International Journal of Advanced Research in Biological Sciences
ISSN: 2348-8069
www.ijarbs.com
DOI: 10.22192/ijarbs Coden: IJARQG(USA) Volume 4, Issue 10 - 2017

Research Article

DOI: http://dx.doi.org/10.22192/ijarbs.2017.04.10.018

Gastroprotective potentials of aqueous leaf extracts of *Phyllanthus amarus* on ibuprofen-induced ulcer in Wistar rats.

Berezi, E.P*[1]. Uwakwe, A A[2]., Monago-Ighorodje,C.C[2],. Nwauche, K. T[2].
[1]Department of Chemistry, Isaac Jasper Boro College of Education, Sagbama, Bayelsa State, Nigeria.
[2]Department of Biochemistry, University of Port Harcourt, Choba, Port Harcourt. Rivers State. Nigeria.
*Corresponding author: *sirepberezi@yahoo.com*

Abstract

This study investigated the gastroprotective potential of aqueous leave extracts of *Phyllanthus amarus* against ibuprofen, a non-steroidal anti-inflammatory drug (NSAID) induced gastric mucosal injury in wistar rats. Male and female adult rats of average weight 200g were divided into five groups for the protective treatment. The rats were pre-treated with distilled water, omeprazole (20mg/kg as reference drug) and 250mg/kgbw and 500mg/kgbw extracts of *P. amarus* leaves. After 7days NSAID (Ibuprofen (20mg/kg) was orally administered to induce ulcer. Evaluation of the untreated (Ulcer group) rats showed severe mucosal damage. The ulcer surface area and ulcer index of experimental rats administered with *P. amarus* were significantly ($p \leq 0.05$) decreased. There was a significant ($p \leq 0.05$) increase in the mucus weight and percentage inhibition of rats pre-treated with the extracts compared with the untreated group. The values of the enzymatic antioxidant and oxidative stress marker, superoxide dismutase (SOD) was significantly ($p \leq 0.05$) increased while the lipid peroxidation (MDA) was decreased. Histopathological assessment of the stomach of experimental rats showed restoration of the mucosal fold suggesting the cytoprotective effect of *P. amarus* as an anti-ulcer agent. This property may be attributed to the combined action of the various antioxidant components of secondary metabolites like alkaloids, phenolic acids, glycosides, flavonoids, saponins and tannins present in the leaves extract.

Keywords: Gastroprotective, *Phyllanthus amarus*, Ibuprofen, Omeprazole Gastric mucosa.

Introduction

Phyllanthus amarus (PA) is a herb of about 2cm-30cm in height that is widely found in most tropical and subtropical country. The plant has approximately 550 to 750 species which are subdivided into 10 to 17 subgenera (Calixto *et al.*, 1998). It is a medicinal plant of interest that is rich in antioxidants and has been widely used by traditional medicine practitioners for the treatment of a wide variety of ailments (Grieve, 2008; Calixto *et al.*, 1998). *Phyllantus amarus* has long been used for the treatment of the liver (Kamble *et al.*, 2008) and active components of the plant have shown hepatoprotective properties (Padma and Sethy, 1999) and employed in Ayurvedic formation (Ratna, 2002; Jain *et al.*, 2009). It exhibit anti-viral properties and used as a remedy for hepatitis B virus infection (Eldeen *et al.*, 2010). The leaves are used as expectorant, diaphoretic, laxative diuretic (Kiritikar and Basu., 2001). The phenolic constituent alleviated the effect of anti-mycin A-induced apoptotic cascade (Guha *et al.*, 2010). The gastroprotective activity effect of other *phallantus* species was studied by Shokunbi and Odetola (2008), the acute toxicity study (Pingale and Shewale., 2011) and its ability to lower blood pressure had been reported (Siridya and Periwal., 1995; Amonkan *et al.*, 2013; Amaechina and Omoybai., 2007).

Gastric and duodenal ulcers are the most prevalent gastrointestinal disorders (Somasundaram,, 2013). Ulcer is primarily caused by an imbalance between the endogenous aggressive and protective factors in the stomach (Paguigan *et al.*, 2014). These protective factors induce acid-pepsin secretion, mucus secretion, reduction of gastric mucosal blood flow, integrity of the mucosal barrier impairment of cellular regeneration, suspension of prostaglandin synthesis, and growth factors (Freitas *et al.*, 2008). Research have shown that the aggressive factors involves the continuous use of non-steroidal anti-inflammatory drugs (NSAID) such as ibuprofen, aspirin, indomethacin, naproxen, piroxicam, fenoprofen, salsalate, exaprozin etc, cause the erosion and injury of the gastric mucosal epithelia (Wallace., 2000).

Materials and Methods

Plant material

Fresh leaves of *Phyllantus amarus* [PA] were obtained from a bush farm in Kaiama town in Kolokuma/Opokuma Local Govt. Area of Bayelsa State, Nigeria. The plants were identified and authenticated by Dr, Nwosu of the Plant Science and Biotechnology Dept. of the University of Port Harcourt, Choba, Port Harcourt, Rivers State, Nigeria.

Extract Preparation

Freshly harvested leaves *P.amarus* (PA) was sun dried and coarsely powdered with a blender. 100gm of the powdered leaves were boiled in 500ml of distilled water for 15 minutes. The decoction was taken and allowed to cool for 45minutes at room temperature. It was then filtered twice using Whatman No1 filter paper, then evaporated to dryness in an oven at 50^0C, to produce 38.13g of the aqueous extract. Stock solution of the concentrated plant samples were constituted with distilled water at 250mg/ml and different doses (250 and 500mg/kg).

Experimental animals

For this study wistar rats of both sex weighing between 150-200g body weights were purchased from animal house of the Department of Biochemistry, Federal University of Agriculture, Abeokuta (FUNAAB), Ogun State, Nigeria. The rats were randomly divided into five (5) groups of 4 rats per group, kept in metal cages at room temperature and allowed to acclimatize for one week under standard environmental conditions. The rats were fed with balanced rodent pellet diet and allowed free access to water *ad libitum*.

Acute toxicity test

Preliminary acute toxicity studies of *P.amarus* leave extract were performed on the rats in accordance to the OECD guideline no 423 (Acute Toxic Class Method) to determine the safe dose concentration of the extract to be administered. The rats were fasted for 24 hours prior to dosing with the leave extract in increasing dose up to 5000mg/kg body weight. The rats were observed at an interval of 4 hours daily for 3 days for any clinical or toxicological manifestation. It was observed that at this dose no abnormal behavior was recorded, hence $1/10^{th}$ (500mg/kg) of this dose was selected for the study.

Ibuprofen induced gastric mucosal injury studies

In this study the rats were divided into five groups of four rats each.

Groups	Treatment		Description
A1.	Normal	-	rats administered with distilled water only
A2.	Negative Control	-	rats induced with 20mg/kg ibuprofen only (Ulcer control)
A3.	Positive Control	-	rats induced with 20mg/kg ibuprofen + 20mg/kg Omeprazole (NSAID)
A4.	Pre – Treated Rats	-	rats induced with 20mg/kg ibuprofen + 250mg/kg aqueous extract of *P.amarus*.
A5.	Pre – Treated Rats	-	rats induced with 20mg/kg ibuprofen+ 500mg/kg aqueous extract of *P.amarus*.

Estimation of gross gastric lesion

Gastric mucosa ulcer appears as dark hemorrhagic lesions of the stomach. The stomach of the experimental rats was dissected along the greater curvature and examined for damage. Each damage was measured using a planimeter (10 x10 mm^2 = ulcer area) by viewing under microscope magnification (1.8X). The length and breadth of the ulcer area was evaluated by counting the number of small squares (2mm x2mm) of the stomach. The total number of these lesions multiplied by 4 x 1.8= ulcer area (UA mm^2) (Mahmood *et al.*, 2011).

The gastric lesions were counted and ulcer index (UI) was calculated using the expression (Singh., 1999);

UI = (n + lesion I) + (n+ lesion II) + (n+ lesion III)

Where;

I = Presence of edema, hyperaemia and single submucosal, puntiform hemorrhage (petechiae);
II = Presence of submucosal, hemorrhage lesions with small erosions;
III = Presence of deep ulcer with erosions and invasive lesions (Szelenyl and Thiemer, 1978).
n = Number of ulcer.

The percentage ulcerated surface was calculated as the total area covered by all lesions expressed as a proportion of the total corpus mucosa surface area. The percentage of inhibition (I%) was calculated as described by Nguelefack *et al.*, (2005) and Ateufack *et al.*, (2006) using the formula;

Percentage ulcer inhibition

$$(\%UI) = \frac{USc - Ust}{USt} \times 100$$

Where;

USc = Ulcer surface area of control
USt = Ulcer surface area of treated

Statistical Analysis

All values were reported as mean ± standard deviation (SD). The statistical significance of differences between groups was assessed using one-way analysis of variance (ANOVA), followed by Dunnett's test. A value of $P \leq 0.05$ was considered significant difference between the groups. Statistical computations were calculated using Statistical Package for Social Sciences (SPSS) Version 20,(SPSS Inc, Chicago, IL, USA).

Results

Qualitative and quantitative phytochemical composition of *P.amarus* extract.

Results of the preliminary phytochemical study of *P.amarus* extract showed the presence of secondary metabolites like alkaloids, flavonoids, glycosides, phenolic acid, saponins and tannins, (Table 1). Tables 2 and 3 shows the quantitative analysis of the phenolic acid and alkaloid content of *P.amarus* leave extract respectively.

Table 1. Qualitative Phytochemical analysis of *P. amarus* leave extracts.

S/No.	Constituents	Aqueous leave extract
1.	Phenolic acid	+
2.	Alkaloids	+
3.	Tannins	+
4.	Glycosides	+
5.	Flavonoids	+
6.	Saponins	+

(+) Presence of phytoconstituent in *P.amarus* leave extract.

Table 2. Quantitative phytochemical analysis of Phenolic Acid in *P.amarus*.

S/No.	Constituents	Aqueous (mg/100g)
1.	Salicylic acid	0.000738
2.	Gentisic acid	0.000306
3.	Protocatechnic acid	0.000329
4.	Vnillic acid	9.63653
5.	p-hydroxybenzoic acid	0.000245
6.	Cinnamic acid	0.765021
7.	Gallic acid	17.95202
8.	3,5-t-butyl phenol	2.90239
9.	Monocaffieyltartic acid	0.0130296
10.	Ferulic acid	0.595809
11.	Syringic acid	0.000064
12.	Caffeic acid	22.51520
13.	4-Caffoeylquinic acid	0.002575
14.	Piperic acid	0.000106
15.	Sinapinic acid	0.000459
16.	Ellagic acid	19.33133
17.	Chlorogenic acid	9.23744
	Total	**82.95360**

Table 3. Quantitative Phytochemical results of Alkaloids in *P.amarus* leave.

S/No.	Constituents	Aqueous (mg/100g)
1.	Phyllantene	257.72318
2.	Phyllantidine	142.12625
3.	Securinine	33.85396
4.	9-Octadecenamide	0.000007
5.	Dihydro-oxo-demethoxy haeman thamine	0.000005
6.	Norsecurinine	22.94634
7.	Isobubialine	7.00728
8.	Oxoassoanine	0.000004
9.	Epibubbialine	3.16560
10.	Crinane-3alpha-ol	0.000003
11.	Sinactine	0.002037
12.	Protopine	0.000060
13.	Cryptopine	0.000115
	Total	**466.82484**

Effect of aqueous leave extract of *P.amarus* on ibuprofen induced ulcer.

The aqueous *P.amarus* extract (P.A.E) showed significant anti-ulcer effect against ibuprofen induced ulcer in a dose dependent manner. Mean ulcer area of the ulcer (negative) control group was 120.13 ± 0.41, pre-treatment with *P.amarus* extract at a dose of 250 and 500mg/kgbw significantly ($p \leq 0.05$) reduced this to 65.87 ± 0.61 and 60.43± 0.37 respectively, while the reference drug, omeprazole treated group was reduced to 50.53± 0.40. The ulcer index result showed that the ulcer group recorded 5.83±0.05 while the omeprazole group, 250mg/kgbw and 500mg/kgbw of *P.amarus* extract was reduced ($p \leq 0.05$) to 2.10± 0.10, 3.03±0.05 and 2.71±0.80 respectively (Table 4).

The percentage inhibition and mucus weight as shown in Table 5 indicate that the negative control group was reduced to 12.2 ± 0.56%,which was increased to 75.2 ± 0.16% for the omeprazole group while the rats administered with extracts of P.amarus recorded 65.3 ± 0.70% and 70.2 ± 0.30% for 250mg/kgbw and 500mg/kgbw dose respectively. The mucus weight was significantly ($p \leq 0.05$) increased to 144.5 ± 2.28mg for the reference drug, omeprazole from 56.80 ± 1.47mg recorded for the ulcer control group. The values recorded for the mucus weight of rats pre-treated with *P.amarus* extract showed no difference with the normal control and the reference drug group rats.

Effect of *P. amarus* extract on some oxidative stress and enzyme marker.

The level of the lipid peroxidation product MDA was elevated in the ulcer control group by the ulcerogenic agent, ibuprofen (40.30 ± 0.30µmol/mg protein, $p \leq 0.05$) compared to the normal control (10.53 ± 0.15µmol/mg protein) (Table 6). The MDA value in rats pre-treated with PAE and the reference drug (omeprazole) were significantly ($p \leq 0.05$) reduced to 13.6 ± 0.20µmol/mg protein, (500mg/kgbw) and 13.00 ± 0.11µmol/mg protein for omeprazole group. In contrast to the results of MDA, the activity level of superoxide dismutase (SOD) was significantly ($p \leq 0.05$) lower in the ulcer control group (15.10±0.15µmol/mg protein). The administration of PAE increased the SOD level 33.10±0.45µmol/mg protein at dose 500mg/kgbw and 35.60±1.34µmol/mg protein for omeprazole group (Table 6)

Table 4: Effect of *P.amarus* extract on Ibuprofen induced Ulcer on ulcer area and ulcer index.

Group	Treatment	Ulcer Area (mm^2)	Ulcer Index
1	Normal control	0.00 ± 0.00[b]	0.00 ± 0.00[b]
2	Ulcer control	120.13 ± 0.41[a]	5.83 ± 0.05[a]
3	Omeprazole	50.53 ± 0.40[a b]	2.10 ± 0.10[a b]
4	P.A.E 250mg/kg bw	65.87 ± 0.61[a b]	3.03 ± 0.05[a b]
5	P.A.E 500mg/kg bw	60.43 ± 0.37[a b]	2.70 ± 0.80[a b]

Values are mean ± S.D of triplicate determination. Values with the same column with superscripts alphabets 'a' and 'b' are significantly different at P≤0.05 when group 1 and group 2 are compared with other groups respectively.

Table 5: Effect of *P.amarus* extracts on Ibuprofen induced Ulcer on % Inhibition and mucus weight

Group	Treatment	% Inhibition	Mucus weight(mg)
1	Normal control	0.00 ± 0.00[b]	124.36 ± 3.68[b]
2	Ulcer control	12.2 ± 0.56[a]	56.80 ± 1.47[a]
3	Omeprazole	75.20 ± 0.16[a b]	144.50 ± 2.28[a b]
4	P.A.E 250mg/kg bw	65.30 ± 0.70[a b]	120.60 ± 1.24[a b]
5	P.A.E 500mg/kg bw	70.20 ± 0.30[a b]	145.50 ± 2.24[a b]

Values are mean ± S.D of triplicate determination. Values with the same column with superscripts alphabets 'a' and 'b' are significantly different at P≤0.05 when group 1 and group 2 are compared with other groups respectively.

Table 6: Effect of P.*amarus* extract on enzymatic antioxidant

Group	Treatment	Superoxide Dismutase (SOD) (µmol/mg protein)	Lipid Peroxidation (MDA) (µmol/mg protein)
1	Normal control	39.20 ± 0.92[b]	10.53 ± 0.15[b]
2	Ulcer control	15.10 ± 0.15[a]	40.30 ± 0.30[a]
3	Omeprazole	35.60 ± 1.34[a,b]	13.10 ± 0.11[a,b]
4	P.A.E 250mg/kg bw	30.20 ± 0.32[a,b]	16.50 ± 0.40[a,b]
5	P.A.E 500mg/kg bw	33.10 ± 0.45[a,b]	13.60 ± 0.20[a,b]

Values are mean ± S.D of triplicate determination. Values with the same column with superscripts alphabets 'a' and 'b' are significantly different at P≤0.05 when group 1 and group 2 are compared with other groups respectively.

Histopathology

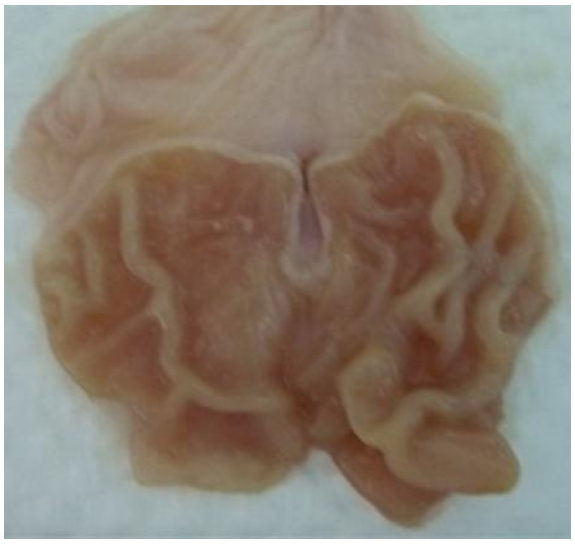

Figure 1: Normal group rats. No injuries to the gastric mucosa are seen. X200

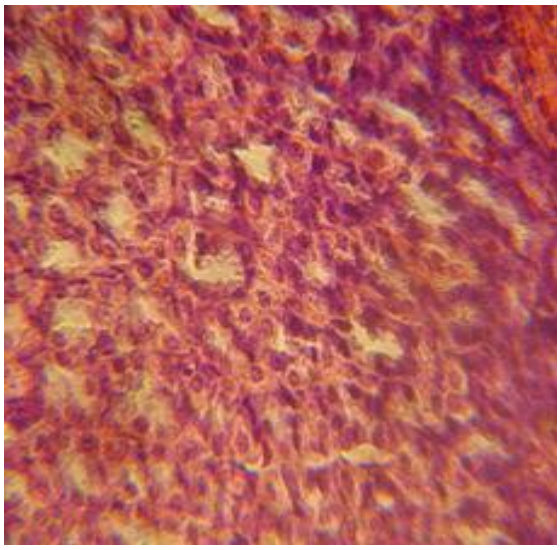

Figure 1a: Normal group rats showed normal gastric mucosa with normal glands, Nucleus appears distinct. X100

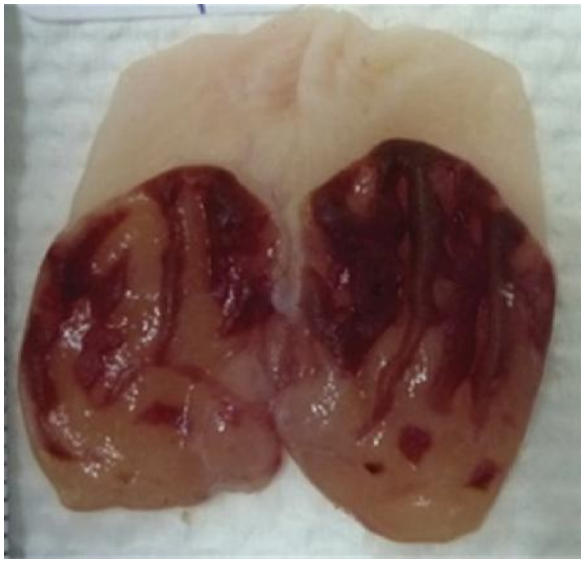

Figure 2: Untreated group rats (ulcer control). Severe injuries are seen in the gastricmucosa. NSAID (Ibuprofen) and absolute ethanol produced extensive visible hemorrhagic necrosis of gastric mucosa. X200.

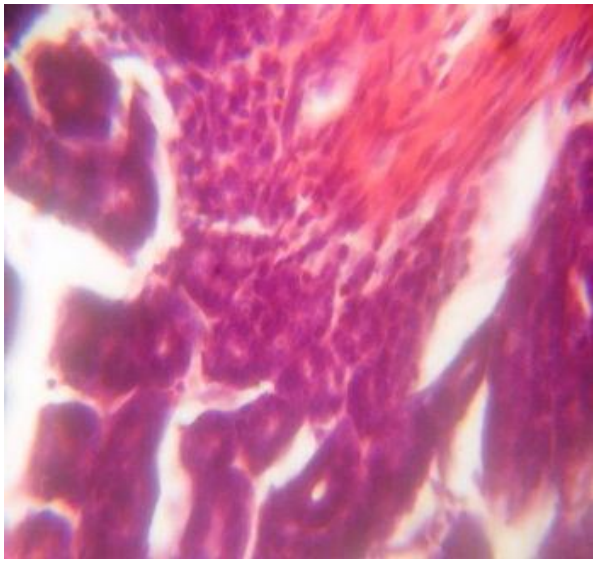

Figure 2a: Untreated ulcer group showed mucosal ulceration with sub mucosal edema, inflammation and polymorphonuclear infiltrate at the ulcer site as well as in the oedematous submucosa. X100

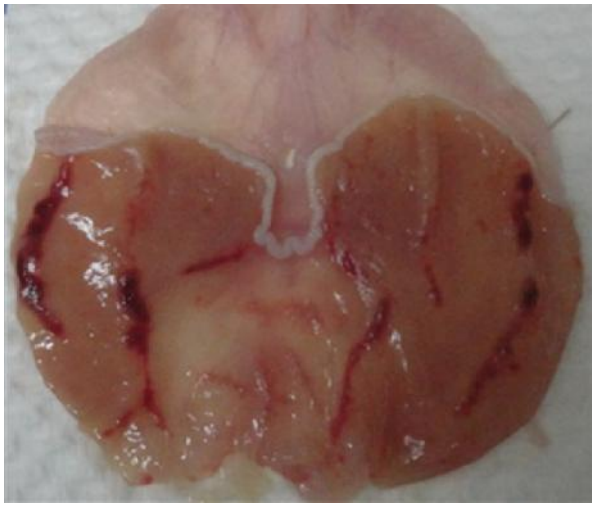

Figure 3: Rats pretreated with omeprazole (20mg/kg). Injuries to the gastric mucosa are milder compared to the injuries seen in the ulcer control rats.

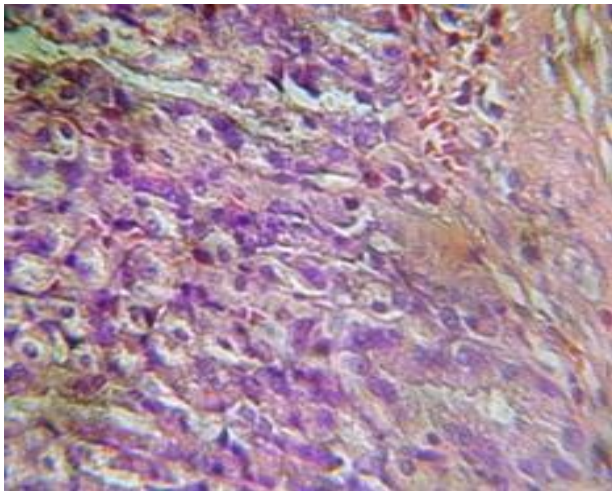

Figure 3a: Treated with standard drug (omepSrazole). Omeprazole (20mg/kg) treated group: There is a mild distruption to the surface epithelium and mild infiltration and haemorrhages to the submucosal layer.

Discussion

The stomach is exposed to various aggressive and damaging agents like the prolong intake of non-steroidal anti-inflammatory drugs (Ibuprofen etc), absolute ethanol, smoking, HCl, bile acid etc, which induces gastric mucosa lesions causing erosion, ulceration, hemorrhage and loss of epithelial cells (Shin *et al*. 2013). These features were evident in this study as observed by the action of the ulcerogenic agent, ibuprofen in the ulcer control group. To maintain the integrity of the stomach, gastric mucosa damage is usually treated with antacids, proton pump inhibitors, histamine H2 receptor type, prostaglandins, cytoprotective agents, gastric antisecretory agents and antibiotics to reduce gastric acid secretion, increasing the production of gastric mucus, increase bicarbonate production and providing defense mechanism to protect the surface epithelial cells (Ateufack *et al*. 2015). In this study, pre-treatment with increasing dose of *P.amarus* extract demonstrated cytoprotective tendency to the gastric mucosa, due to increased mucus weight accompanied by a proportional increase in proteins, this agrees with the study of Thirunavukkarasu *et al*., (2009). The gastro protective effect of *P.amarus* may be attributed to the various secondary metabolites present in the plant. Phenolic compounds are known to stimulate the production of prostaglandins based on their action as co substrate for the peroxidase reaction (Alanko *et al*., 1999). The action of phenols, alkaloids and tannins contribute in precipitating microproteins on the ulcer site forming a thick layer to cover the surface of the epithelial cells thereby hindering gut secretions and protect the mucosa from damage. The following active components, chlorogenic, gallic and ellagic acids of phenols as well as phyllantene and phyllantidine of alkaloids are characterized by their astringent and antimicrobial action to exhibit cytoprotective and anti-ulcer activity as reported in other plants by Gonzales *et al*.,*(*2000); Konig *et al*.,*(*1994); and Ramirez and Roa. (2003). Since, *P.amarus* have also shown similar cytoprotective and anti- ulcer activity, this property can be attributed to the actions of these secondary metabolites present in the plant. This is consistent with the findings on *Phyllanthus niruri* by Abdulla *et al*., (2010); *Acanthopanax trifoliatus* by Roslida *et al*., (2010). Histopathological examinations of tissues of the stomach showed flattening of the mucosal folds indicating gastroprotective effect of the plant extract. This causes a relaxation of the circular muscles and increases the production of prostaglandin (Takeuchi and Nobuhara, 1985).

The level of lipid peroxidation (MDA) was increased while the enzymatic antioxidant defense component like superoxide dismutase (SOD) was decreased due to the effect of ibuprofen. Pre-treatment with aqueous extracts of *P.amarus* reduced the MDA level and in contrast elevated the level SOD activity. Superoxide dismutase is an important antioxidant that converts singlet oxygen, reactive oxygen species (ROS) and free radicals to hydrogen peroxide and molecular oxygen, thus protecting tissues and cells from necrotic effect of ibuprofen (Devi et al, 2007).

Conclusion

The results from this study revealed that *P.amarus* possess gastroprotective and anti-ulcer potentials. Such protection was shown to be dose dependent as shown by the reduction of ulcer area and ulcer index and a simultaneous increase in the mucus weight. The cytoprotective effect of aqueous *P.amarus* extract may be due to the action of bioactive phytochemical components present in the plant extract which results in increasing the antioxidant activity and reducing the effect of the aggressive agent.

References

Alanko, J., Riutta, A., Holm, P., Mucha, I., Vapatalo, H., and Metsa-Ketela, T. 1999. Modulation of Arachidonic acid metabolism by Phenols: relation to their structure and antioxidants/prooxidant properties. *Free Radical Biol. Med*. 26: 193-201.

Amaechina, F.C. and Omogbai, E.K. 2007. Hypotensive effect of aqueous extract of the leaves of *Phyllantus amarus* Schum and Thomn (Euphobiaceae).*Acta Poloniae Pharmaceutica-drug Research*.**64**: 547-552.

Amonkan, A.K., Kamagate, M., Yao, A.N.R., Konan, A.B., Kouame, M.N., Koffi, C., Kati, C. and Die-Kakou, H. 2013. Comparative Effects of Two Fractions of *Phyllantus amarus* (Euphorbiaceae) on the Blood Pressure in Rabbit.*Greener Journal of Medical Sciences*.**3**(4): 129-134.

Ateufack, G., Dongmo-Feudjio, B.R., Yousseu, W.N., Atsamo, A.D. and Kamanyi, A. 2015. Ulcer protective and ulcer healing activities of aqueous and methanolic extracts of leaves of *Rumex Bequaertii*De Wild (Polygonaceae) in rats. *Journal of Biology and life science*.**6**(2).

Ateufack, G., Nguele-fack, T.B., Wabo, H.K., Watcho, P., Tane, P., Kamanyi, A. 2006. Antiulcer effects of the aqueous and organic extracts of the stem bark of *Anthocleista vogelii* in rats. *Pharmaceutical Biology***44**:1-6.

Calixoto, J.B., Santos, A.R.S., Filbo, V.C. and Yune, R.A. 1998. A Review of the plants of the genus *Phyllanthus* their chemistry, pharmacology, and therapeutic potential. *John Wiley & Son, Inc*. 225-258.

Devi, R.S., Narayan S., Vani, G., Shyamala Devi, C.S. 2007. Gastroprotective effect of *Terminalia anjuna* bark on diclofenac sodium induced gastric ulcer. Chem.. boil. Interact. 167: 71-83.

Freitas, C.S., Baggio, C.H., Finan, J., Angioni, M., Pizzolatti, M.G., Santos, A.R.S. and Marques, M.C.A. 2008.Inhibition of H^+/K^+ ATPase in the gastroprotective effect of baccharis illinita DC.*Journal Pharmacology*.**60**: 1105-1110.

Gonzales , E., Iglesias, I., Carretero, E., and Villar, A. 2000. Gastric cytoprotection of Bolivian medicinal plants. *Journal of Ethnopharmacology*. 70: 329-333.

Grieve, M. 2008. Dandelion (*Taraxacum Officinale* WEBER).A modern herbal.*Botanical.com*. 1-10.

Guha, G., Tamoghna, M. and Rajkumar, R.A. 2010. Antimycin-A induced mitochondrial apoptotic cascade is mitigated by phenolic constituents of *Phyllantus amarus* aqueous extract in Hep3B cell. *Food and Chemical Toxicology***48**: 3449-3457.

Jain, S., Gill, V., Vasudera, N. and Singla, N. 2009. Ayurvedic Medicine in treatment of cancer.*Journal of Chinese Integrated Medicine*.**7**(11): 1096-1099.

Kamble, M.B., Dumbre, R.K. and Ranyari, V.D. 2008. Hepatoprotective studies of herbal formations. *International Journal of Green Pharmacy*.**2**: 147-151.

Kirtikar, K.R. and Basu, B.D. 2001. Indian Medicinal Plants.2nd ed. Vol 1x.Oriental Enterprises. Uttranchal, India. 3068-3069.

Konig, M., Scholz, E., Hartmann, R., Lehmann, W. and Rimpler, H. 1994. Ellagitannins and complex tannins from *Quercus petraca* bark. *Journal of natural products*. 57: 1411-1415.

Mahmood, A.A.,Al-Bayaty, F.H., Salmah, I., Nor-Syuhada, A.B.and Harita, H. 2011. Enhancement of gastric ulcer by Areca catechu nut in ethanol-induced gastric mucosal injuries in rats. *Journal of Medical Plant Research*,**5(**12):2562-2569.

Nguelefack, T.B., Watcho, P., NgueIta, M.M., Wansi, S.L. and Kamanyi, A. 2005. Effects of the methanol leaf extract of Alchonca cordifolia (Schum & Thonn). Muell. Arg. On different gastric ulcer models in rats.*Cameroon Journal of Experimental Biology*, **I.** 54-56.

OECD 2002.Acute oral toxicity. Acute oral toxic class method guidelines 423 adopted 23/03/1996. In: Eleventh addendum to OECD, guidelines for the testing of chemicals organisation for economical cooperation and development, Paris, June 2000.

Padma, P. and Setty, O.H. 1999. Protective effect of *Phyllantus fraternus* against carbon tetrachloride-induced mitochondrial dystruction.Life Science.**64**: 2411-2417.

Paguigan, N.D., Castillo, D.H. and Chichioco-Hernandez, C.L. 2014. Anti-Ulcer activity of Leguminosae Plants. Arq Gastroenterol. **51**(1): 64-68.

Pingale, S.S. and Shewale, S.S. 2011. Acute Toxicity study of *Phyllantus amarus*. *International Journal of Pharmaceutical Sciences Review and Research*.**9** (1): 81-84.

Ramirez, R.O. and Roa, C.C. 2003. The gastroprotective effect of tannins extracted from duhat (*Syzygium cumini skeels*) bark of HCl/ethanol induced gastric mucosal injury in Spargue-Diwley rats. *Clinical Hemorheology and Microcirculation*. 29: 253-261.

Ratna, B. 2002. Chyawanprash market in for healthier glow. Available from: http://www.blonnet.com.

Satoskar, R.S., Bhandkar, S.D, and Ainapure, S.S., 1997. Pharmacology and pharmacotherapeutics.2: 565.

Shin, I.S., Woo-young, J., Shin, H.K., Cha, S.W. and Lee, M.Y. 2013. Banhabaekchulchunma-tay, a traditional herbal formula attenuates absolute ethanol-induced gastric injury by enhancing the antioxidant status.*Biomed Central (BMC) Complementary and AlternativeMedicine*.13(170):2-8.http://www.biomedcentral.com/1472-6882 | 13 | 170.

Shokumbi, O. and Odetola, A. 2008. Gastroprotective and Antioxidant activities of *Phyllantus amarus* extracts on absolute ethanol induced ulcer in albino rats. *Journal of Medicinal Plant Research*.**2**: 261-267.

Siridya, N. and Periwal, S. 1995. Diuretic, hypotensive and hypoglycaemia effect of *Phyllantus amarus*. *Indian Journal of Experimental Biology*.**33**: 861-864.

Somasundaram, J. 2013. Anti-Ulcer Activity of Aqueous extract of *Alphitonia zizyphoides* Bark in Experiment Rats. *International Journal of Pharmacotherapy*.**3**(1): 28-33.

Szenlenyl, I. and Thiemer, K. 1978.Distention Ulcer as a model for testing drugs for ulcerogenic side effects.*Archives of Toxicology*.**41**. Pp 99-105.

Takeuchi, K. and Nobuhara, Y. 1985. Inhibition of gastric motor activity by 16, 16-dimethyl prostaglandin E2. A possible explanation of cytoprotection. *Digestive Diseases and Sciences.* 30: 41-46.

Thirunavukkarasu, P., Ramkumar, L., and Ramanathan, T. 2009. Anti-ulcer activity of Excoecaria Agallocha bark on NSAID- induced Gastric Ulcer in Albino Rats. *Global Journal of Pharmacology*. 3(3): 123-126.

Wallace , J.L. and Tigley, A,W. 1995. New insights into Prostaglandins and mucosal defence. Alimentary pharmacology and therapeutics. 9: 227-235.

Wallace, J.L. 2000. How do NSAIDs cause ulcer diseases. **14**(1): 147-159.

Access this Article in Online

Website: www.ijarbs.com

Subject: Biochemistry

Quick Response Code

DOI:10.22192/ijarbs.2017.04.10.018

How to cite this article:

Berezi, E.P., Uwakwe, A A., Monago-Ighorodje,C.C,. Nwauche, K. T. (2017). Gastroprotective potentials of aqueous leaf extracts of *Phyllanthus amarus* on ibuprofen- induced ulcer in Wistar rats. Int. J. Adv. Res. Biol. Sci. 4(10): 138-146.

DOI: http://dx.doi.org/10.22192/ijarbs.2017.04.10.018