

ANTI-ULCER POTENTIALS OF METHANOL EXTRACT OF *ARTOCARPUS ALTILIS* (BREADFRUIT) ON ASPIRIN INDUCED GASTRIC ULCER IN ALBINO WISTER RATS.Ajah A. A.*¹, Amah-Tariah F. S.¹, Obia O.¹ and Iwu I. C.¹

Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port-Harcourt. Rivers State, Nigeria.

***Corresponding Author: Ajah A. A.**

Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port-Harcourt. Rivers State, Nigeria.

Article Received on 20/07/2017

Article Revised on 10/08/2017

Article Accepted on 31/08/2017

ABSTRACT

This study was carried out to evaluate the anti-ulcer activities of methanol extract of breadfruit (*Artocarpus altilis*) on aspirin induced gastric ulcer. A total of 30 male albino rats weighing about 120- 200kg were used. Animals were divided into five groups of six rats each. Group I was the control group (Aspirin induced only), Group II, III IV are Low, Medium and High dose of extract (100mg/kg, 200mg/kg and 300mg/kg) respectively and Group V (Omeprazole), the standard drug used. The parameters recorded were percentage of animals with gastric ulcer (UP), ulcer index (UI) and percentage protection of ulcer (%P). From the results, the control group had highest (100%) percentage ulcer incidence (UI) while the percentage ulcer incidence decreased drastically with increasing dose of the methanol extract of breadfruit (83.32 ± 0.005 , 66.66 ± 0.005 , 33.33 ± 0.004) and omeprazole (16.16 ± 0.004). Similarly, there was a significant ($p \leq 0.005$) decrease in ulcer index from Group I through II, III, and IV to V (11.67 ± 0.00 ; 9.51 ± 0.005 ; 7.51 ± 0.005 ; 3.66 ± 0.005 and 1.82 ± 0.005) respectively and a corresponding dose dependent increase in % protective ability of the extract in comparison to the control and omeprazole (Group I 0.01 ± 0.005 ; Group II 18.58 ± 0.005 ; Group III 35.73 ± 0.004 ; Group IV 68.58 ± 0.005 and Group V 84.32 ± 0.004) However statistical analysis showed that this increase percentage protection in ulcer incidence with increasing amount of doses of extract was significant ($p \leq 0.005$). Hence, the results concluded that methanol extract of breadfruit has significant anti-ulcer activities.

KEYWORDS: breadfruit (*Artocarpus altilis*), aspirin, omeprazole, gastro protective, gastric ulcer, ulcer index.**INTRODUCTION**

Ulcer is an open sore or lesion, usually found in the skin or mucous membrane lining the alimentary tract and if it is within the stomach or duodenum, it is referred to as peptic ulcer.^[1,2] Peptic ulcer arises from an imbalance between damaging factors within the Lumen and protective mechanisms within the mucosa of the stomach and duodenum, occurring most commonly (98-99%) in either the duodenum or the stomach in the ratio of 4:1.^[3]

Ulceration lesions of GI tract are one of major side effect associated with the use of NSAIDS, alcohol, stress and ischemic reperfusion. Several herbal drugs and preparations have been shown to protect against the drug-induced gastric mucosal injury.^[3]

Since the dawn of history, mankind has relied on plants as the primary sources food and medicines. However, the last two centuries have witnessed an explosion of understanding of these natural products and how they interact with other organisms. World Health Organization estimates that 80% of the world's inhabitant rely on traditional medicines for health care; these traditional medicines are primarily plant-based.^[4]

Breadfruit is a common name for fruits belonging to the genera *Artocarpus*^[5] although it usually refers to *Artocarpus altilis*.^[6,7] Research on the efficacy of breadfruit extracts from various parts of the plants has shown promising results. *Artocarpus* extracts and metabolites from leaves stem, fruit and bark contain numerous beneficial biologically active compounds and these compounds are used in the various biological activities including antibacterial, antitubercular, antiviral, antifungal, antiplatelet, antiarthritic, tyrosinase inhibitory and cytotoxicity.^[8]

In the West Indies the yellowing leaf is brewed into tea and taken to reduce high blood pressure.^[9] The tea is also thought to control diabetes. A complex organic acid in the leaf extract (gamma-amino butyric acid) is the active ingredient, but it is not clear whether the extract is effective in lowering blood sugar. The leaves are used to treat liver disease and fevers in Taiwan^[10], and an extract from the flowers was effective in treating ear edema.^[11] Bark extracts exhibited strong cytotoxic activities against leukemia cells in tissue culture.^[12] Extracts from roots and stem barks showed some antimicrobial activity

against gram-positive bacteria and may have potential use in treating tumors.^[13]

A decoction of the leaves has been used traditionally in Indonesia for the treatment of liver cirrhosis, hypertension and diabetes^[14], but characterization of the active principles responsible for these biological effects has not yet been determined. The roots have been used as a component in Thai folk remedies for venereal diseases and cancer.^[15] Whereas in Taiwan, the stems and roots have been used traditionally for the treatment of liver cirrhosis and hypertension.^[16]

Previous research on the chemical constituents of *Artocarpus altilis* has resulted in the isolation of several classes of compounds such as flavonoids^[10] and triterpenoids.^[17] A previous study indicated that some flavonoids from *artocarpus altilis* could inhibit 5-lipoxygenase of cultured mastocytoma cells.^[11] The aqueous leaf extract *Artocarpus altilis* proved has an antihypertensive as it produces negative chronotropic and hypotensive effects through α -adrenoceptor and Ca^{2+} channel antagonism.^[18]

The ideal aim of treatment for peptic ulcer disease, are to relieve pains, heal the ulcer and delay ulcer reoccurrence. Till date, no drug meets all the goals of therapy.^[2] Despite the myriad of literature on the medicinal properties of different extracts of *Artocarpus altilis*, its effects on gastric ulcer has been poorly documented hitherto this study. The present study tends to investigate the anti-ulcer properties of methanol extract of *Artocarpus altilis* (breadfruit).

MATERIALS AND METHOD

The study was carried out in the Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences in the University of Port Harcourt, Nigeria.

Drugs: Aspirin and omeprazole were obtained from a local pharmacy duly registered by the Pharmacists' Council of Nigeria (PCN).

Animals: A total of thirty (30) male albino rats of Wister strain weighing (120-200g) were used for the study. The animals were housed under standard conditions of temperature ($23\pm 2^{\circ}C$), humidity ($55\pm 15\%$) and 12 h light (7.00 am-7.00 pm). The animals were put into a wire meshed wooden and were allowed to acclimatize for 14 days while fed with normal commercial rodent chew and allowed water *ad libitum*.

Artocarpus altilis (Parkinson) Fosberg (Moraceae) known as breadfruit is widely distributed in tropical and subtropical regions, including Indonesia. A decoction of the leaves has been used traditionally in Indonesia for the treatment of liver cirrhosis, hypertension and diabetes (Kasahara and Hemmi, 1986), but characterization of the active principles responsible for these biological

effects has not yet been determined. Previous research on the chemical constituents of *A. altilis* has resulted in the isolation of several classes of compounds such as flavonoids (Lin and Shieh, 1992; Ashok et al., 2002) and triterpenoids (Altman and Zito, 1976). A previous study indicated that some flavonoids from *A. altilis* could inhibit 5-lipoxygenase of cultured mastocytoma cells (Koshihara et al., 1988). To our knowledge, no reports have been recorded of antiatherosclerotic phytochemicals from this plant. *Artocarpus altilis* (Parkinson) Fosberg (Moraceae) known as breadfruit is widely distributed in tropical and subtropical regions, including Indonesia. A decoction of the leaves has been used traditionally in Indonesia for the treatment of liver cirrhosis, hypertension and diabetes (Kasahara and Hemmi, 1986), but characterization of the active principles responsible for these biological effects has not yet been determined. Previous research on the chemical constituents of *A. altilis* has resulted in the isolation of several classes of compounds such as flavonoids (Lin and Shieh, 1992; Ashok et al., 2002) and triterpenoids (Altman and Zito, 1976). A previous study indicated that some flavonoids from *A. altilis* could inhibit 5-lipoxygenase of cultured mastocytoma cells (Koshihara et al., 1988). To our knowledge, no reports have been recorded of antiatherosclerotic phytochemicals from this plant.

Plant Materials

The fruit of *Artocarpus altilis* were bought from local vendors in Choba Market in Port-Harcourt, identified and authenticated by a staff of the Forestry Research Institute of Nigeria (FRIN), Ibadan, where the Voucher No FHI 110483 was given. Fresh breadfruit seeds were thoroughly cleaned with deionized water, air dried at room temperature, powdered by a Willey Miller, sieved and the fine powder was stored in a clean glass container.^[20] The ground powder (260g) was extracted by cold extraction for 72 hours using methanol (MeOH). The MeOH extract provides a semi-solid residue (ms; 47.8G) and the percentage yield is 18.4%. this residue was dried in a rotary evaporator and stored in a dry sample container.

Preparation of Stock Solution and Reagents:

Omeprazole (OMP): 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).

Aspirin (Asp): Four tablets of aspirin weighing 300mg each was dissolved in 10ml of distilled water to make a stock of 30mg/ml to be administered at a dose of 150mg/kg Po.

Treatment: The animals were randomly divided into five groups of six rats each. Groups I and V served as positive and negative controls administered with normal saline and standard drug omeprazole; 10mg/kg per oral (Po). Group II, III and IV served as the test groups (low, medium and high dose groups) administered with

100mg/kg, 200mg/kg and 300mg/kg of MEAA respectively.^[21] The rats were fasted for 24 hours before the experiments, but were allowed free access to clean drinking water.

Anti-Ulcer Study: Aspirin, at a dose of 150mg/kg, po was administered to induce ulcer after 45 minutes of treatment with methanol extract of *Artocarpus altilis* (MEAA) at low, medium, and high doses of 100, 200, and 300mg/kg po respectively and omeprazole (10mg/kg, po). The animals were sacrificed by cervical dislocation 5 hours after aspirin treatment^[2] and the stomach was dissected out and the lesion was scored.

Measurement of ulcer index

Ulcers were scored with the help of magnascope under 5X magnification using the ulcer scoring criteria. The following criteria were used to grade the incidence and severity of the lesions:

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

Ulcer index (UI) is calculated from scorings described as follows:

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

Where US = mean severity of ulcer score.

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:

$$\text{Percentage protection index and healing index} = (Uc - Ut) C^{-1} \times 100$$

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 and 0.001 as highly significant respectively.

RESULT

The result of the study to evaluate the anti-ulcer activities of methanol extract of *Artocarpus altilis* (breadfruit) on aspirin induced ulcer in albino Wister rats is presented in the tables below. Results were presented as mean values \pm S.E.M. Mean extract effects.

TABLE 1: Shows the Percentage of animals with ulcer (UP).

GROUP	UP
Control	100 \pm 0.005
100mg/kg	83.32 \pm 0.005
200mg/kg	66.66 \pm 0.005
300mg/kg	33.33 \pm 0.004
Omeprazole	16.16 \pm 0.004

TABLE 2: Shows the Ulcer index (UI) in animals.

GROUP	UI
Control	11.67 \pm 0.00
100mg/kg	9.51 \pm 0.005
200mg/kg	7.51 \pm 0.005
300mg/kg	3.66 \pm 0.005
Omeprazole	1.82 \pm 0.005

TABLE 3: shows the percentage of protection (% protection).

GROUP	% PROTECTION
Control	0.01 \pm 0.005
100mg/kg	18.58 \pm 0.005
200mg/kg	35.73 \pm 0.004
300mg/kg	68.58 \pm 0.005
Omeprazole	84.32 \pm 0.004

DISCUSSION

The anti-ulcer activities of methanol extract of breadfruit was experimented in albino Wister rats where aspirin was used to induce ulcer. The statistical result obtained shows a significant decrease ($P \leq 0.005$) in ulcer incidence in all the experimental groups treated with breadfruit extract compared to the control group which is in concordance to earlier reports^[6], that all doses of breadfruit extract administered were able to decrease stomach pains (which could be related to ulcer).

Artocarpus altilis showed a dose dependent decrease in percentage incidence of ulcer. From table 1, It is clear that the percentage of animals with ulcer (stomach inflammation) decreases with increasing dose of the extract, but there was a drastic decrease in the omeprazole group (Standard drug) in comparison with control group that shows a 100% ulcer incidence since there was induction of ulcer with aspirin and without treatment. In comparison, the mean values obtained show that at low dose (100mg/kg) the percentage of animals with ulcer decreased from the (100 \pm 0.005) in control group to (83.32 \pm 0.005) but lesser when compared to the standard drug. At medium and high doses of 200mg/kg and 300mg/kg, the percentage of animals with ulcer further decreased to (66.66 \pm 0.005) and (33.33 \pm 0.004) respectively and also to (16.16 \pm 0.004) in the Omeprazole group (Standard drug).

In table 2, the mean values obtained for ulcer index (UI) showed a significant decrease ($P \leq 0.005$) in the ulcer incidence in the respective groups treated with the methanol extract of breadfruit. The ulcer incidence in the

control group showed the highest ulcer index (11.67 ± 0.005) since no extract nor drug was administered to animals in that group.^[19] However, in comparing the control group and 100mg/kg group in the previous chapter, there was a slight decrease in the ulcer index from (11.67 ± 0.005) to (9.51 ± 0.005). This clearly shows the slight effect of the extract at low dose of 100mg/kg on ulcer. The table for ulcer index showed that the 200mg/kg group, 300mg/kg group and omeprazole group also had a slight decrease in ulcer index from (7.51 ± 0.005), to (3.66 ± 0.005), and (1.82 ± 0.005) for the Omeprazole group (standard drug). This clearly shows that the potency of MEAA in aspirin induced gastric ulcer is dose dependent.

The values obtained in group 2 (100mg/kg) of table 3 for ulcer protection showed a significant increase in % protection (18.58 ± 0.005) when compared to the control (group 1) with % protection of (0.01 ± 0.005) but less efficacious when compared to the standard drug (group 5) from (18.58 ± 0.005) to (85.35 ± 0.004) but the mean values in group 3 and 4 (200mg/kg) and 300mg/kg) also showed a very significant increase in % protection (35.73 ± 0.004 and 68.58 ± 0.005) respectively in comparison with the control group. The result also shows that group 3 and 4 have increasing efficacy or high therapeutic effect but not as the standard drug (omeprazole). It is clear from this table that the higher the dose of the extract administered, the higher the decrease in ulcer incidence. This shows that breadfruit (*Artocarpus altilis*) extract has potential values in the treatment of gastrointestinal problems.^[22,19] The results obtained reveal that the breadfruit (*Artocarpus altilis*) extract truly has some anti-ulcer properties.

CONCLUSION/ RECOMMENDATION

Conclusively, the results show that the methanol extract of breadfruit (*Artocarpus altilis*) has potential anti-ulcer activities. Its mechanism might be through the release of prostaglandins and possibly free radical scavengers which protect the gastric mucosa. Breadfruit (*Artocarpus altilis*) could be recommended to patients with ulcer but as a supplement, especially to patients who cannot rely only on anti-ulcer drugs to manage or cure ulcer. Though the mechanisms of action of the methanol extract of breadfruit on gastric mucosa is not known from the parameters studied in this research. Therefore, I recommend that further research should be carried out to ascertain the mechanism of action of the gastro-protective activity of methanol extract of breadfruit.

REFERENCE

1. A. A. Mahmood, Abdalbasit A. Mariod, Fouad Al-Bayaty and Siddig Ibrahim Abdel-Wahab. Anti-ulcerogenic activity of *Gynura procumbens* leaf extract against experimentally-induced gastric lesions in rats. *Journal of Medicinal Plants Research*, 18 April, 2010; 4(8): 685-691.
2. R.K. Goel, K. Sairam, M. Dora Babu, I.A. Tavares, A. Raman. *In vitro* evaluation of *Bacopa monniera* on anti-*Helicobacter pylori* activity and accumulation of prostaglandins. *Phytomedicine*, 2003; 10(6-7): 523-527.
3. AJ Vanisree, K Mitra, Devi CS Shyamala. Antiulcerogenic effect of UL-409 against experimentally induced gastric ulcer in rats. *Indian Journal of Pharmacology*, 1996; 28(4): 265-268.
4. Akah, P.A, Orisakwe, O.E, Gamaniel, K.S, Shittu, A.J *Ethnopharmacol*, 1998; 62: 123-7.
5. Morton, J. Breadfruit, 1987; 50-58 in fruits of warm climates. morton collectanea. university of miami, coral gables, florida.
6. Ragone, D. Breadfruit: Diversity, conservation and potential. In proceedings of the 1st International Symposium on Breadfruit Research Development. *Acta Horticulture*, 2007; 757: 19-30.
7. Bailey, L.H., The standard Encyclopedia of Horticulture. The Mac-millan co. New York, 1942; 401-402.
8. Jagtap U.B., Bapat VA. Artocarpus: A review of its traditional uses, phytochemistry and pharmacology. *Journal of Ethnopharmacology*, 2004.
9. McIntoch, C. and P.Manchew. The breadfruit in nutrition and health. *Tropical Fruits Newsl*, 1993; 6: 5-6.
10. Lin, C.N., W.L. Shieh and T.T. Jong. a pyranodihydrobenzoxanthone epoxide from artocarpus communi. *Phytochemistry*, 1992; 31(7): 2563-2564.
11. Koshihara, Y., Y. Fujimoto and H. Inoue, A new 5-lipoxygenase selective inhibitor derived from *Artocarpus communis* strongly inhibits arachidonic acid-induced ear edema. *Biochem. Pharmacol*, 1988; 37: 2161-2165.
12. Fujimoto, Y., X.X. Zhang, M. Kirisawa, J. Uzawa and M.Sumatra. New flavones from artocarpus communi forest. *chem, and pharmac. Bull*, 1990; 38(6): 1787-1789.
13. Sundarro, K., I. Burrows, M. Kuduk, Y.D. Yi, M.H. Chung, N.J. Suh and I.M. Chang. preliminary screening of antibacterial and antitumor activities of papua new guinean native medicinal plants. *int. J. Pharmacognosy*, 1993; 31: 1, 3-6.
14. Kasahara S and Hemini S. Medicinal Herb Index in Indonesia, Bogor, Indonesia, P.T. Eisai Indonesia., 1986; 1-2.
15. Wutthithammaweach W. *Encyclopedia of herb: compilation of Thai pharmaceuticals*, Edn, Odion store, Bangkok, 1997; 123.
16. Chen C.C., Huang Y.L., and Ou J.C. Three new prenylflavones from *Artocarpus altilis*, *J. Nat. Prod.*, 1993; 56: 1594-7.
17. Altman, L.J. and S.W. Zito. Sterols and triterpenes from the fruit of *Artocarpus altilis*. *Phytochemistry*, 1976; 15(5): 829-830.
18. Nwokocho CR, Owu DU, McLaren M, Murray J, Delgoda R, Thaxter K, McCalla G, Young L. Possible mechanisms of action of the aqueous extract of *Artocarpus altilis* (breadfruit) leaves in producing hypotension in normotensive Sprague-

- Dawley rats. *Pharmaceutical Biology*, 2012; 50(9): 1096-1102.
19. Navarro, M, S. Malres, S.P. Labouisse & O, Rounsard. Vanuatu breadfruit project: Survey on botanical diversity and traditional uses of *Artocarpus altilis* in proceeding of the 1st International symposium on Breadfruit Research and development. *Acta Horticulture*, 2007; 757: 81-88.
 20. Ajayi IA, Ajibade O, Oderinde RA. Preliminary phytochemical analysis of some plant seeds. *Res. J Chem Sci.*, 2011; 1(3): 58-62.
 21. Ajah Austin A, Olorunfemi O Joyce, Onasanwo A. Samuel Gastro-Protective Effect of Ethanolic Extract of *Artocarpus Altilis* (Breadfruit) on Alcohol Induced Acute Ulcer Model in Albino Wistar Rats. *Am. J. PharmTech Res.*, 2015; 5(1): 1-9.
 22. Ragone Diane. Breadfruit. *Artocarpus altilis* (Parkinson) Fosberg. Promoting the conservation and use of underutilized and neglected crops, 1997.