Original

Gastric Ulceration in Albino Wistar Rats Following Chronic Consumption of Lime

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ABSTRACT

Background: Gastric ulceration is a common health problem caused by a defect in the factors that protect the gastric mucosa or an excess of those that damage it. Lifestyle and diet have been associated with the development of gastric ulcers. The use of lime juice with its high acidic content in cuisines and as a remedy for various health conditions is a common practice. This study was aimed at demonstrating the possible effects of long-term consumption of lime juice concentrate on basal gastric acid secretion, gastric mucous output, pepsin concentration, and ulcer formation in Wistar rats.

Methods: Ten (10) adult male Wistar rats weighing between 160 and 180g were used for the experiments. The rats were randomly divided into 2 groups of five (5) rats each. Group one (1) was the control group and was administered 1ml of distilled water daily; group two (2) was the test group and was administered 1ml of lime juice concentrate daily for 28 days. Gastric acid secretion, pepsin secretion, gastric mucous output, and ulcer formation were evaluated.

Results: The results showed that the mean basal acid secretion was significantly higher in the test group, compared with the control ($p<0.05$). The mean ulcer score was significantly higher in the test group compared with the control ($p<0.05$). The mean gastric pepsin concentration was significantly higher in the test group compared with the control($p<0.05$). The ulcer score was significantly higher in the test group($p<0.05$).

Conclusion: In conclusion, long-term consumption of lime juice predisposes Wistar rats to the development of gastric ulcers.

Keywords: Lime, gastric ulceration, gastric acid, ulcer score, gastric mucosa

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INTRODUCTION

Lime is a fruit that belongs to the Rutaceae family and the Citrus genus. Limes are a part of the Order *Sapindales,* which includes other citrus fruits like oranges, lemons, and grapefruits. Limes are typically round, light green in color, and contain acidic vesicles, making them strongly acidic (1). Limes are known by different names in various languages. In Spanish, it is called "lemon," and in French, it is known as "citron vert". In Nigeria, it has several names, including "lemu tsami" in Hausa. They are rich in vitamin C, citric acid, and antioxidants (1). They contain flavonoids, limonoids, quercetin, polyphenols, terpenes, thiamine, iron, calcium, Calcium and Vitamin B6 (1).

Lime is traditionally used in cuisines. It is said to have a low glycemic index, hypoglycemic property, antiseptic, antispasmodic, anti-inflammatory, and astringent activities (2). Due to the organoleptic properties of lime (flavor and odour), it is used as a food additive and for seasoning. Lime also plays a key role in boosting immunity, wound healing (2), and protecting the body from free radicals (3).

Lime is a key component in traditional medicine, food, and the cosmetic industries; it is known to cause gastrointestinal symptoms, including nausea, heartburn, vomiting, difficulty in swallowing, and acid reflux due to its acidity (3). Chronic use of lime predisposes to tooth cavities because the acid in it can erode the enamel of the tooth (4).

Gastric ulceration is a break in the mucosal barrier of the stomach that penetrates through the muscularis mucosa, extending more than 5 mm in diameter (5). Alterations in the mucosal protective defense mechanisms result in changes to the gastric mucosa, leading to erosion and ultimately ulceration. Prostaglandins protect the gastric mucosa by increasing bicarbonate ion secretion, mucous, growth factors, and adequate blood supply (5,6). Gastric mucous is primarily secreted by surface epithelial cells of the stomach (7). The secretion of gastric mucus is regulated by various factors, including prostaglandins, mucin, growth factors such as epidermal growth factor (EGF) and hepatocyte growth factor (HGF) (8). Its functions include protecting the stomach lining from the corrosive effects of hydrochloric acid, maintaining pH balance, facilitating nutrient absorption, and promoting healthy gut flora (9). Studies have shown that a reduction in mucus production increases susceptibility to gastric injury (10).

The epidemiology of gastric ulceration varies worldwide. In Spain, the prevalence of gastric ulceration is 141.8/100,000, while in the United Kingdom, it is 23.9/100,000 (11). This makes gastric ulceration with its complications like bleeding, perforation, peritonitis, and gastric outlet obstruction a serious medical condition (11).

The etiopathophysiology of gastric ulceration is multi-factoral. The key factors associated with gastric ulceration include bacterial infection with *Helicobacter pylori,* which is found in most patients with gastric ulcers, and gastric prostaglandin loss linked to the use of non-steroidal anti-inflammatory drugs (5,12). Other but less frequent causes include Zollinger-Ellison syndrome, chemotherapy, radiotherapy, smoking, and Crohn's disease (5). Gastrinomas (Zollinger-Ellison syndrome) cause increased secretion of gastrin, resulting in increased production of gastric acid (12). Infection with *Helicobacter pylori* causes gastric mucosal inflammation, epithelial degeneration, and injury. This results in mucosal damage (12). Non-steroidal anti-inflammatory drugs inhibit the cyclooxygenase enzyme, which increases prostaglandin synthesis, gastric bicarbonate secretion, mucus barrier formation, mucosal blood flow, increased epithelial cell restitution, and cell repair after injury. (5). The breakdown of the mucosal barrier, which exposes the mucosa to the damaging effect of gastric acid, is the final pathway, irrespective of the causes of ulceration. Ingestion of acids has been known to cause gastric ulcers (13).

This research was conducted to investigate the effects of long-term lime consumption, known to be acidic, specifically its impact on peptic ulceration, and to elucidate factors that may provoke ulceration, including gastric acid secretion, pepsin secretion, and gastric mucous output.

MATERIALS AND METHODS

Ethical approval: Ethical approval was obtained from the Animal Ethics and Research Committee of the Faculty of Basic Medical Sciences, University of Calabar on 26th of June, 2025. Ethical approval number: BOT/HERB/UCC/196A.

Preparation/dosage of lime juice concentrate: Lime fruits were purchased from Watt Market in Calabar South Local Government Area. They were cut into small pieces and blended. The resulting juice was strained through a muslin cloth to remove any particles. It was then stored in an airtight plastic container, which was kept in a cool, dry place. Fresh samples of the juice were prepared daily.

Dose of administration of lime juice concentrate

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1ml of lime juice = Ag/ml
Weight of mice = 250g = 0.250kg
Therefore 0.250kg = Ag/ml/0.250kg = Rg/kg body weight
Lime juice administered = Rg/kg body weight

Experimental animals: Ten male adult Wistar rats weighing between 160 and 180g were used for these experiments. They were housed in a well-ventilated room in the animal facility of the Department of Physiology, University of Calabar. They were kept at a temperature of 28 °C in a 12/12, dark/light cycle and acclimatised for 2 weeks before the onset of the experiments. The rats were fed standard feed pellets and were allowed access to water and food *ad libitum*.

Experimental design: Ten (10) Wistar rats were used for this study. The animals were randomly divided into 2 groups of 5 rats each. Group one served as the control group and was administered 1ml of distilled water/0.25kg, while group two served as the test group and was administered 1ml of lime juice concentrate/0.25kg. This administration was done orally, every morning for a period of 28 days.

Measurement of gastric acid: Measurement was done using the continuous perfusion method (14,15). Gastric acid output in the effluent sample was measured by titrimetric analysis. Gastric acid secretion was measured at the basal state, with histamine, and following administration of histamine + cimetidine. The calculation of acid in millimoles per hour (mMol/Hr) was by the principle that states that a gram equivalent of acid balances a gram equivalent of the base at the neutralization point.

Measurement of pepsin: The determination of the proteolytic activity of gastric acid secretion (which is the basis for the measurement of pepsin) was done using Casein as a substrate (16).

Measurement of mucus concentration: The weight of adherent gastric mucous was determined using the method of Tan *et al.* (9).

Induction of gastric ulcers/scoring: Ulcers were induced by gastric instillation of acid-ethanol. The stomach of each animal was spread and pinned to a dissecting board to provide a good view of the stomach's mucosa (174). A careful macroscopic examination for any ulcerative lesions was carried out, and scoring of ulcer spots was done (18). Ulcer scoring was done according to the following grading system, as shown in Table 1 below.

Table 1: Grading of ulcer points

GRADE	INTERPRETATION
0.0	No less
0.5	Pin-sized ulcer
1.0	2 or more small linear or hemorrhagic ulcers
2.0	Ulcer spots greater than 3mm

Statistical analysis: Data were expressed as mean ± SEM. One-way analyses of variance (ANOVA) were employed to analyze the data, and Tukey's post hoc test was performed to compare the mean values. All data was evenly distributed after testing with Levene's test of homogeneity of variance. Statistical Package for Social Sciences (SPSS, v.25) was used to analyze the data. A p-value of $p<0.05$ was considered statistically significant (19).

RESULTS

Comparison of mean basal gastric acid output between the control and the test groups

The mean basal gastric acid output (BGAO) in the control group and test groups was 6.30 ± 0.12 uMOL/ 10 min and 9.45 ± 0.08 µmol / 10 min, respectively. It was significantly increased in the lime-fed group compared with the control ($p<0.001$). Figs 1 and 2.

Comparison of the mean histamine-mediated gastric acid output

The mean histamine-mediated gastric acid output (Hist-GAO) in the control and test groups was 11.40 ± 0.08 µmol/10min and 12.03 ± 0.04 µmol/10min, respectively. No significant differences in the Hist-GAO between the two groups as shown in Figs 1 and 2.

Comparison of the mean Histamine + Cimetidine-mediated gastric acid output

The mean Histamine + Cimetidine-mediated gastric acid output (Hist+Cim-GAO) in the control group and test groups was 9.05 ± 0.11 µmol/10 min and 10.15 ± 0.04 µmol/10 min, respectively. There was a significant increase in the mean Hist+Cim-GAO in the test group ($P<0.05$) compared with the control group, as shown in Figs 1 and 2.

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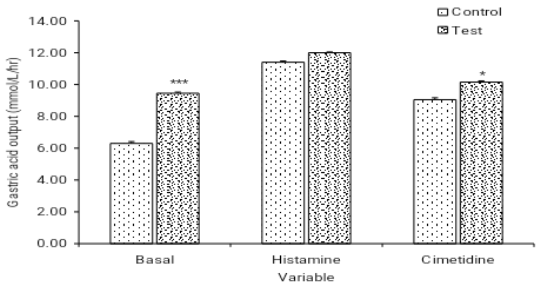
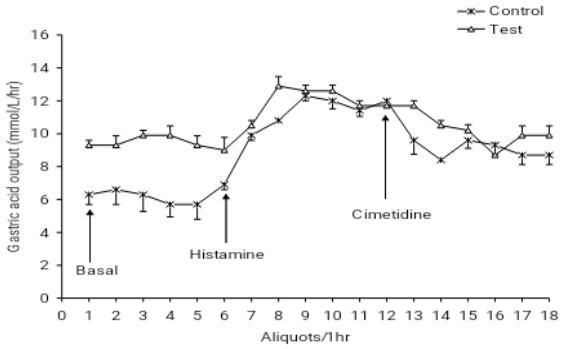


Values are expressed as mean ± SEM, n = 5.
* = p<0.05 vs control, *** = p<0.001vs control

Fig 1: Comparison of basal, histamine, and cimetidine-induced gastric acid secretion between the control and test groups.

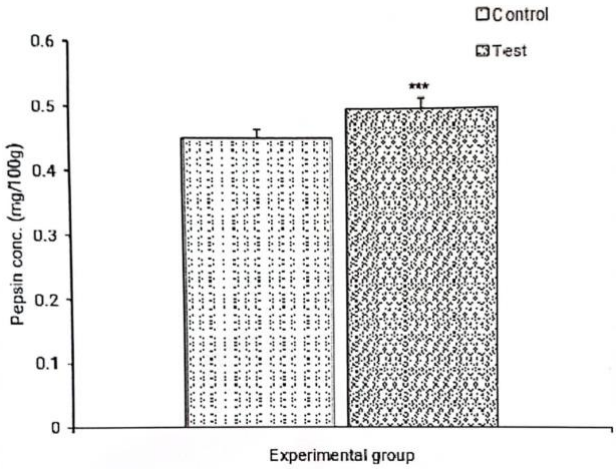


Values are expressed as mean ± SEM, n =

Fig**. 2:** Gastric acid secretion in the control and test groups.

Gastric pepsin secretion in the control and the test groups

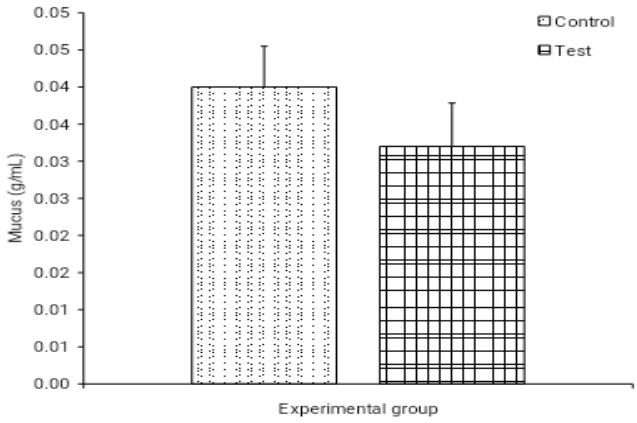
The mean concentration of gastric pepsin in the control and test groups was 0.45 ± 0.01mg/100ml and 0.50 ± 0.01mg/100ml, respectively. The mean concentration of gastric pepsin in the test group was significantly higher (p<0.001) when compared with the control group (Figure 3).



Values are expressed as mean ± SEM, n = 5.
*** = p<0.001 vs control

Fig. 3: Pepsin concentration in the different experimental groups

The mean gastric mucous output in the control and test groups was 0.04 ± 0.01g and 0.03 ± 0.01g, respectively.



The mean gastric mucous output in the test group was not significantly different when compared to the control group (Figure 4)

Values are expressed as mean +SEM, n = 5
No significant difference between groups

Fig. 4: Gastric mucus secretion of the different experimental groups

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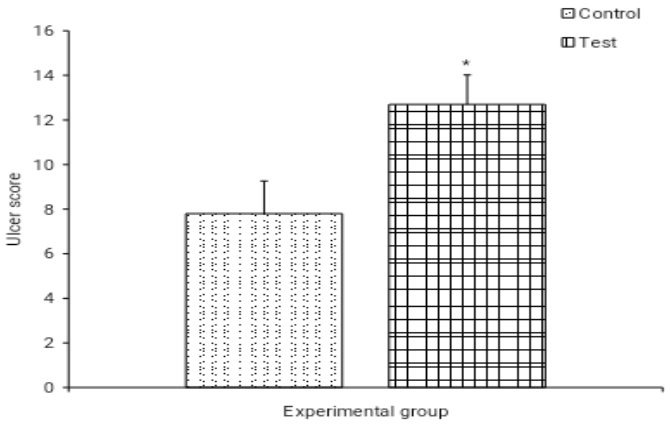
Gastric ulcer scores in the control and the test group
The mean gastric ulcer score in the control and the test group was 7.78 ± 1.46 and 12.70 ± 1.32, respectively.



The mean gastric ulcer score in the test group was significantly higher ($p<0.05$) when compared with the control group (Figure 5).
Values are expressed as mean ± SEM, n = 5.
*= $p<0.05$ vs control
Fig. 5: Gastric ulcer score of the different experimental groups.

DISCUSSION

This study investigated the effect of long-term ingestion of lime juice concentrate on peptic ulceration. Aggressive factors that could provoke gastric ulceration - low mucous secretion, high pepsin secretion, high basal acid secretion, and ulcer score- were investigated.
Peptic ulcer disease is common both in humans and animals. It occurs as a result of the imbalance between protective and aggressive factors present in the gastric mucosa. Every day, the gastric mucosa is exposed to factors that can cause injury, including gastric acid, certain types of food, pepsin, bacterial agents (*Helicobacter pylori*), bile acids, and certain drugs (19).
The mean basal gastric output was significantly higher in the test group when compared to the control group. When histamine was administered, there was no significant difference between the two groups. When cimetidine was administered, a significant difference in acid secretion was observed. The acid secretion was significantly higher in the test group when compared to the control group. This result suggests that H2 receptors are not involved in gastric acid secretion in this instance. Cimetidine did not affect stimulated acid production (stimulated by the consumption of lime). There is an increase in the presence of free hydrogen ions in the stomach, which may damage the gastric mucosa (20).
The test group had significantly reduced adherent gastric mucus when compared to the control group. This may be due to several reasons, including the destruction of epithelial cells caused by oxidative injury, disruption of Prostaglandin function, and increased acidity in the stomach. All of the above would negatively affect the ability of the epithelial cells to secrete mucus (18).
Mean gastric ulcer scores were significantly higher in the test group when compared to the control group. This may be because there is comparatively more acidity in this group. Ulcer scores are used to assess mucosal damage. This result signifies a higher propensity for the development of peptic ulceration in the test group (21).
The mean pepsin concentration was significantly higher in the test group when compared to the control group. Pepsin solubilizes gastric mucous, thus exposing the gastric mucosa to acid attack (19). Increased pepsin concentration, combined with increased gastric acid secretion, may be the reason for the higher incidence of gastric ulceration observed in the test group when compared to the control group.

Strengths of the study

1. **Controlled experimental design:** The use of a control and treatment group allowed for a clear comparison of the physiological effects of chronic lime juice consumption on gastric parameters.
2. **Assessment of multiple ulcer-related parameters:** This study evaluated several key determinants of gastric ulceration, including basal gastric acid secretion, histamine-mediated acid secretion, pepsin concentration, mucus output, and ulcer score. This provides a comprehensive assessment of gastric mucosal aggression and defense mechanisms.
3. **Use of standard experimental methods:** Standard laboratory techniques such as the continuous perfusion method for gastric acid measurement and casein digestion for pepsin estimation improved the reliability of the findings.

Limitations of the Study

1. **Small sample size:** Only ten Wistar rats were used in the study, which may limit the statistical power and generalizability of the findings.

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2. **Short experimental duration:** Although 28 days represents chronic exposure in experimental models, longer-term studies may provide better insight into progressive gastric mucosal changes.
3. **Limited translation to humans:** As the study was conducted in rats, the findings may not fully reflect the physiological effects of lime consumption in humans.

Implications of the Findings of the Study

The findings of this study suggest that chronic consumption of lime juice concentrate increases susceptibility to gastric ulceration by increasing basal gastric acid secretion and pepsin concentration while reducing protective mucosal factors. These results highlight the potential gastrointestinal risks associated with excessive or prolonged intake of highly acidic foods, particularly in individuals who may already be predisposed to peptic ulcer disease. Furthermore, the findings of this study also contribute to the understanding of dietary influences on gastric mucosal integrity, emphasizing that natural food products traditionally considered beneficial may have adverse effects when consumed in large quantities or over long periods.

CONCLUSION

Chronic consumption of lime juice concentrates significantly increased basal gastric acid secretion, pepsin concentration, and gastric ulcer scores in Wistar rats, suggesting an increased susceptibility to gastric mucosal injury. Although lime possesses several nutritional and medicinal benefits, prolonged intake in concentrated form may disrupt the balance between gastric mucosal protective and aggressive factors. These findings highlight the need for moderation in the consumption of highly acidic foods.

Declarations

Authors' contribution: Authors' contributions: Irene Okpoene Atim conceptualized the study, participated in the experimental work, data collection, data analysis, and preparation of the initial manuscript draft. Polycarp Unim Adie supervised the study, contributed to the study design and methodology, interpreted the data, and critically revised the manuscript. Ekpe Okpata Aribo contributed to the methodology, data interpretation, literature review, and critical revision of the manuscript. All authors read and approved the final manuscript.

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Declaration of Conflicts of Interest: The authors declare that they have no conflicts of interest.

Disclosure in AI use: Generative AI was not used in the design, conduct, data analysis, interpretation, or original drafting of the manuscript.

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