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Evaluation of Anti-ulcer Effects of the Methanol Extract of *Mangifera indica* L Stem Bark

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Authors' contributions

This work was carried out in collaboration between the both authors. Author HDK designed the study, wrote the protocol checked the manuscript and managed literature searches and analyses of the data. Author OA carried out the research in the laboratory and was monitored by author HDK. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aims: The anti-ulcer effects of methanol extract of *Mangifera indica* L stem bark was investigated on wistar rats.
Place and Duration of Study: The study was carried out between August and November 2013 in the Pharmacology Laboratory of Department of Pharmacology, Faculty of Basic Medical Sciences, University of Port Harcourt, Nigeria.
Methodology: The methanol extract of *Mangifera indica* was prepared. The doses of the extract administered to the rats were 100, 200 and 400 mg/kg p.o. respective, and cimetidine (100 mg/kg; p.o.) was the reference drug. Ulcer was induced with ethanol and indomethacin. Ulceration was assessed by the degree of ulceration, total ulcer scores and ulcer index of the various treatment groups.
Results: The extract showed a significant ($p < 0.001$), dose dependent inhibition of ulceration (reduction in ulcer index values) relative to control, in both the ethanol and indomethacin models.
Conclusion: This study therefore suggested that *M. indica* stem bark has ulcer-reducing properties.

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Keywords: Gastric ulcer; ethanol-induced ulcer; indomethacin-induced ulcer; Mangifera indica stem bark.

1. INTRODUCTION

Peptic ulcers are inflammations of the stomach or duodenal lining. They usually occur as mucosal erosion equal to or greater than 0.5 cm. As many as 70-90% of such ulcers are associated with *Helicobacter pylori*, a spiral-shaped bacterium that lives in the acidic environment of the stomach. The etiology of peptic ulcer disease has implicated local environmental factors and customs that are diet dependent, therefore diets and dietary habit could provide a clue to incidences of peptic ulcer disease [1].

Medicinal plants and plant-derived medicines are widely used in traditional cultures around the world, and are also becoming increasingly popular in modern societies as natural alternatives to synthetic chemicals [2]. Medicinal plants are known to be the principal health care resources for a significantly large number of people all over the world [3]. About 70 - 80% of the rural population in many tropical countries still depend on traditional medicines for their primary health care, which also mean that the people have to depend on medicinal plants for treatment [2]. There are many traditional medicinal uses for the bark, roots and leaves of *Mangifera indica L* throughout the globe [4,5]. *M. indica* is used medicinally to treat ailments such as asthma, cough, diarrhea, dysentery, leucorrhoea, jaundice, pains and malaria [6].

The current study seeks to investigate the anti-ulcer properties of *Mangifera indica* stem bark in rats.

2. MATERIALS AND METHODS

2.1 Animal Maintainance and Handling

Adult male albino rats (weighing 165–250 g respectively) were used in this study. The animals were obtained from Faculty of Basic Medical Sciences Animal house, University of Port Harcourt, Nigeria. They were housed in plastic cages and maintained under standard laboratory conditions (12 h light and dark cycles) with food and water given *ad libitum*. They were taken out of the animal house and acclimatized to the laboratory environment for about 2 h prior to commencement of the tests. The care and handling of these animals were carried out in strict compliance with international best practices [7]. The “Principle of Laboratory Animal Care” (National Institute of Health-NIH publication No. 85-23) guidelines and procedures were followed in this study. The Ethical Committee of the Faculty of Basic Medical Sciences, University of Port Harcourt, approved this research work.

2.2 *Mangifera indica* Stem Bark Collection and Extraction Procedures

Mangifera indica stem bark was obtained from Choba (the host community of University of Port Harcourt, Nigeria) within the month of August 2013. The plant part was identified and authenticated by Dr. N. Edwin-Wosu of Department of Plant Science and Biotechnology, University of Port Harcourt. It was then cut into smaller piece, and oven dried for 5 days at temperature interval of 36 - 40°C. The dried stem bark of *Mangifera indica* was pulverized using electric blender. The resulting powdered material was macerated with 70% methanol (the methanol to plant powder (v/w) ratio was 3:1). The mixture was shaken intermittently and kept for 72 h after which it was filtered with Whatman No. 1 filter paper and the filtrate was concentrated in a carefully regulated water bath (maintained at temperature of 90°C), to yield dark solid extract which was stored in a refrigerator pending the time for biological investigations.

2.3 Experimental Procedures

2.3.1 Effect of extract on ethanol-induced gastric ulceration

Five groups of male rats (6 per group) were fasted for 18 h, though water was given *ad libitum* till 2 hours before the commencement of the experiment [8]. The animals were treated as follows:

Group 1 (control) received only 0.5 ml of 99% ethanol.
Group 2 – 4 were pre-treated with the extract (100, 200 and 400 mg/kg p.o. prepared with 10% Tween 80; respectively).
Group 5 was given cimetidine orally (100 mg/kg dissolved in 10% Tween 80).

30 minute later, groups 2-5 were administered with 0.5 ml of 99% ethanol to induce ulcer. 4 h after ethanol administration, the rats were anaesthetized with light ether and sacrificed by cervical dislocation. The stomach was removed and opened along the greater curvature. Macroscopic examination of the stomach was carried out with a hand lens for the presence of ulcer lesions, which were scored using standard methods [9,10].

The observed ulcers were scored as shown below

Ulcer score	Scoring system criteria
5	Multiple ulcer along the entire length of gastric fold
4	Lesions which followed approximate 80% of the fold
3	Ulcer 1- 4mm in length of the fold
2	At least two ulcers approximate 2 mm in length
1	The presence of one ulcer and generalize erythema
	No visible damage

The Ulcer Index (UI) and Degree of ulceration (DU) were calculated with the method shown below [11,12].

$$\text{Ulcer Index (UI)} = \frac{\text{Degree of Ulceration x Percentage of Group Ulcerated}}{100}$$

$$\text{Degree of ulceration (DU)} = \frac{\text{Total Ulcer Score}}{\text{Number of animal ulcerated}}$$

2.3.1 Effect of extract on indomethacin-induced gastric ulceration

Male rats randomized into five groups of five rats each, were fasted for 18 h and water withdrawn only 2 h before the commencement of experiment [8].

The groups were treated as follows:

Group 1 (control) was given only indomethacin orally, (60 mg/kg dissolved in 5% Na_2CO_3).

Group 2 –4 were pre-treated with extract (100, 200 and 400 mg/kg p.o. prepared with 10% Tween 80, respectively).

Group 5 received cimetidine orally (100 mg/kg dissolved in 10% Tween 80).

30 minute later groups 2 – 5 were administered with indomethacin.

4 hours after indomethacin administration, the rats were anaesthetized with light ether and sacrificed by cervical dislocation. The stomachs were removed and opened along the greater curvature.

Macroscopic examination was carried out with a hand lens and the presence of ulcer lesion scored as shown below [9,10].

Ulcer	Scoring system criteria
0.0	Normal
0.5	Punctuate or pinpoint haemorrhagic ulcer
1.0	Two or more small haemorrhagic ulcer less than 3mm.
2.0	Ulcer greater than 3mm in diameter.
3.0	Several ulcers.

2.4 Statistical Analysis of Data

The data obtained were analyzed using the Graphpad Prism, version 5.01. Data were expressed as mean ± SEM. The statistical significance of the difference between the mean ulcer index of the treated group and that of the control group was tested with one way analysis of variance (ANOVA) followed by Dunnett's post-test.

3. RESULTS

3.1 Effect of Extract on Ethanol-Induced Gastric Ulceration

The effect of extract on ethanol-induced ulceration in rats is as shown in Table 1.
The extract inhibited ethanol-induced gastric ulceration. The inhibition was statistically significant ($p<0.001$).

3.2 Effect of Extract on Indomethacin-Induced Gastric Ulceration

The effect of extract on indomethacin-induced ulceration in rats is as shown in Fig. 1. The extract inhibited indomethacin-induced gastric ulceration. The inhibition was statistically significant ($p<0.001$).

Table 1. Ulcer parameters of ethanol-induced ulcerated male rats treated with *M. Indica* methanol extract

Control	Doses (mg/kg)	Total ulcer	Degree of ulceratn (DU)	Ulcer index (UI)
		35	7	7.00±0.58
Extract	100	15	3	1.80±0.35***
	200	15	3	1.80±0.46***
	400	10	2	0.66±0.35***
Cimetidine	100	8	1.6	0.53±0.26***

*Values are expressed as Mean ・ SEM; (n=5); Significance relative to control: ***p< 0.001*

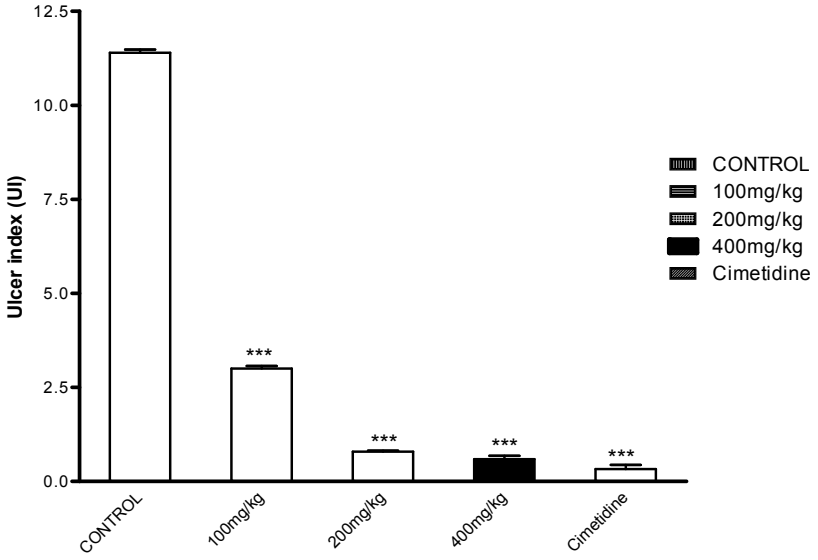

Fig. 1. Effect of methanol extract of *Mangifera indica* stem bark on indomethacin-induced ulcer in rat

*Values are expressed as Mean ・ SEM; (n=5); Significance relative to control: ***p< 0.001*

4. DISCUSSION

The results of the current investigation showed that the methanol extract of *Mangifera indica* significantly inhibited the development of indomethacin- and ethanol-induced acute gastric ulcers in a dose-dependent mannerrats.

Indomethacin is known to induce ulcers by inhibition of prostaglandin synthetase through the cycloxygenase pathway [13]. The drug typically produce haemorrhagic ulcers caused by the rupture of small blood vessels around the gastric mucosa. Ethanol, however, is believed to induce stasis of gastric blood flow [14,15] as well as having a direct necrotizing action on tissues which results in a reduction of mucosal defensive factors such as the secretion of bicarbonate ions and production of mucus, thereby producing necrotic lesions [16,10].

Since ulcers are known to be due to an imbalance between offensive factors such as acid and pepsin, and defensive factors such as mucin secretion, cell proliferation and prostaglandins production [17,10], it is possible that the protective effect of *M. indica* extract against indomethacin and ethanol-induced gastric ulceration is produced through actions that increase prostaglandin formation thereby preventing or reducing the impact of the aggressive factors [15]. This may be due to the ability of the extract to mobilise prostaglandins in the gastric mucosa by increasing its microcirculation or through an unknown mechanism [18,10]

The extract has been shown to contain tannins and flavonoids [19,20], substances known to affect the integrity of mucous membranes [21,9]. Tannins has protein precipitating and vaso-constrictory effects which could be of advantage in preventing ulcer development [22,9]. Tannins being an astringent may have precipitated microproteins on the site of the ulcer thereby forming an impervious protective pellicle over the linning to prevent absorption of toxic substances and resist the attack of proteolytic enzymes [23,12]. Flavonoids have been reported to offer some protection in ulcer development by increasing capillary resistance. Flavonoids improve microcirculation which renders the cells less injurious to precipitating factors [24,25].

5. CONCLUSION

These findings show that the methanol stem bark extract of *Mangifera indica* has a dose dependent ulcer reducing properties on both necrotizing and haemorrhagic ulcers induced by ethanol and indomethacin (Non steroidal antiinflammatory drugs –NSAIDs) respectively.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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