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COMPARATIVE GASTRO-PROTECTIVE EFFECTS OF *CARICA PAPAYA*, ALOE VERA, AND TURMERIC EXTRACTS ON ALCOHOL-INDUCED GASTRIC ULCER IN WISTAR RATS

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ABSTRACT
Gastric ulcer is a significant global health concern, often aggravated by alcohol-induced oxidative stress and mucosal injury. Although proton pump inhibitors provide symptomatic relief, their use is constrained by side effects and recurrence, creating the need for safer alternatives. This study evaluated the gastro-protective effects of *Carica papaya,* Aloe vera, and Turmeric extracts in Wistar rats with ethanol-induced gastric ulcer. Acute toxicity (LD_{50}) was assessed according to OECD guidelines, and thirty-six rats were distributed into six groups: normal control, ulcer control, omeprazole-treated, and three extract-treated groups. Gastric ulcers were induced using ethanol (95% v/v, 1 ml/100 g), and gastric parameters (pH, pepsin activity, total acidity), ulcer indices, and inhibition rates were determined. Toxicity results revealed no mortality or major adverse effects up to 50 ml/kg, indicating wide safety margins. Ethanol caused severe gastric lesions in ulcer control rats, reflected by increased ulcer index, total acidity, and pepsin activity with a reduction in pH. Treatment with extracts significantly improved these parameters, with *Carica papaya* demonstrating the strongest gastro-protective effect and highest ulcer inhibition (46%), followed by Turmeric (37%), Aloe vera (9%), and omeprazole (29%). These findings indicate that *Carica papaya* may surpass omeprazole in effectiveness, supporting its promise as a natural therapy for gastric ulcer.
Keywords: Aloe vera, *Carica papaya,* ethanol-induced ulcer, Turmeric, Wistar rats.

INTRODUCTION
Peptic ulcer disease (PUD) is one of the most prevalent gastrointestinal disorders worldwide, characterized by mucosal injury in the stomach or duodenum due to an imbalance between protective and aggressive factors (Sung *et al*., 2020). Among the many etiological agents, alcohol is a major contributor to gastric ulceration because it directly damages the gastric mucosa, induces oxidative stress, and disrupts mucosal blood flow (Salim, 2019). Alcohol-induced gastric ulcer models are widely employed in biomedical research to evaluate gastro-protective and anti-ulcer therapies (Asha *et al*., 2021and Bhavnagar *et al*.,2021).
Despite the availability of synthetic anti-ulcer drugs such as proton pump inhibitors and H_2-receptor antagonists, limitations including side effects, relapse, and long-term complications necessitate the search for safer and more effective alternatives (Wagner & Ulrich-Merzenich, 2019). Medicinal plants have been used traditionally for gastrointestinal ailments and are rich sources of phytochemicals with antioxidant, anti-inflammatory, and cytoprotective properties (Nwankwo *et al*., 2019).
Carica papaya (pawpaw), Aloe vera, and Turmeric (*Curcuma longa)* are among the most studied plants for gastrointestinal health. *Carica papaya* contains flavonoids, alkaloids, and proteolytic enzymes with demonstrated wound-healing and anti-inflammatory activities (Olagunju *et al*., 2021and Hamza *et*

al.,2015). Aloe vera gel contains anthraquinones, polysaccharides, and phytosterols that enhance mucosal regeneration and inhibit oxidative damage (Hamman, 2008). Turmeric, through its bioactive compound curcumin, has potent anti-inflammatory and antioxidant properties that support gastric mucosal defense (Prasad *et al*., 2014 and Alqasoumi *et al*.,2011).
A comparative study of these three extracts against alcohol-induced gastric ulcer will provide valuable insights into their efficacy and potential therapeutic application in ulcer management.

MATERIALS AND METHOD

Study Area

The study was carried out at the Animal House and Laboratory Unit of the Department of Microbiology, Ogbonnaya Onu Polytechnic, Aba, Abia State, Nigeria.
Experimental Animals
Healthy adult Wistar rats (150‑200 g) were procured and acclimatized for two weeks under standard laboratory conditions (12-hour light/dark cycle, 25 ± 2 ° C, free access to water and feed). Ethical approval was obtained from the departmental Animal Care and Use Committee.
Plant Collection and Preparation of Extracts
Fresh leaves of Carica papaya and Aloe vera, and rhizomes of Turmeric were collected and authenticated by a botanist. The plant materials will be washed, air-dried, and ground into powder. Extraction was carried out using aqueous solvents via maceration or Soxhlet extraction, followed by concentration using a rotary evaporator.

Experimental Design

Thirty-six rats will be randomly divided into six groups (n=6):

- Group 1: Normal control (distilled water).
- Group 2: Ulcer control (ethanol only).
- Group 3: Standard drug (omeprazole 20 mg/kg).
- Group 4: *Carica papaya* extract (200 mg/kg).
- Group 5: Aloe vera extract (200 mg/kg).
- Group 6: Turmeric extract (200 mg/kg).

Ulcer Induction

Gastric ulcer was induced by administering 1 ml of 95% ethanol orally after 24 hours of fasting.

Parameters to be Evaluated

- Ulcer Index and % Inhibition: Measured using standard ulcer scoring systems.
- Gastric pH and Mucus Content: Determined from gastric juice.
- Biochemical Assays: Superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), and malondialdehyde (MDA) will be measured.
- Histopathology: Gastric tissues will be fixed in 10% formalin, sectioned, and stained with hematoxylin and eosin for microscopic examination.

Statistical Analysis

Data will be expressed as mean ± standard deviation (SD). Statistical significance will be determined using one-way ANOVA followed by Tukey’ s post hoc test. A p-value < 0.05 will be considered statistically significant.

RESULTS

No mortality was observed in all groups treated with the extract at all doses administered, even at 50 ml/kg body weight. Animals instead remained active and showed no obvious signs of toxicity throughout the period of the acute toxicity test. Therefore, the lethal dose (LD_{50}) value of the extract was adjudged to be >5,000 mg/kg body weight. Details on observed behaviours of the animals during the acute toxicity test are presented in tables 1&2.

Table 1: Results of phase 1 LD_{50} evaluation of Carica juice

Group	Dose (ml/kg)	No. of death	Observation
1	1	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
2	5	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
3	10	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.

Table 2: Results of phase 2 LD_{50} evaluation of Carica juice

Group	Dose (ml/kg)	No. of death	Observation
1	16	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
2	29	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
3	50	0/3	Animals were calm and physically inactive for about 1 hour, but regained physical activity thereafter. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.

LD_{50} > 5,000 mg/kg body weight

Note: the above result is same for all the extracts provided.

EXPERIMENT 1: *Carica papaya,* Tumeric and Aloe vera
Effect of Carica papaya, *Tumeric* and *Aloe vera* juices against ethanol-induced ulcer in rats

Treatment groups	UN	US	UP	UI	Percentage inhibition of ulcer
Normal control	0.00 ± 0.00^{a}	0.00 ± 0.00^{a}	0.00 ± 0.00	0.00 ± 0.00^{a}	100.00 ± 0.00^{f}
Ulcer control	13.67 ± 1.53^{e}	38.83 ± 2.08^{e}	100.00 ± 0.00	15.25 ± 0.36^{f}	0.00 ± 0.00^{a}
Carica papaya juice 10 ml/kg body weight	4.33 ± 0.58^{b}	8.00 ± 1.00^{b}	70.00 ± 0.00	8.23 ± 0.15^{b}	46.01 ± 1.00^{e}
Tumeric juice 10 ml/kg body weight	$5.33\pm0.58^{b,c}$	10.33 ± 1.53^{b}	80.00 ± 0.00	9.57 ± 0.15^{c}	37.26 ± 1.00^{d}
Aloe vera juice 10 ml/kg body weight	10.67 ± 1.16^{d}	32.67 ± 4.75^{d}	95.00 ± 0.00	13.83 ± 0.49^{e}	9.29 ± 3.19^{b}
Omeprazole, 20 mg/kg body weight	7.00 ± 1.00^{c}	16.17 ± 1.61^{c}	85.00 ± 0.00	10.82 ± 0.26^{d}	29.07 ± 1.68^{c}

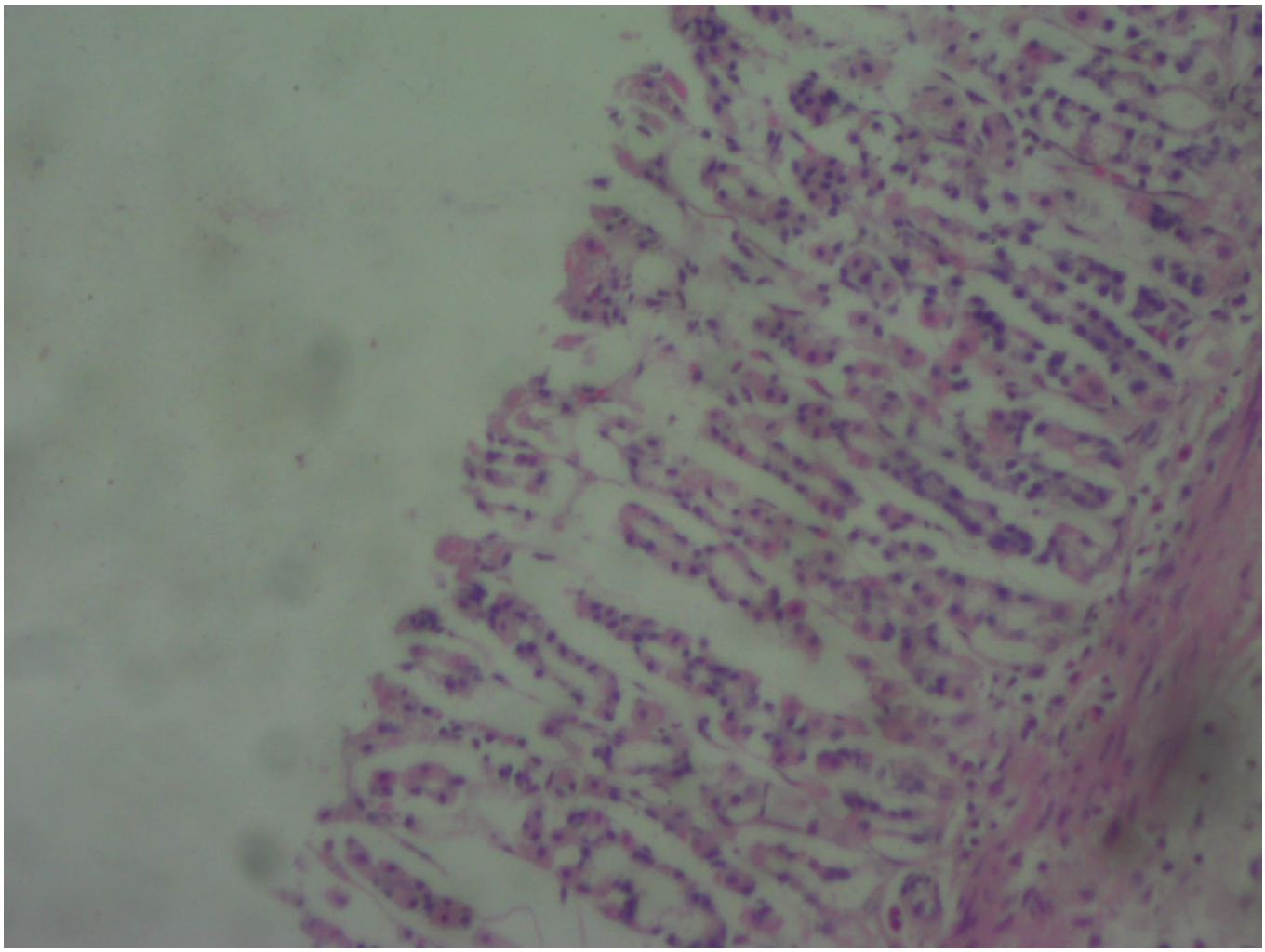
Results are presented as mean ± standard deviation (n = 3); and values with different letter superscripts are significantly ($P < 0.05$) different within the column.

Effects on some gastric juice parameters (pH, pepsin activity and total acidity) for exp 1

Treatment groups	pH	Pepsin activity (µmol tyrosine/ml)	Total acidity (mmol/L)
Normal control	2.76±0.05[b]	17.47±0.58[a]	79.01±0.24[a]
Ulcer control	2.49±0.10[a]	27.10±0.59[e]	116.86±3.12[f]
Carica papaya juice 10 ml/kg body weight	3.16±0.04[d]	20.38±0.23[b]	89.71±3.51[b]
Tumeric juice 10 ml/kg body weight	3.04±0.06[c]	22.85±1.08[c]	100.49±1.94[c]
Aloe vera juice 10 ml/kg body weight	2.77±0.08[b]	24.86±0.30[d]	112.34±1.32[e]
Omeprazole, 20 mg/kg body weight	3.05±0.03[c]	24.19±0.62[d]	107.71±2.99[d]

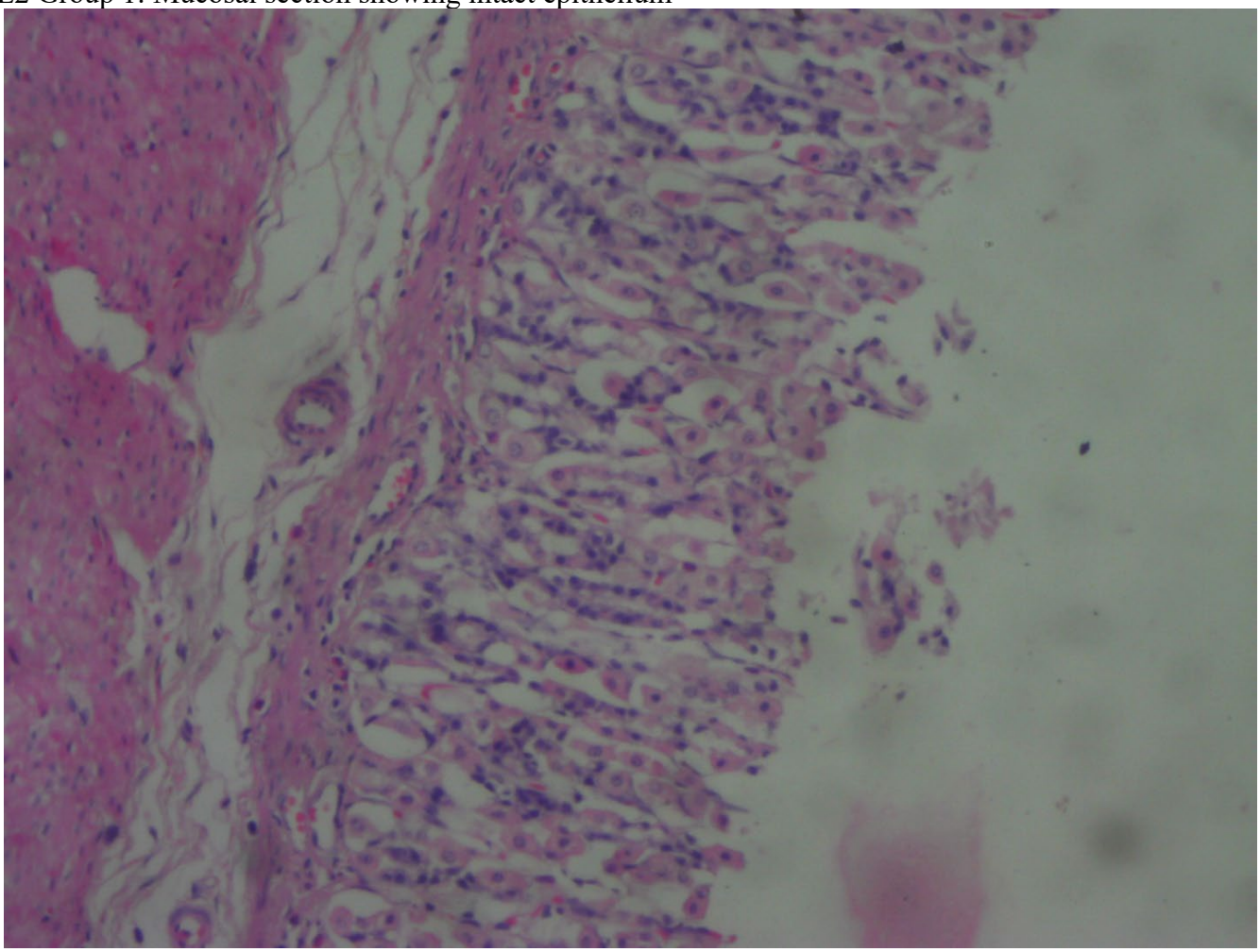
Results are presented as mean ± standard deviation (n = 3); and values with different letter superscripts are significantly ($P < 0.05$) different within the column.

E2 SOLO



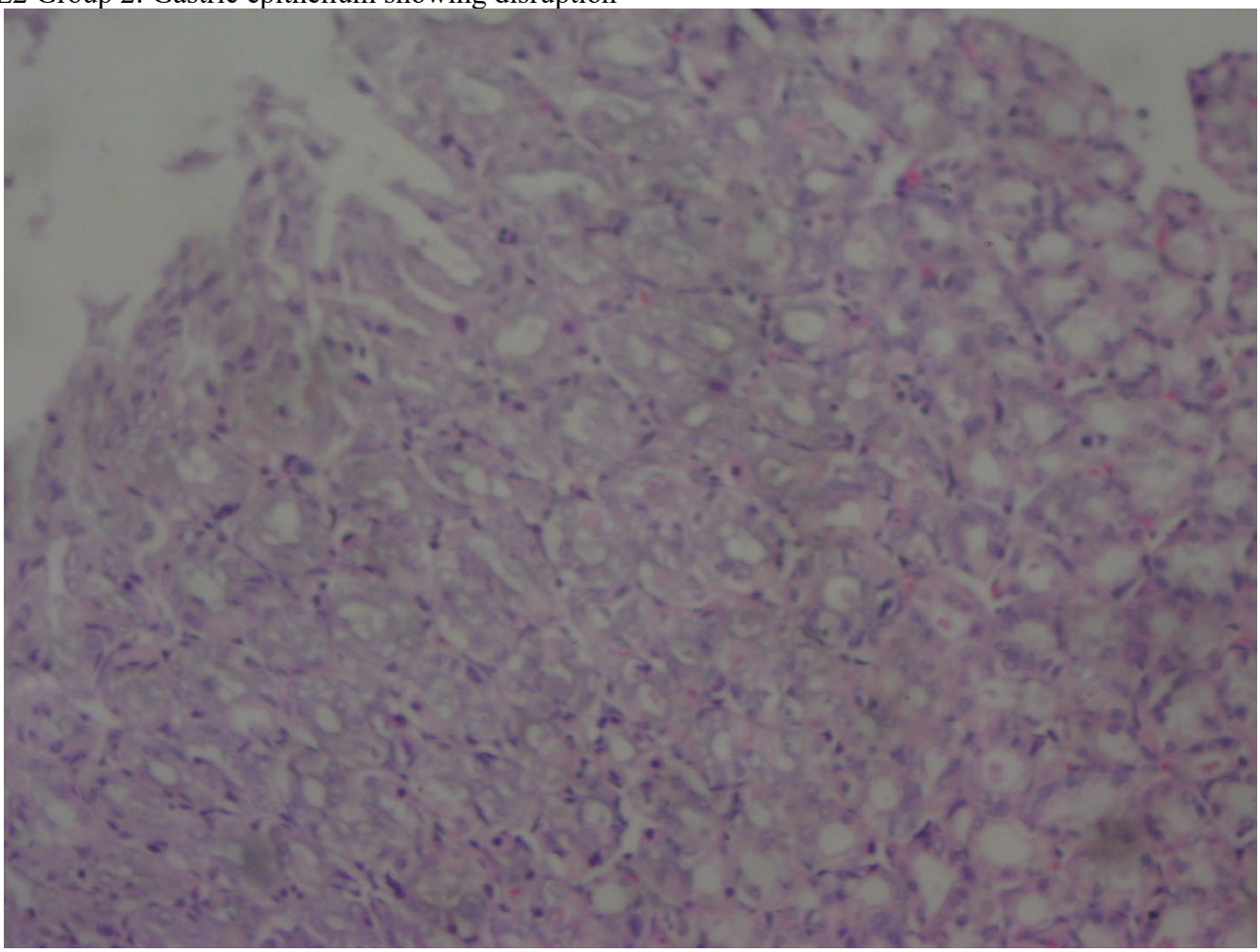
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E2 Group 1: Mucosal section showing intact epithelium



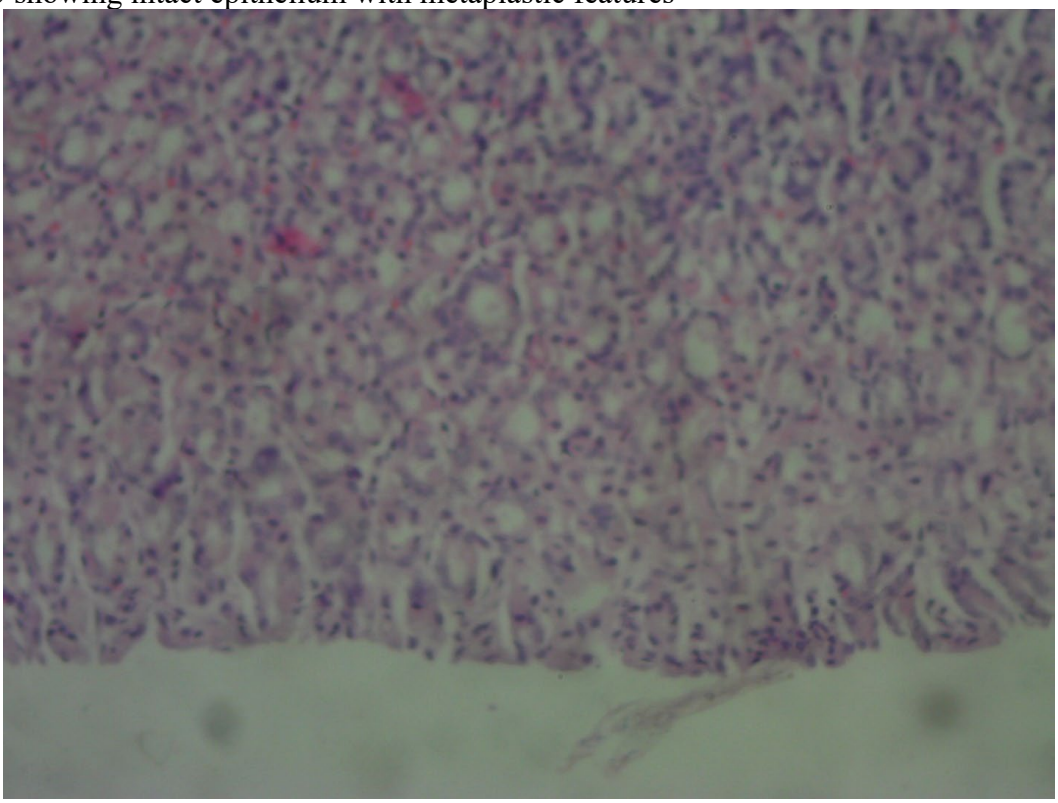
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E2 Group 2: Gastric epithelium showing disruption

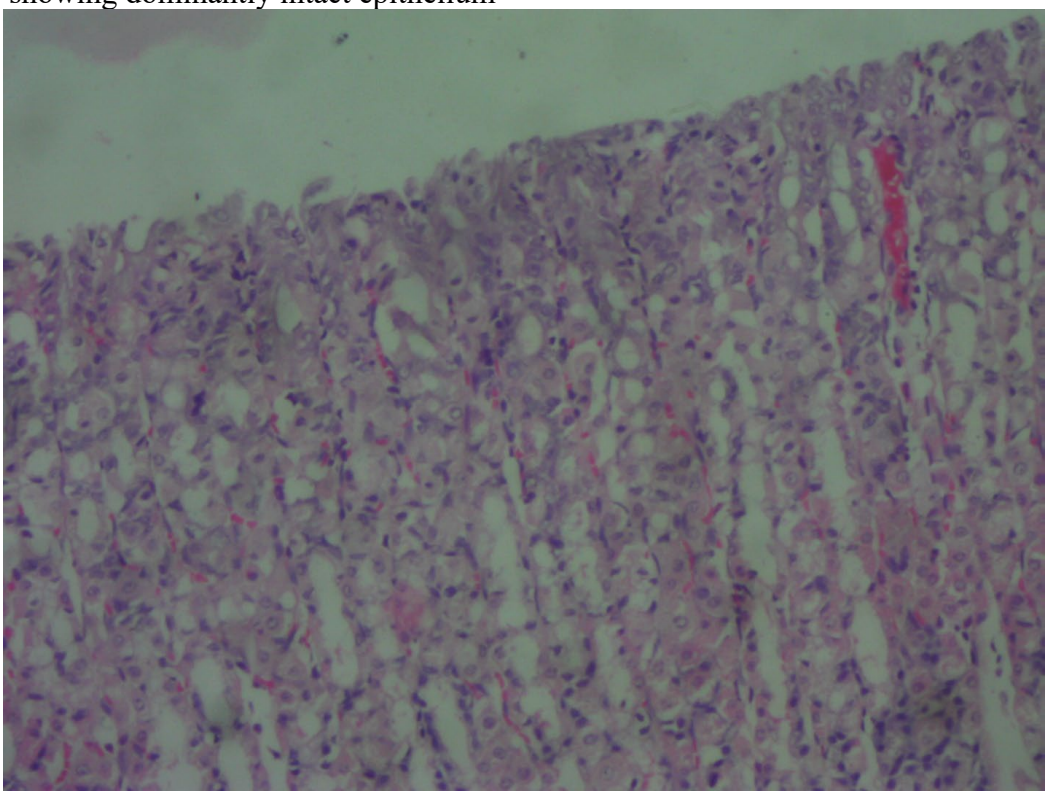


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E2 Group 3 showing intact epithelium with metaplastic features

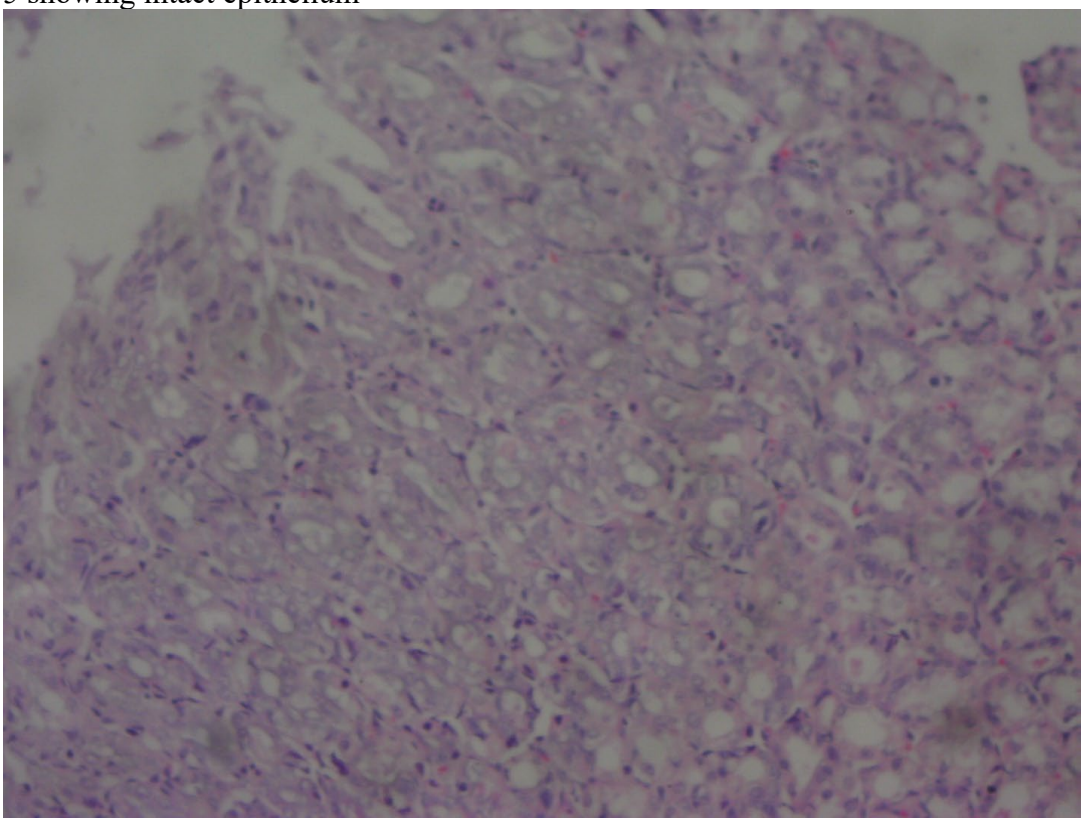


E2 Group 4 showing dominantly intact epithelium



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E2 Group 5 showing intact epithelium



The present study evaluated the gastro-protective effects of Carica papaya, *Aloe vera*, and Turmeric extracts against alcohol-induced gastric ulcer in Wistar rats. Acute toxicity testing revealed no mortality or observable signs of severe toxicity at doses up to 50 ml/kg (equivalent to >5,000 mg/kg body weight), suggesting a wide margin of safety for the three extracts. This finding aligns with earlier reports that papaya extracts are non-lethal even at high doses in rodents (Akinmoladun *et al*., 2020), thereby supporting their potential application as safe therapeutic agents.

Ethanol administration induced severe gastric mucosal injury in ulcer control rats, characterized by elevated ulcer index, increased gastric acidity and pepsin activity, and decreased gastric pH, reflecting oxidative and ulcerogenic stress. Among the test agents, *Carica papaya* juice showed the most potent anti-ulcer activity, producing 46% ulcer inhibition. This effect can be attributed to its rich content of flavonoids, papain, and other antioxidant phytochemicals that enhance mucosal defense and suppress free radical damage. Turmeric extract demonstrated 37% inhibition, comparable to omeprazole (29%), consistent with previous evidence that curcumin exerts gastro-protection by attenuating oxidative stress and inflammatory cascades (Rahmani *et al*., 2018). In contrast, *Aloe vera* exhibited only 9% inhibition, indicating a relatively weaker effect, though its moderate reduction of gastric acidity suggests a possible mucosal healing action that may be dose-dependent or slower in onset.

Analysis of gastric juice parameters further reinforced these outcomes. While ethanol significantly lowered gastric pH and increased acidity and pepsin activity, *Carica papaya* markedly increased gastric pH (3.16 vs. 2.49 in ulcer control), reduced pepsin activity, and suppressed gastric acidity, indicating both antisecretory and mucosal protective properties. Turmeric also improved gastric parameters, albeit less effectively than papaya, while *Aloe vera* produced minimal improvement, correlating with its low ulcer inhibition percentage. As expected, omeprazole raised gastric pH (3.05) and reduced acidity, validating its standard pharmacological profile.

Overall, the comparative order of gastro-protective effectiveness was *Carica papaya* > Turmeric > *Aloe vera*, with papaya not only surpassing the other natural extracts but also outperforming omeprazole in ulcer inhibition. This superior effect may be attributed to the synergistic activity of its bioactive compounds, which confer strong cytoprotective and antioxidant benefits.

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