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Gastro-Protective Effect of Ethanolic Extract of *Artocarpus Altilis* (Breadfruit) on Alcohol Induced Acute Ulcer Model in Albino Wistar Rats

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ABSTRACT

The study was designed to investigate the gastro protective effects of fruit extracts of *Artocarpus altilis* (Breadfruit), using alcohol induced acute ulcer model. The extracts were administered at doses 100mg/kg, 200mg/kg and 300mg/kg. 10mg/kg of Omeprazole was used as a reference standard. The parameters used for this were percentage of animals with gastric ulcer (UP), ulcer index (UI) and percentage protection of ulcer (%P). The percentage of animals with ulcer was lowest in both the groups treated with 300mg/kg (16.67 ± 0.004) of extract and those treated with omeprazole (16.67 ± 0.004). While the animals in control group and those treated with 100mg/kg of extract had the highest percentage of animals with ulcer (100.01 ± 0.005). The gastro protective activity was accessed by determining and comparing the ulcer index in the test group with that of the control group. Animals pretreated with *Artocarpus altilis* extract showed significant reduction in ulcer index in a dose dependent manner when compared to the control group having an ulcer index of 11.51 ± 0.005 when treated 100mg/kg of extract, 3.66 ± 0.004 & 1.83 ± 0.004 for 200mg/kg & 300mg/kg of extract respectively. The gastro protective effect of 300mg/kg had the same potency as the standard drug Omeprazole. The administration of 100mg/kg, 200mg/kg, 300mg/kg and Standard drug (Omeprazole) reduced Gastric lesions by 9%, 71%, 85.5% and 85.5% respectively. The results suggest that the extract possesses significant protective properties against ulcer in albino rat compared to the control group.

Keyword: *Artocarpus altilis*, Omeprazole, gastro protective, gastric ulcer, ulcer index.

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INTRODUCTION

There is a balance in the stomach between the aggressive digestive capabilities of acid plus pepsin and the mucosal barrier. Mucus serves as the first line of the defense against ulcerogens. The protective effects of mucous barrier depend not only on the gel structure but also on the amount or thickness of the layer covering the mucosal surface. The ability of the gastric mucosa to resist injury caused by endogenous secretions (acid, pepsin and bile) and by ingested irritants such as alcohol, aspirin and NSAIDs can be attributed to a number of factors that have been generally referred as mucosal defense¹. Ulceration occurs when there is a disturbance in equilibrium caused by enhanced aggression or reduced gastro- protective agents even when there is normal rate of acid secretion². Peptic ulcer may be classified mainly into four types they are gastric, duodenal, esophageal and Meckel's Diverticulum ulcers. Gastric ulcer is a peptic ulcer that develops in the stomach, Duodenal and esophageal ulcers occur in the duodenum and esophagus respectively. Meckel's Diverticulum ulcer is a less common type of ulcer that develops in the Meckel's Diverticulum(a vestigial remnant in the form of a small bulge in the small intestine)³. Patients with Zollinger Ellison syndrome are also susceptible to peptic ulcer in which there are multiple peptic ulcerations in the stomach, duodenum, and even jejunum, owing to excess gastrin secretion by a tumor and, hence, excess gastric acid production. Acid and pepsin secretion must be considered together because in practice it is difficult to distinguish the effects of each alone⁴.

There are several implications in the pathogenesis of gastric ulcer. These include. Acid-pepsin secretion, impaired mucous secretion, impaired bicarbonate secretion and precipitate lesions on the mucosal layer⁵. Also, the prolonged use of Non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin causes ulcer. Drug treatment of peptic ulcers is targeted at either counteracting aggressive factors (acid plus pepsin, active oxidants, PAF, leukotrienes, endothelins, bile or exogenous factors including NSAIDs) or stimulating the mucosal defenses (mucus, bicarbonate, normal blood flow, prostaglandins, nitric oxide)⁶. The ideal aims of treatment of peptic ulcer disease are to relieve pain, heal the ulcer and delay ulcer recurrence. To date, no drug meets all the goals of therapy. In recent years, infection with gram negative bacteria such as *Helicobacter pylori* also leads to peptic ulcer⁷. About 70% of patients with peptic ulcer disease are infected by *Helicobacter pylori* & the eradication of this microorganism seems to be the best curative measure for this disease. Fruits represent an abundant source of nutrients and non-nutritive bioactive compounds which are mostly associated with reduced risk of many non-communicable/chronic diseases. The name *Artocarpus* is derived from the greek words *artos*(‘bread’) and

karpos ('fruit')^{8,9}. Bread Fruit belongs to the genus *Moraceae* which consists of approximately 60 species native to the Indian subcontinent, south-east Asia and Australasia^{10,11}. The botanical name of Bread fruit is *Artocarpus altilis*¹².

MATERIALS AND METHOD

Animals

A total of thirty (30) male albino rats of wistar strain weighing between one hundred and eighty to two hundred and fifty (180-250g) were obtained from the central animal house, faculty of Basic Medical Science, College of Health Sciences, University of Port Harcourt, Nigeria. Animals were kept in ventilated cages at room temperature (28-30°C) and 12hrs light/dark cycle. They were fed with standard rat's pellet (finisher's) and tap water ad libitum. They were acclimatized for 2 weeks after which they were divided into five groups of six animals each. Animal experimental studies were conducted according to the guidelines of Institutional Animal Ethical Committee (IAEC) of University of Port Harcourt, Nigeria. The study was approved by Faculty of Basic Medical Sciences, University of Port Harcourt animal ethics committee.

Drugs

Omeprazole was obtained from the University Of Port Harcourt Teaching Hospital Pharmacy Department, and was used as the reference anti- ulcer drug. The proton pump is the final stage in stomach acid secretion where H^+ produced from H_2O is pumped into canaliculus within parietal cell by H^+/K^+ ATPase where it binds to Cl^- to form HCl. Proton pump inhibitors act by binding to the H^+/K^+ ATPase and irreversibly blocks the system thereby resulting in non-pumping of H^+ into canaliculus. Thus complete inhibition of H^+/K^+ ATPase inhibits all HCl formation i.e abolishes HCl formation¹³. Proton-pump inhibitors are given in an inactive form, which readily crosses cell membranes and enters into parietal cells, where they become activated by the acidic environment. Example of a prototype of proton pump inhibitor (PPI) is Omeprazole. It diffuses across the parietal cell and eventually becomes protonated. Omeprazole tablet weighing 20mg was dissolved in 10ml of distilled water to make a stock solution of 2mg/ml to be administered at a dose of 10mg/kg per oral (po).

Plant material and preparation of extract

Artocarpus altilis (breadfruit) were purchased from local food vendors in Port Harcourt. The fruits were identified and confirmed for use by a botanist of the department of plant science biotechnology (PSB) herbarium, University of Port Harcourt, Nigeria. Afterwards, sample specimens were deposited in the herbarium of the department for future references. The altocarpus

altilis samples were dried under room temperature, after which, were weighed and grinded into powder form. The powdered altocarpus altilis was soaked in a glass container of ethanol and left for a period of 72 hours. After which the powdered breadfruit settles and the clear liquid is decanted. Filtrate was then evaporated using rotatory evaporator. The extract was evaporated to semi-solid form and stored in the refrigerator throughout the period of the experiment to preserve the prepared extract.

Alcohol induced gastric ulcer model in rats

Gastric ulcer was induced in rats by administering absolute alcohol (1ml/200g po)¹⁴ (Method of Suleyman). Omeprazole and Ethanolic Extract of *Altocarpus Altilis* were administered 45 minutes before alcohol treatment. After a lapse of 1 h the animals were sacrificed by cervical dislocation and stomachs were removed and opened along the greater curvature. The stomach was gently rinsed with water to remove the gastric contents and blood clots for subsequent ulcer scoring.

Measurement of ulcer index; ulcers were scored with the help of magnascope under 5x magnification using the ulcer scoring criteria described by Srivastava *et al.*,¹⁵

The following criteria were used to grade the incidence and severity of the lesions;

No ulcer	=	0
Shading of epithelium	=	10
Petechial and Franck haemorrhages	=	20
One or two ulcers	=	30
More than two ulcers	=	40
Perforated ulcers	=	50

Ulcer index is calculated from the scorings described as follows;

$$UI = US + UP \times 10^{-1}$$

Where,

US = severity of ulcer scored

UP = percentage of animals with ulcer incidence.

Percentage protection index [in case of anti- ulcer studies] and healing index [ulcer-healing study] is calculated as follows;

$$\text{Percentage protection index} = [Uc - Ut] C^{-1} \times 100$$

Where Uc = ulcer index in control group; Ut = ulcer index in treated group.

Statistical Analysis

The values are expressed as mean \pm SEM. Hypothesis testing method included one way analysis of variance (ANOVA) followed by post hoc performed with Least Significant Difference (LSD)

dunnett. p value of less than 0.005 was considered to indicate statistical significance.

RESULTS AND DISCUSSION

Several plants and herbs have been reported for the treatment of gastro-intestinal disorders including ulcers¹⁶. There are reports that ethanol-induced ulcer is due to increase secretion of proteins in the gastric juice reduced GSH and GPH levels in gastric mucosa and producing toxic oxygen derived from free radicals¹⁷. In the literature survey reports are indicating that the fruit extracts contain tannins and flavonoids which have antioxidant property and anti-oxidants have gastroprotective role against experimentally induced ulcer^{16,17}. Findings from this study showed that ethanolic fruit extracts of *Artocarpus altilis* has an effective gastroprotective activity against ethanol induced rats. Extracts contained Phenolics, Flavonoids and anti-oxidants¹⁷. The results obtained indicated that there was a decrease in ulcer incidence in all group treated with the extract in a dose dependent manner. From the statistical results showed that there was 100% ulcer incidence in both control group (100.01 ± 0.005) and 100mg/kg of extract (100.01 ± 0.005). This is because there was no administration of any kind in the control group. In the case of 100mg/kg of extract, there was no reduction in the percentage of animals with ulcer. The incidence was still very high because the dose administered was not strong enough to cause protection. The reduction of ulcer incidence may be due to the presence of flavonoids. Administration of 200mg/kg of extract showed significant reduction of ulcer incidence (33.33 ± 0.004) when compared to the control group (100.01 ± 0.005)¹⁸. While 300mg/kg of extract had the same reduction in the percentage of ulcer (16.67 ± 0.004) as the standard drug Omeprazole (16.67 ± 0.004)¹⁹. From the mean values obtained showed the ulcer index of the various groups. The fruit extract of *Artocarpus altilis* showed significant gastro-protective effects in a dose dependent manner when compared to the control group (12.67 ± 0.004) which is evident by the decrease in ulcer index^{20,21}. At dose 100mg/kg of breadfruit extract, there was a slight decrease in ulcer index (11.51 ± 0.005) when compared to ulcer index in control group (12.67 ± 0.004). At a dose of 200mg/kg of extract, there was significant decrease in ulcer index (3.66 ± 0.004) while 300mg/kg of extract had the same ulcer index (1.83 ± 0.004) as that of Omeprazole (1.83 ± 0.004) showing same potency²². From table 3, the result obtained indicated that there was zero percentage (0%) protection of animals in control group (0.01 ± 0.005) due to no administration of drug or extracts. At a dose of 100mg/kg the percentage protection was still very low (9.22 ± 0.005) when compared with Omeprazole (85.55 ± 0.004). 200mg/kg of extract had a significant percentage of ulcer protection (71.11 ± 0.004) when compared to standard drug Omeprazole (85.55 ± 0.004) while 300mg/kg of extract

had percentage ulcer protection of 85.55 ± 0.004^{23} . Apparently, the 300mg/kg of extract (85.55 ± 0.004) has the same percentage ulcer protection with that of standard drug Omeprazole (85.55 ± 0.004)²⁴. Previous studies have showed that hot water extract of *Artocarpus altilis* leaves, allowed to stand for 24hrs cures ulcer²⁵, and that ethanolic extracts of bread fruit contain flavonoids and anti-oxidants which have gastro protective effect^{16,17}, Therefore this extract possessed significant gastroprotective abilities.

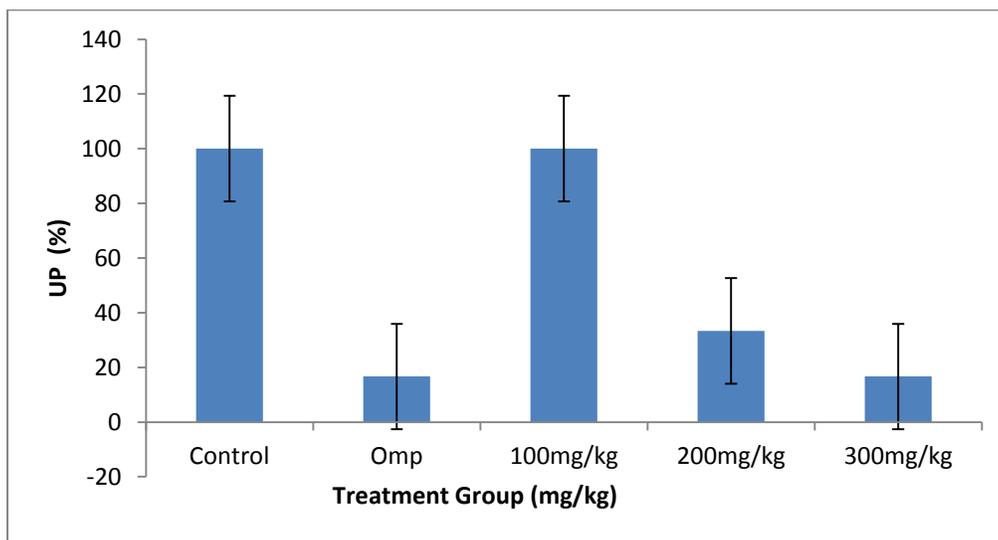
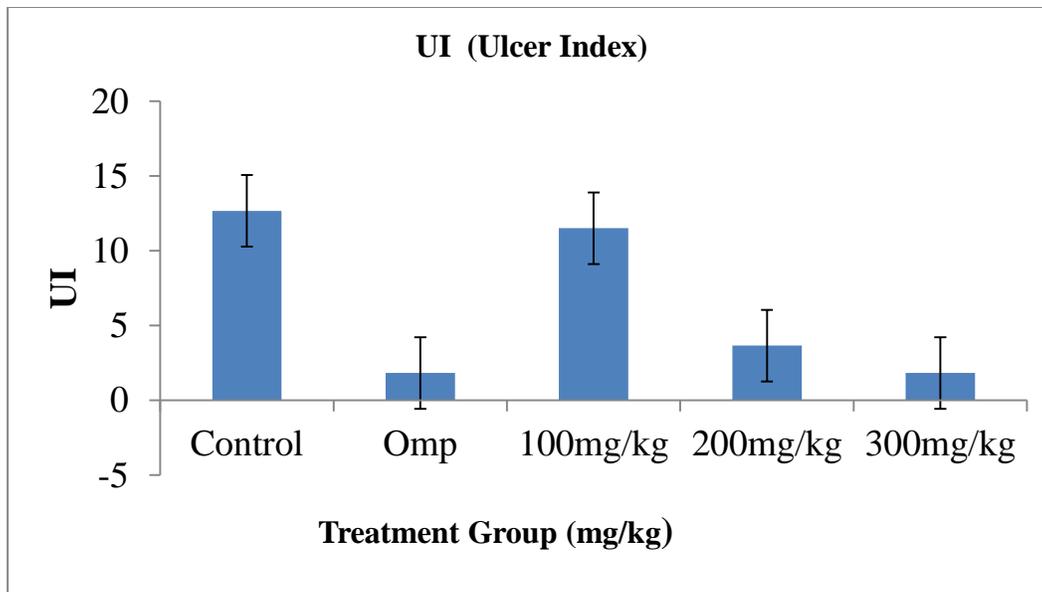


Figure 1: Chart showing percentage of animals with ulcer



Percentage of Animals With Ulcer

Figure 2: Chart showing ulcer index of animal

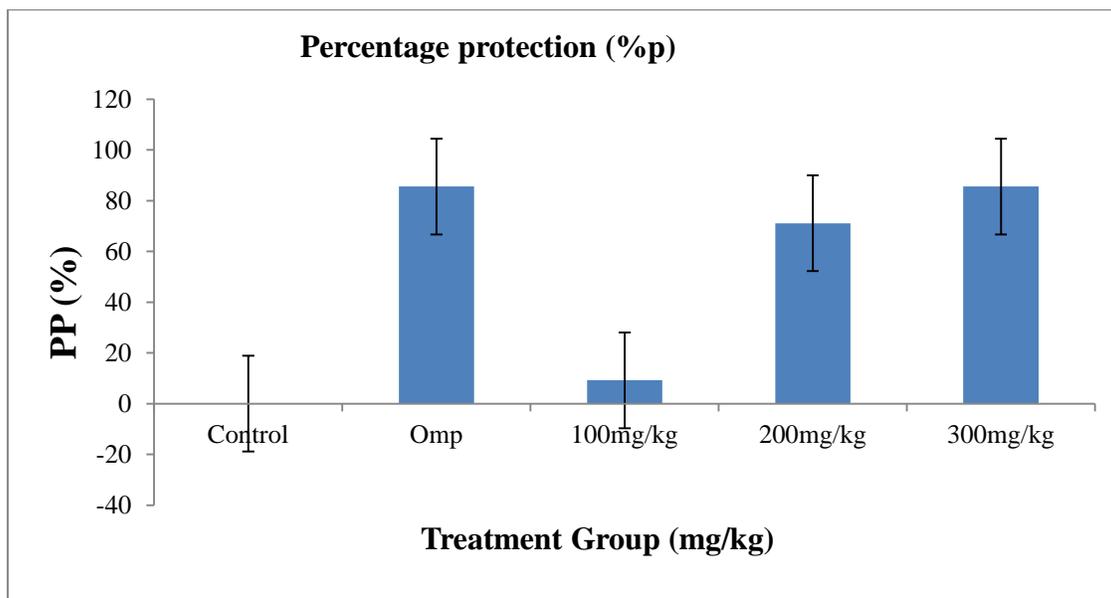


Figure 3: Showing the Ulcer Index of the Treatment Groups.

CONCLUSION

In conclusion, the studied fruit extract has appreciable decrease in ulcer incidence with the administration of 300mg/kg of ethanol extract of *Artocarpus altilis* having same potency as the standard drug (Omeprazole). It was observed also that the percentage protection was in a dose dependent manner and 300mg/kg of extract had the same protective ability as the standard drug Omeprazole. This study has shown that the ethanol extract of breadfruit possess some gastroprotective effects and can be used in the management of gastric ulcer. Also the degree of gastric protection is significantly high (85.5%).

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