



## AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: <http://www.ajptr.com/>

### Anti-Ulcer Activities of Methanolic Extract of *Artocarpusaltilis* (Breadfruit) on Alcohol Induced Acute Ulcer Model in Albino Wistar Rats

Ajah AA<sup>1\*</sup>, Olorunfemi OJ<sup>1</sup>, Chike CPR<sup>1</sup>, Balogun ME,<sup>2</sup> Obia O<sup>3</sup>, Adienbo O<sup>3</sup>

1. Department of Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt, Choba, Port Harcourt, Nigeria.

2. Department of Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Ebonyi State University, Abakaliki, Nigeria.

3. Department of Anatomy, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt, Choba, Port Harcourt, Nigeria.

#### ABSTRACT

The present work was designed to investigate the anti-ulcer activities of methanolic extract of *artocarpusaltilis* [breadfruit] on alcohol induce ulcer in male albino rats. Animals were administered orally with a single dose of 98% alcohol [depending on the animals' weight] to induce ulcer. This resulted in significant increase in ulcer occurrence [exacerbation]. Both the induced and normal rats were divided into six groups of 5 rats each. Group 1 was the control group [induced but not treated] while group 2 received 100mg/kg dose of aqueous extract of *artocarpusaltilis*. Group 3 and 4 received 200mg/kg and 300mg/kg dose of aqueous extract of *artocarpusaltilis* respectively. Group 5 received 10mg/kg per oral dose of omeprazole [standard drug]. Administration of methanolic extract of *artocarpusaltilis* produce a decrease in ulcer occurrence in induced rats. The decrease in ulcer occurrence was significant [ $p < 0.005$ ] with all the groups treated with methanolic extract of *artocarpusaltilis* when compared to the control group. But group 3 and 4 exclusively showed same potency when compared to group 5 [standard drug]. The decrease in ulcer incidence when compared to the control group [ulcer induced but not treated] and for exhibiting same potency with the standard drug shows that the extract of *artocarpusaltilis* is effective in controlling ulcer and can be used as a substitute for the standard drug in managing or treating/controlling ulcer. Conclusively, methanolic extract of *artocarpusaltilis* has tremendous beneficial anti-ulcer values in the treatment of ulcer following oral administration.

**Keyword:** *Artocarpusaltilis*, Omeprazole, anti-ulcer activities, gastric ulcer, ulcer index.

\*Corresponding Author Email: [Atriplaus@gmail.com](mailto:Atriplaus@gmail.com)

Received 07 February 2015, Accepted 15 March 2015

Please cite this article as: Ajah AA *et al.*, Anti-Ulcer Activities of Methanolic Extract of *Artocarpusaltilis* (Breadfruit) on Alcohol Induced Acute Ulcer Model in Albino Wistar Rats. American Journal of PharmTech Research 2015.

## INTRODUCTION

Ulcer disease is a problem of the gastrointestinal tract characterized by mucosal damage secondary to pepsin and gastrin acid secretion, it usually occurs in the stomach and proximal duodenum; less commonly, it occurs in the lower oesophagus, the distal duodenum, or the jejunum as in oppose hyper secretory state such as Zollinger- Ellison syndrome, in hiatal hernia (Bipat *et al.*, 2008)<sup>1</sup>. Approximately 500,000 persons develop peptic ulcer disease in the United States each year (Sundarrao *et al.*, 1993)<sup>2</sup>. In 70 per cent of patients it occurs between the ages of 25 and 64 years (Sonnenberg & Everhart. 1996)<sup>3</sup>. However, the incidence of peptic ulcers is declining, possibly as a result of the increasing use of proton pump inhibitors and a little diversification into natural medicinal plants and decreasing rate of helicobacter pylori infection (Bipat *et al.*, 2008)<sup>1</sup>. The incidence of duodenal ulcers has dropped significantly during the last few decades, while the incidence of gastric ulcers has shown a small increase in recent years, which is mainly caused by the wide spread use of NSAIDs (Bashinskaya *et al.*, 2011)<sup>4</sup>. The two most important developments associated with the overall decreased rates of peptic ulcers disease are the discovery of effective and potent acid suppressants and the identification of H. pylori as the main causative agent (Malfertheiner *et al.*, 2009)<sup>5</sup>. In essence, as the infectious cause of gastric ulceration is being successfully fought, a higher percentage of the U.S medication primarily NSAIDs. In most industrialized countries, the prevalence of H. pylori infections leading to symptoms roughly matches age (i.e. 20 percent at age 20, 30 percent at age 30, 60 percent at age 60 etc.), although prevalence is even higher in third world countries (Brown, 2000)<sup>6</sup>. Only a minority of cases of H. pylori infection will eventually lead to ulceration, but a large proportion will develop non-specific discomfort, abdominal pain/gastritis. Gastric ulcers are more common in males; especially those within the ages of 55 and 65. approximately, 500,000 new cases of peptic ulcers are diagnosed yearly, with gastric varieties comprising about 16 per cent of those. Breadfruit (*artocarpusaltilis*), is a member of moraceae plant family. The family moracea contain over 50 genera and over 800 plant species, which are mostly tropical and subtropical, also include a number of economically important species. The name artocarpus is derived from Greek words "artos-bread" and "carpus-fruit" (Bailey, 1942)<sup>7</sup>. the genus 'artocarpus' contains about 50-60 species distributed throughout the indo-Malaysia and in south china (Campbell, 1984)<sup>8</sup>

## MATERIALS AND METHOD

### Preparation of Stock Solution

OMEPRAZOLE(OMP); omeprazole tablet weighting 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 Materials**

*Artocarpusaltil* is (breadfruit) were purchased from Port Harcourt local market. The fruits were identified and confirmed for use by a botanist of the department of plant science and biotechnology herbarium, university of port-Harcourt.

### **Preparation of the Plant Extract**

#### **Methanol Extract**

Powdered dried *altocarpusaltil* is (7.5kg) extracted by cold extraction for 72 hours using methanol (meoH). The meoH extract provide a semi-solid residue (AA; 7.2kg) and the percentage yield is 96 per cent.

#### **Procedures Involved**

The powdered *altocarpusaltil* is fruit seed was soaked in a glass container and left for a period of 72 hours after which the powdered dried breadfruit settles and the clear liquid is decanted and then evaporated using rotatory evaporator. The extract was evaporated to semi-solid form (Odec, 2001)<sup>9</sup>.

#### **Phytochemical Screening**

*Artocarpusaltil* is contain an array of biologically active plant chemicals including; tannins, phenolics,  $\beta$ -sitosterol, flavonoid, glycosides, saponins, gums and resins, were screened in the laboratory (Harbone, 1998; Raaman 2006; Jamunaet *al.* 2001)<sup>10,11,12</sup>. The anti-ulcer effect is more pronounced in the seed of *artocarpusaltilis* were these chemicals are found in greater abundance (Enoset *al.*2009)<sup>13</sup>.

#### **Experimental Animals**

A total of thirty (30) male albino rat of wistar strain weighing (120-200g) were obtained from the central animal house, faculty of basic medical sciences, college of health sciences, university of port-Harcourt, port-Harcourt, Nigeria. They were maintained under standard laboratory conditions and were feed with standard rat's pellet and tap water ad libitum. They were acclimatized for 2 weeks after which they were divided into groups. Wistar strain albino rats were used for this work because of the following merits it has over other laboratory/ experimental animals. It is easily accessible, cheap, and it's physiology in terms of the gastrointestinal tract is almost identical to that of humans.

#### **Experimental Procedures**

The rats were fasted of food for two days (48hours) before the experiment, but allow free access to clean drinking water. The study was carried out with the introduction of ulcer under acute model

thus;

### Anti-Ulcer Study

Gastric ulcer was induced in rats by administering absolute alcohol (1ml/200g po) (Suleyman et al., 2002)<sup>14</sup>. OMP and MEAA were administered 45 minutes before alcohol treatment. The animals were sacrificed 1hr after the treatment and the stomachs were excised to observe gastric lesions, and ulcer scored. Measurement of ulcer index; ulcers were scored using the ulcer scoring criteria described by Srivastava *et al.*, 1991<sup>15</sup>. The following criteria below 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;

$$UI = US + UP / 10$$

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;

$$\text{Percentage protection index} = \frac{Uc - Ut}{Cx} \times 100$$

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

### Experimental Design

30 male albino rat of wistar strain were divided into five groups of six animals each.

Group 1 [control]; 6 rats [ulcer was induced but was not treated]

Group 2 [low dose]; 6 rats [ulcer was induced but treated with 100mg/kg of MEAA]

Group 3 [medium dose]; 6 rats [ulcer was induced but treated with 200mg/kg of MEAA]

Group 4 [high dose]; 6 rats [ulcer induced but treated with 300mg/kg of MEAA]

Group 5 [OMP]; 6 rats [ulcer induced, treated with a standard drug, Omeprazole].

### Acute Toxicity Test

To determine the lethal dose of methanol extract of *artocarpusaltit is* to be administered to experimental animals, series of dose dependent test were carried out which are summarized in the table below;

**Table 2: Result of Acute Toxicity Test for methanol extract of *artocarpusaltilis***

Media	Qty IN grams	Observations	No of death	Lethal concentrations	Lethal Dose	Safe dose
Methanol	0.5	Normal, stable,	Not sig.	>1g (1, 2,3g) etc.	0.5g	100, 200, 300mg or less per kg b.w.
	1	Sluggish, tail wagging, anorexic, death	Sig.			
	2-3	Neurological deficit, slow, death	Sig.			

### Calculation of Concentration/ Dosage

The calculation of the concentration was mainly based on the highest weight of the animals (rats) in each cage, (ISO, 1989b) as follows ; (Hodge and Sterner scale (1980)<sup>16</sup>. In preparation of methanol extract of altocarpusaltil is high dose (300mg/kg)

Volume (vol.) = weight x dose/1000 x concentration(c)

$$1\text{ml} = 200 \times 300/1000 \times c = 60\text{mg/ml} = 360\text{mg}/6\text{ml}$$

I.e. for every 60mg of the extract measured, 1ml of distilled water was mixed with it.

And for every 360mg of the extract measured, 6mls of distilled water was added.

For medium dose (200mg/kg)

$$\text{Vol,} = 200 \times 200/1000 \times c = 40\text{mg/ml} = 240\text{mg}/6\text{ml}$$

Again, for every 40mg of the extract correctly measured, 1ml of distilled water was added for medium dose. And for every 240mg of extract, 6mls of distilled water was added.

For low dose (100mg/kg)

$$\text{Vol.} = 200 \times 100/1000 \times c = 20\text{mg/ml} = 120\text{mg}/6\text{ml}$$

This means that, in every 20mg of extract well measured, just an ml of distilled water was added and for 120mg of extract, 6mls of distilled water was added.

In total, in 720mg [360 for high dose + 240 for medium dose + 120 for low dose] of extract measured, 18 mills of distilled water be added to it.

In preparation of omeprazole (OMP);

Omp tablet weighing 20mg was dissolved in 10mls of distilled water to make a stock solution of 2mg/ml to be administered at a dose of 10mg/kg.

$$\text{Vol.} = 200 \times 10/100 \times C = 2\text{mg/ml}$$

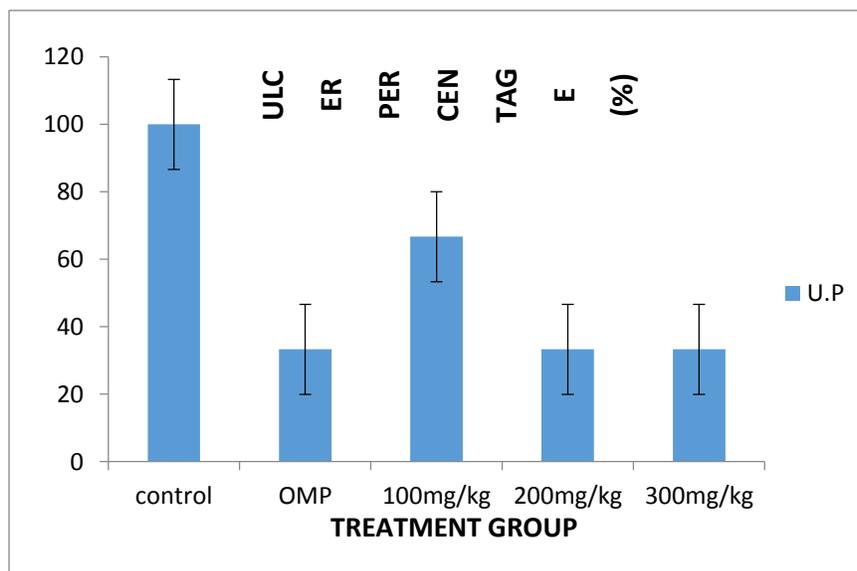
I.e. in 20mg of omp 10mls of distilled water was added.

### RESULT AND DISCUSSION

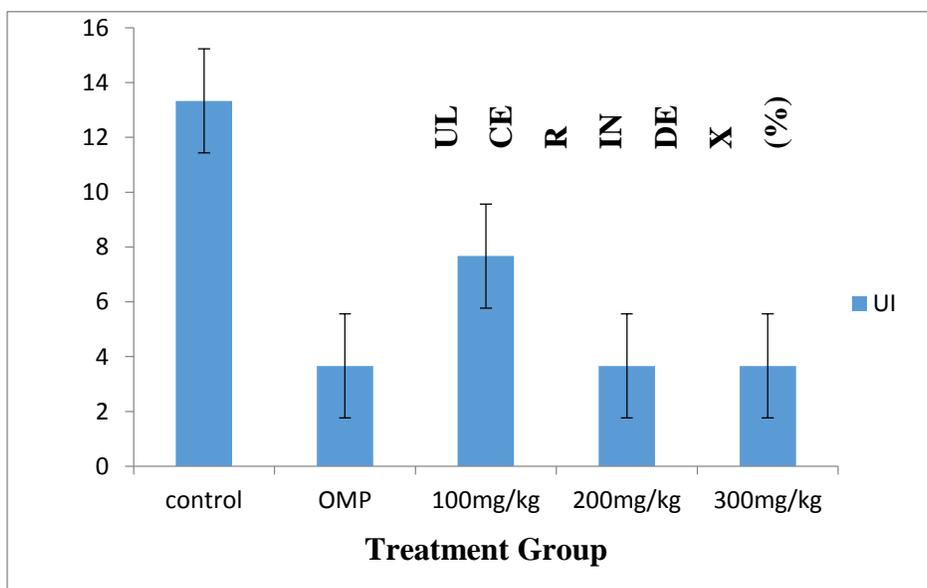
The values are expressed as mean  $\pm$  SEM. Hypothesis testing method included one way analysis of variance (ANOVA) followed by post hoc performed with Least Significant Difference (LSD) dunnnett. p value of less than 0.005 was considered to indicate statistical significance. Effect of

anti-ulcer activities of methanolic extract of *artocarpusaltilis* was experimented in rats where alcohol (98%) was used to induce ulcer. The statistical result obtained revealed a mark/significant decrease ( $P \leq 0.005$ ) in ulcer incidence in all the experimental groups treated with *artocarpusaltilis* extract as compared to the control group which corresponds with Ragone (2007)<sup>17</sup> in concluding that all doses of *altocarpusaltilis* extract administered were able to decrease the incidence of stomach aches (which could be related to ulcer) significantly. From the statistical result, it is clear from the first table in chapter 4 that the percentage of animals with ulcer (stomach inflammation and pain) decreases drastically with increasing dose of the extract (McClatchey, 1993)<sup>18</sup>. The table shows a 100% of animals with ulcer in the control group since it were without any form of protection. By way of comparison, the mean values obtained showed that at dose 100mg/kg the percentage of animals with ulcer decrease from the (100±0.005) in control to (66.67±0.004), but higher when compared to the standard drug. At the dose of 200mg/kg and 300mg/kg the percentage of animals with ulcer further decrease to (33.31±0.005) and (33.31±0.005) respectively for the 200mg/kg, 300mg/kg and the standard drug (omeprazole). It can be deduce from the forgoing, that after the administration of the extract, there was a gradual reduction in the percentage of animals with ulcer. And at dose 200mg/kg and 300mg/kg equal efficacy was witnessed, and these same doses, are as efficacious as the standard drug itself with exactly the same efficacy according to the work. The mean values obtained for ulcer index showed a significant decrease ( $p \leq 0.005$ ) in the incidence of ulcer in the respective groups treated with the extract of breadfruit as epitomise in the second table in the previous chapter. The ulcer incidence in the control group (group 1) showed the highest ulcer index (13.33±0.004) since no extract was administered to the animals in that group (Navarro *et al.*, 2007)<sup>19</sup>. However, comparing the group 1 above to group 2, there was a slight decrease in the ulcer index from (13.33±0.004) for control to (7.67±0.004) for the group 2. This is a clear manifestation of the slight effect of the extract at dose 100mg/kg on ulcer. A clear picture of the table for ulcer index showed that group 3 and 4 has the same values as group 5 (standard drug) from (3.66±0.004) for group 3 and 4 respectively and (3.66±0.004) for group 5. This implies that the extract containing 200mg/kg and 300mg/kg has same efficacy as the standard drug (omeprazole) looking at their potency on alcohol induced ulcer. The statistical values obtained in group 2 (100mg/kg) in the previous chapter for percentage protection showed a significant decrease in ulcer incidence when compared to the control group (group 1) from (42.45±0.005) to (0.005±0.003) respectively but less efficacious when compared to the standard drug (group 5) from (42.45±0.005) to (72.54±0.003). but the mean values in group 3 and 4 (200mg/kg) and (300mg/kg) showed a very significant decrease in the incidence of ulcer

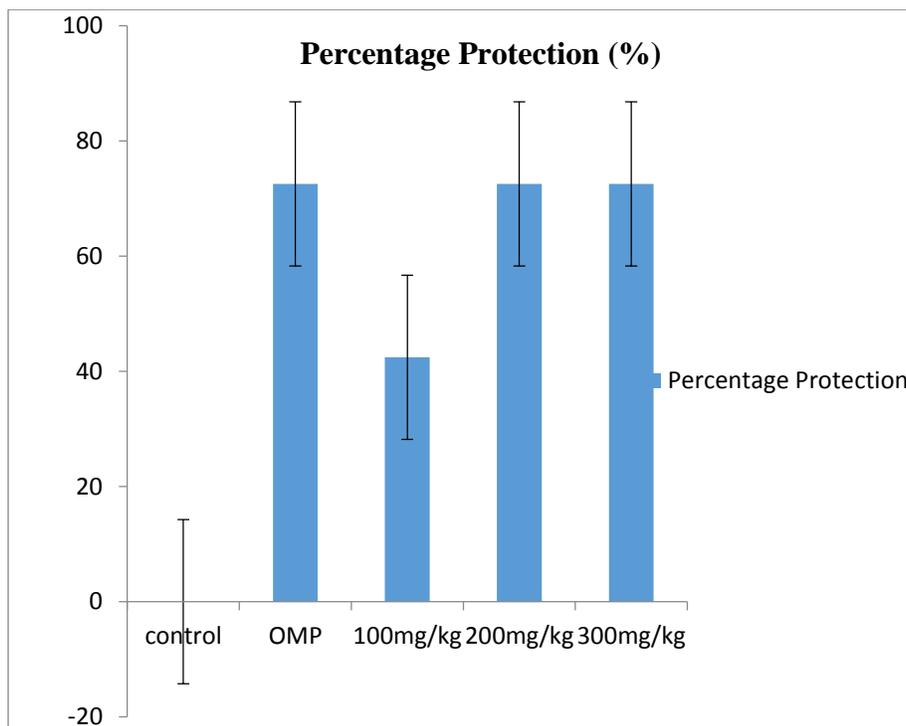
(high therapeutic effect) when compared to the standard drug (group 5), in fact the statistical result revealed that both group 3 and 4 have the same efficacy/potency or therapeutic effect as the standard drug (group 5) from  $(72.54 \pm 0.003)$  for group 3 and 4 respectively to  $(72.54 \pm 0.003)$  for the standard drug (group 5), it is clear from the above discussion that the higher the dose of the extract administered the higher the level at which it decreased the incidence of ulcer in rats. This anchored that artocarpusaltilis extract has tremendous beneficial values in the treatment of gastrointestinal problems (Ragone, 1997; Navarro *et al.*2007). The result obtained for the anti-ulcer activities revealed that the methanolic extract of artocarpusaltilis have same potency compared to the known anti-ulcer drug (omeprazole).



**Figure 1: Chart Showing the Percentage of Animals with Ulcer**



**Figure 2: Chart Showing the Ulcer Index of Animals**



**Figure 3: Showing the Percentage Protection of Animals to Ulcer Treatment Group**

## CONCLUSION

The result of this study indicated that methanolic extract of artocarpusaltilis at an oral dose of 200mg/kg and 300mg/kg body weight can alleviate alcohol induced ulcer in a rat model for a period of two hours and above. However, with the speculation on the unidentified mechanism of action of the methanolic extract, I do not eliminate the possibility of mark beneficial effects in the treatment of ulcer. Methanolic extract of artocarpusaltilis administration may be useful as an adjunct therapy or supplement to oral anti-ulcer agents in the management of ulcer.

## RECOMMENDATION

In the light of the above conclusion, methanolic extract of artocarpusaltilis could be recommended to ulcer patients, but most especially as a supplement to patients that cannot rely only on anti-ulcer drugs to control ulcer in preventing the onset of secondary complications. Therefore, more study should be carried out to examine its safety in treatment. Hence, it is hereby necessary that further studies should be carried out to evaluate the mechanism of action of methanolic extract of artocarpusaltilis in Anti-ulcer activities.

## REFERENCES

1. Bipat, R, JR. Toelsie, RF. Joemmanbaks, JM. Gummels, J. Klaverweide, N. Jhanjan, S. Orie & K. Ramjiawan. Effects of plants popularly used against hypertension on norepinephrine-stimulated guinea pig atria. *Pharmacognosy Magazine* 2008; 4(13):12.

2. Sundarrao K Burrows I, Kuduk M. Preliminary screening of anti-bacterial and anti-tumor activities of Papuan new Guinean active medicinal plants. *Pharm. Biol* 1993; 31: 3-6.
3. Sonnenberg A, Everhart JE. The prevalence of self-reported peptic ulcer in the United States. *Am J Public Health* 1996; 86:200-5.
4. Bashinskaya B. et al. Trends in Peptic Ulcer Disease and the Identification of *Helicobacter Pylori* as a Causative Organism: Population-based Estimates from US Nationwide Inpatient Sample. *J Global Infectious Diseases*. 2011; 3 (4):36 370.
5. Malfertheiner P, Chan FK, McColl KE. Peptic ulcer disease. *Lancet*, vol. 2009; 374:1449-1461.
6. Brown LM. “*Helicobacter pylori*: epidemiology and routes of transmission.” *Epidemiological Review*, 2000;22(2):283–97.
7. Bailey, LH. The standard Encyclopaedia of Horticulture. The Macmillan co. New York, 1942:401-402.
8. Campbell, CW. Tropical fruits and nuts in: CRC hand book of tropical crops. CRC press Inc., Boca Raton Florida, USA. 1984.
9. Odec J. Guidelines for testing of chemicals, acute oral toxicity-fixed dose procedure. OECD, 2001:1-3.
10. Harbone JB.1998. Phytochemical methods; a guide to modern techniques of plant analysis. Chapman and hall, 1998:279.
11. Raaman N. phytochemical techniques. New India Publishing Agency2006: 306.
12. Jamuna KS, Ramesh CK, Srinivasta TR, Raghu KL. In vitro antioxidant studies in some common fruits. *Int J Pham Sci* 2011; 3[1]; 60-63.
13. Enos T, Britanto D, Yohana A. anti-ulcer properties of diethyl ether extract of wood from *artocarpusaltilis*. *Tropical J Pharma Res* 2009; 8[4]: 317-324.
14. Suleyman H, Banoglu N, Ahmet K. Melatonin prevents ethanol induced gastric mucosal damage possibly due to its antioxidant effect. *Plenum Publishing Corporation* 2002:856-861.
15. Srivastava S, Vijay K, Sharad S. evaluation of ulcerogenic and ulcer-healing properties of *ocinum sanctum linn*. *J ethnopharmacology*1991:197-206.
16. Hodge, H.C. and Sterner, J. H. Determination of substances acute toxicity by LD B50B. *Amer. Industrial Hyg. Assoc.* 1943; 10:93.
17. Ragone D. Breadfruit, *Artocarpusaltilis (Parkinson) Fosberg*. International Plant Genetic Resources Institute, Rome. 1997.

18. McClatchey, WC. The Traditional Rotuman Medicinal System. Brigham Young University, Provo, Utah. 1993.
19. Navarro M, S. Malres JP. Labouisse & O. Rroupsard. Vanuatu breadfruit project: Survey on botanical diversity and traditional uses of *Artocarpusaltilis*. In Proceedings of the 1st International Symposium on Breadfruit Research and Development. Acta Horticulture 2007; 757:81- 88.

***AJPTR is***

- Peer-reviewed
- bimonthly
- Rapid publication

Submit your manuscript at: [editor@ajptr.com](mailto:editor@ajptr.com)

