: H&E: X400]

Figure 1: Plate 1A and 1B show the histological section of the stomach from the control group (Group 1), stained with H&E (Hematoxylin and Eosin) at ×400 magnification. The blood vessels (BV), gastric pits (GP), gastric glands (GG), and muscularis mucosa (MM) are intact.

Figure 2 Histological Analysis of stomach of group 2 mice (plate 2A and 2B)



BV - Blood vessels
GG - Gastric gland
M - Mucosa
Y - Ulceration
Z - Inflammation

Plate 2A- Stomach section of group 2 mice [stain: H&E: X400]

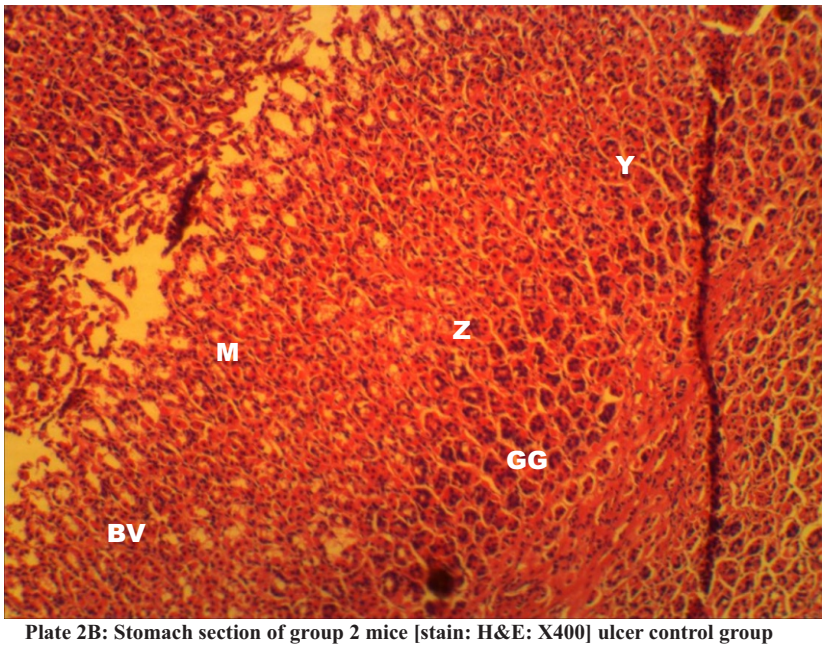
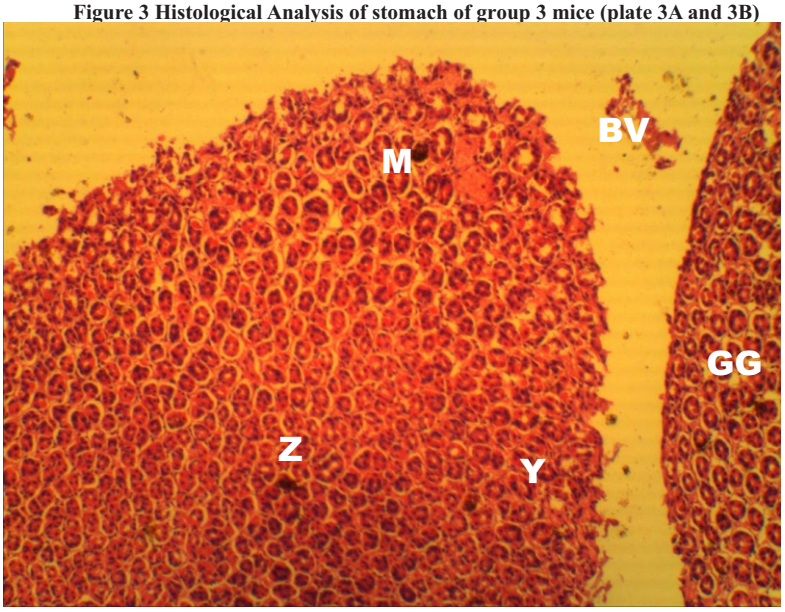


Plate 2B: Stomach section of group 2 mice [stain: H&E: X400] ulcer control group

Figure 2: Plate 2A and 2B depicts the stomach section from Group 2 (indomethacin-treated), showing noticeable ulceration (Y) and inflammation (Z) in the mucosal layer, indicative of NSAID-induced gastric damage.

Figure 3 Histological Analysis of stomach of group 3 mice (plate 3A and 3B)



BV - Blood vessels
GG - Gastric gland
M - Mucosa
Y - Ulceration
Z - Inflammation

Plate 3A- Stomach section of group 3 mice [stain: H&E: X400]

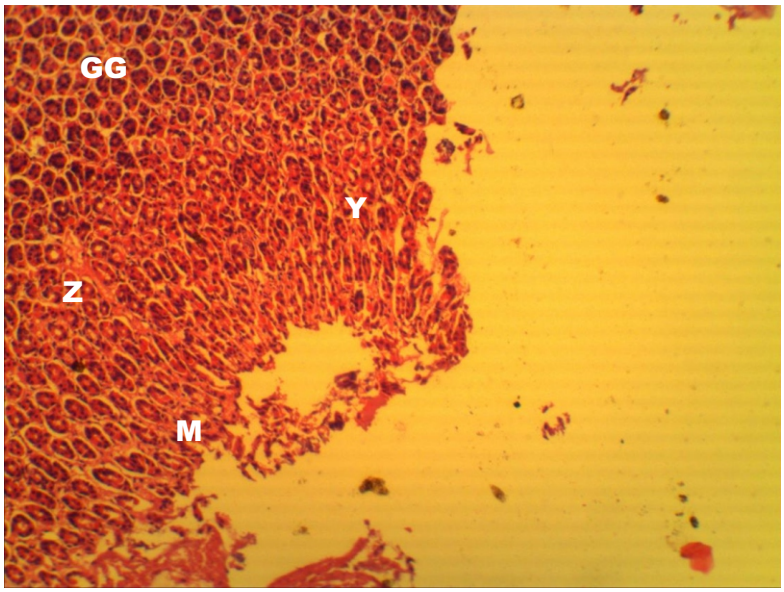
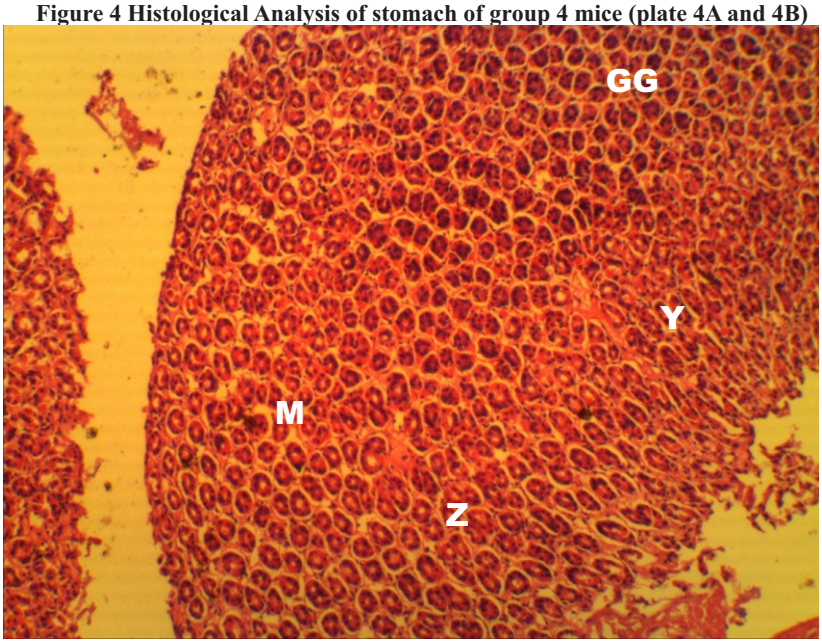


Plate 3B: Stomach section of group 3 mice [stain: H&E: X400]

Figure 3: Plate 3A and 3B presents the stomach section from Group 3 at ×400 magnification, with minimal ulceration and inflammation (Y, Z) compared to group 2

Figure 4 Histological Analysis of stomach of group 4 mice (plate 4A and 4B)



BV - Blood vessels
GG - Gastric gland
M - Mucosa
Y - Ulceration
Z - Inflammation

Plate 4 A: Stomach section of group 4 mice [stain: H&E: X400]

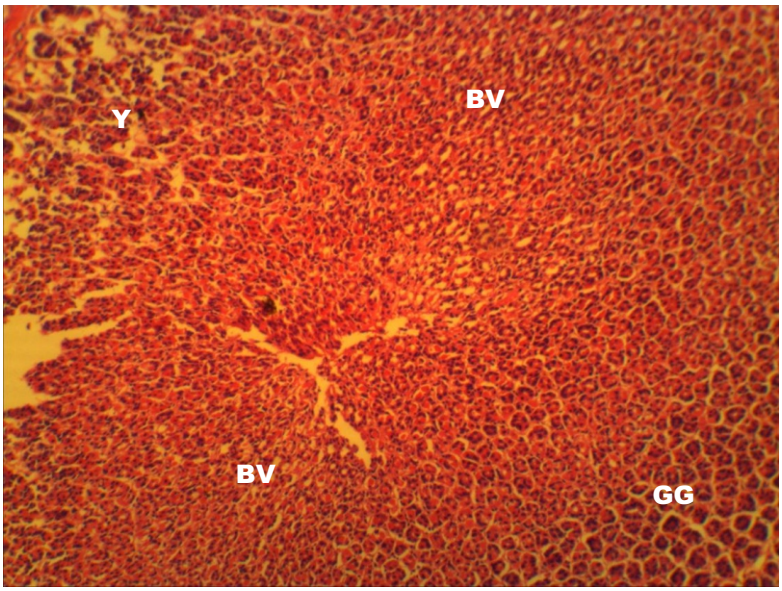
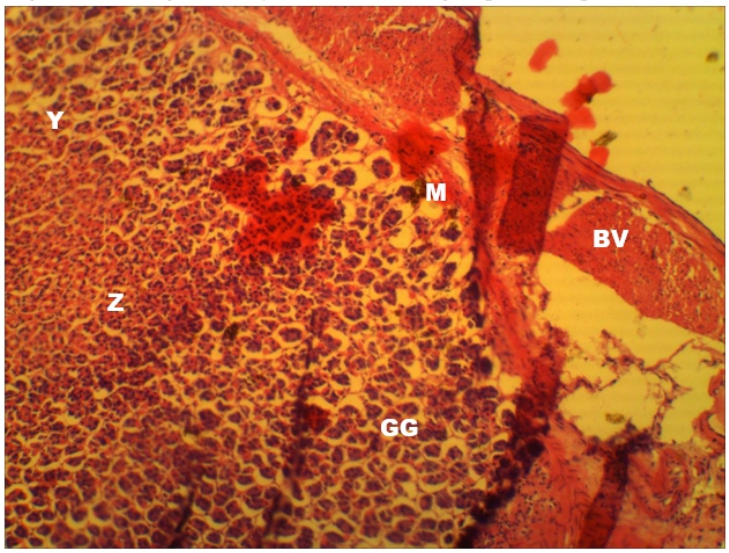


Plate 4B: Stomach section of group 4 mice [stain: H&E: X400]

Figure 4: Plate 4A and 4B shows the mucosal layer is less disrupted, with intact blood vessels (BV) and gastric glands (GG). There is less ulceration and minimal inflammatory cell infiltration.

Figure 5 Histological Analysis of stomach of group 5 mice (plate 5A and 5B)



BV - Blood vessels
GG - Gastric gland
M - Mucosa
Y - Ulceration
Z - Inflammation

Plate 5A: Stomach section of group 5 mice [stain: H&E: X400]

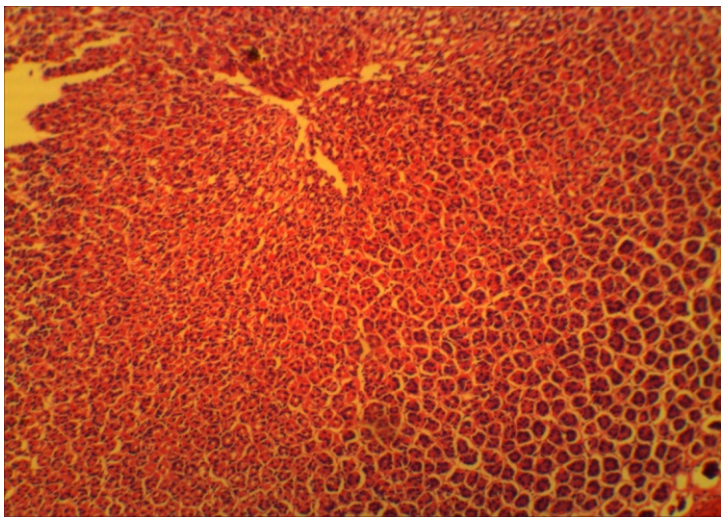


Plate 5B: Stomach section of group 5 mice [stain: H&E: X400]

Figure 5: Plate 5A shows the histological section of the stomach from Group 5, where the protective effect of omeprazole against NSAID-induced gastric injury is observed, with reduced ulceration (Y) and inflammation (Z). Plate 5B shows intact gastric glands and blood vessels.

DISCUSSION

This study aimed to assess the anti-inflammatory and cytoprotective effects of *Jatropha tanjorensis* on indomethacin-induced ulcers in mice. The results demonstrated that the plant extract exhibited significant protective effects, primarily through its anti-inflammatory and antioxidant properties. The findings of the study extend the current understanding of *Jatropha tanjorensis* in several novel ways that distinguish this work from previous investigations. To our knowledge, this is the first study to specifically evaluate the combined anti-inflammatory and cytoprotective effects of the aqueous leaf extract in an indomethacin-induced ulcer model using female mice, providing comprehensive dose-response data alongside integrated biochemical and histopathological findings. Furthermore, our study uniquely demonstrates the

differential modulation of interleukin-1β (IL-1β) versus interleukin-6 (IL-6), suggesting a cytokine-specific anti-inflammatory mechanism that has not been previously reported for this species and that contrasts with findings from studies on related *Jatropha* species.

In this study, there was no significant change in the body weight of the mice across the experimental groups. This finding aligns with previous report that the intake of *Jatropha tanjorensis* extract does not significantly affect body weight.[17] However, while previous studies focused primarily on general toxicity assessments, our study specifically controls for weight changes to confirm that the observed gastroprotective effects are independent of nutritional status. This is a methodological control not consistently applied in earlier investigations. This distinction is important because it strengthens the attribution of the therapeutic effects specifically to the plant extract rather than to secondary nutritional or metabolic changes.

A key novel finding of our study is the significant reduction in IL-1β levels by *Jatropha tanjorensis* treatment. Our data show that both low-dose (200 mg/kg) and high-dose (400 mg/kg) treatments reduced IL-1β from 31.60 ± 1.98 pg/mL to 25.20 ± 1.27 pg/mL and 26.10 ± 1.41 pg/mL, respectively. This magnitude of IL-1β reduction, approximately seventeen to twenty-one percent, is comparable to that observed with omeprazole treatment at 24.59 ± 3.51 pg/mL. IL-1β is a key pro-inflammatory cytokine involved in the inflammatory response, and its reduction suggests that the plant extract may be mitigating the inflammatory pathway activated by NSAID-induced mucosal injury. While previous study on *Jatropha* species have reported anti-inflammatory effects, most focused on generic inflammatory markers rather than specific cytokine profiles.[18] In this study, no significant change in IL-6 levels across treatment groups, suggesting that *Jatropha tanjorensis* may exert its anti-inflammatory effects through selective cytokine modulation. This insight is an important distinction from previous work on *Jatropha curcas*, which reported simultaneous reductions in both IL-6 and IL-1β.[19] The cytokine-selective activity we observed has not been previously described for *J. tanjorensis* and needs further investigation into the specific signaling pathways involved, as it may indicate a more targeted anti-inflammatory mechanism with potentially fewer off-target effects.

Regarding oxidative stress markers, our study provides novel evidence for dose-dependent but non-linear antioxidant effects of *Jatropha tanjorensis*. The administration of indomethacin alone significantly increased malondialdehyde (MDA) levels from 0.70 ± 0.28 nmol/mg protein in the control group to 1.50 ± 0.84 nmol/mg protein, consistent with the established pro-oxidant effects of NSAIDs.[20] This elevation in MDA, a marker of lipid peroxidation, indicates a rise in oxidative stress that damages cell membranes and other cellular components. However, our data demonstrate that *Jatropha tanjorensis* treatment reversed this effect, with the low dose showing superior antioxidant protection as evidenced by an MDA level of 0.91 ± 0.41 nmol/mg protein compared to 1.05 ± 0.21 nmol/mg protein for the high dose. This dose-response pattern, where the lower dose was more effective at reducing lipid peroxidation, is a particularly novel finding that contrasts with previous studies on *Jatropha* species that generally reported linear dose-dependent antioxidant effects.[6, 21] This non-linear dose-response suggests the potential for optimal therapeutic dosing and neccesitates further investigation, as it has significant implications for clinical application where identifying the most effective yet safest dose is recommended.

Furthermore, our analysis of superoxide dismutase (SOD) activity revealed that *Jatropha tanjorensis* treatment significantly supported antioxidant enzyme function. SOD is an effective antioxidant enzyme that neutralizes superoxide radicals, thereby protecting cells from oxidative damage.[9] SOD levels in the indomethacin-only group were reduced to 13.68 ± 2.14 U/mg protein compared to 28.68 ± 3.62 U/mg protein in the control group, indicating that oxidative stress was elevated in this group. Treatment with the low dose of *Jatropha tanjorensis* at 200 mg/kg restored SOD to 25.65 ± 2.05 U/mg protein, which was comparable to omeprazole treatment at 22.65 ± 4.87 U/mg protein. The high dose at 400 mg/kg also improved SOD activity to 18.22 ± 0.01 U/mg protein, though to a lesser extent than

the low dose. This finding is significant because while previous studies have established the antioxidant potential of *Jatropha* species.[5-7] our study provides quantitative dose-response data specific to the gastric ulcer model, demonstrating that the 200 mg/kg dose may be more effective than the 400 mg/kg dose in preserving endogenous antioxidant defenses. This observation represents a practical therapeutic consideration not previously addressed in the literature and suggests that higher doses do not necessarily confer greater benefit, a finding that challenges the conventional assumption of simple dose-dependent efficacy.

The histopathological examination provides visual confirmation of the biochemical findings and offers additional insights into the protective mechanisms. The stomach tissues from the indomethacin-treated group revealed significant damage characterized by epithelial disruption, depletion of the mucus layer, and infiltration of inflammatory cells, which are hallmarks of NSAID-induced gastric ulcers and are consistent with previous studies that have demonstrated indomethacin's capacity to induce severe gastric damage.[22] In contrast, the groups treated with *Jatropha tanjorensis* extract exhibited significantly fewer haemorrhagic lesions and less gastric mucosal damage, suggesting that the plant extract has protective effects against NSAID-induced ulcers. While previous study has documented the gastroprotective effects of *Jatropha* species, [18] our study uniquely demonstrates graded mucosal protection with both low and high doses. The low-dose treatment resulted in minimal ulceration with some inflammatory cell infiltration, while the high-dose treatment showed less disrupted mucosal layers with intact blood vessels and gastric glands. This histological correlation strengthens the evidence for dose-dependent mucosal protection and provides a visual benchmark for future comparative studies.

Unlike previous studies that used ethanol- or stress-induced ulcer models, we employed the NSAID-induced model, which more closely mimics the clinical scenario of NSAID-associated gastric injury and is directly relevant to clinical practice where many patients experience gastrointestinal complications from chronic NSAID use. This study provides dose-response data for *Jatropha tanjorensis* in a gastric ulcer model, revealing a non-linear relationship between dose and therapeutic effect. This is a finding with significant clinical implications for optimal dosing. The demonstration of IL-1β-specific reduction without concurrent IL-6 modulation suggests a novel mechanism of action not previously described for this species, potentially involving selective inhibition of specific inflammatory pathways rather than broad immunosuppression. This study combines quantitative biochemical markers with detailed histopathological analysis, providing an evaluation that links pathological changes with tissue-level protection. Additionally, most previous studies utilized male animal models or did not specify sex,[22] whereas our use of female mice is particularly relevant given the higher prevalence of NSAID-induced ulcers in women and the potential sex-specific responses to phytotherapy. Recent evidence demonstrates that male and female mice respond distinctly to indomethacin-induced damage, with sex-specific inflammatory responses observed in gastrointestinal and other tissues.[23,24] These findings make our results more directly applicable to the population most affected by this condition.

It is important to note that the absence of prominent angiogenic features in the gastric tissue sections is likely attributable to the acute nature of the experimental model. Given that the animals were sacrificed after only 7 days of treatment, the histological assessment primarily captured the acute inflammatory and protective phases of the ulcer. As angiogenesis is a hallmark of the later reparative phase of ulcer healing, its limited presence in our samples is consistent with the expected timeline of the model. Future studies with extended treatment and recovery periods would be better suited to evaluate the role of *Jatropha tanjorensis* in promoting angiogenesis and tissue regeneration.

This study provides evidence for the cytoprotective and anti-inflammatory effects of *Jatropha tanjorensis.* The dose-response patterns observed, particularly the greater efficacy of the low dose for certain parameters, suggest that the therapeutic mechanisms are more complex than simple dose-dependent antioxidant

activity and may involve specific receptor-mediated or signaling pathway interactions that differ from previously characterized species. These findings suggest that *Jatropha tanjorensis* could be a promising therapeutic agent for managing NSAID-induced gastric ulcers, offering an alternative or adjunctive treatment that could complement existing therapies. Future studies should explore the specific molecular mechanisms underlying the selective cytokine modulation, investigate the optimal therapeutic dosing through pharmacokinetic studies, examine the potential synergistic effects with conventional anti-ulcer medications, and evaluate the long-term safety and efficacy in higher mammals before proceeding to human trials. Additionally, isolating and characterizing the specific bioactive compounds responsible for the observed effects could facilitate the development of standardized phytopharmaceutical preparations and potentially identify novel compounds for drug development. Research into the long-term effects and safety of *Jatropha tanjorensis* for ulcer treatment in higher mammals is essential before clinical applications can be considered.

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