

Research Article

## Attenuating Effect of *Telfairia occidentalis* on Oxidative Stress in Indomethacin-induced Gastric Ulcer in Male Rats

Adisa W.A.<sup>1</sup>, Otamere H.O.<sup>1</sup>, Adesina A.A.<sup>2</sup>, Bankole J.K.<sup>4</sup>

Departments of <sup>1</sup>Physiology, <sup>2</sup>Psychology and <sup>3</sup>Medical Laboratory Science, Ambrose Alli University, Ekpoma, Edo State, Nigeria.

**Summary:** Peptic ulcer is a major health challenge with high morbidity and mortality all over the world. This study investigated the involvement of oxidative stress in the healing and protective potentials of aqueous leave extract of *Telfairia occidentalis* (TO) on indomethacin induced gastric ulcers in adult Sprague Dawley male rats. The rats were divided into 6 groups (A-F) of 5 rats each, with A as normal control, B received single oral administration of 40mg/kg indomethacin without treatment for 4 hours; C received 40mg/kg indomethacin without treatment for 4 hours and scarified after 72 hours; D received 100mg/kg aqueous leave extract of TO for 7 days without ulcer induction; E (pre-treated test group) received 40mg/kg indomethacin after being pre-treated with 100mg/kg aqueous leave extract of TO daily for 7 days. Group F (Post treated test) received 40mg/kg of indomethacin and treated four hours later with 100mg/kg aqueous leave extract of TO daily for 7 days. The results revealed changes in gastric macroscopic architecture of the mucosa, and changes in ulcer indices and oxidative stress markers levels in group B-F. These changes comparatively suggested that the leave-extract of *Telfairia occidentalis* has gastro-protective with minimal healing potentials mediated through reduced oxidative stress.

**Keywords:** *Telfairia occidentalis*, gastric ulceration, MDA, indomethacin

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\*Address for correspondence: [williamsadewumi@yahoo.com](mailto:williamsadewumi@yahoo.com); Tel: +234-8056049158

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### INTRODUCTION

Gastric ulcer is one of the major causes of morbidity and mortality (Chaturvedi *et al.*, 2007; Miami *et al.*, 2016) and has remained a worrisome health challenge (Lanas and Chan, 2017), with known capacity to induce gastrointestinal bleeding when not adequately treated (Tortora and Grabowski, 2003; Leontiadis *et al.*, 2013; Lanas *et al.* 2014). It has been reported that the etiology of gastroduodenal ulcers are caused by imbalance between offensive factors such as gastric HCl, pepsin secretion; and defensive factors such as parietal cell, mucosal barrier, mucus secretion, blood flow, cellular regeneration and endogenous protective agents (Repetto and Llesuy, 2002). According to Malysenko *et al.* (2005), factors like inadequate dietary habits, cigarette smoking, excessive ingestion of non-steroidal anti-inflammatory agents, stress, hereditary predisposition and infection by *Helicobacter pylori*, may also be responsible for the development of peptic ulcers. Similarly, Reactive Oxygen Species (ROS) has been implicated as one of the major causes of mucosal lesions and gastrointestinal damage (Bagchi *et al.*, 1999; Pohle *et al.*, 2001; Whittle, 2003).

Noteworthy is the fact that several pharmaceutical products have been employed in the treatment of gastroduodenal ulcer and peptic diseases, resulting in decreasing mortality and morbidity rates; but considering their associated adverse effects, such products cannot be described as completely effective (Rates, 2001; Wedemeyer and Blume, 2014). One widely used drug that has been associated with rare idiosyncratic hepatotoxicity is the histamine H2 receptor antagonist-ranitidine (Bourdet *et al.*,

2005). It is available over the counter for oral administration or by prescription for parenteral administration for treatment of gastric ulcers, hypersecretory diseases, and gastroesophageal reflux disease. Idiosyncratic ranitidine hepatotoxicity occurs in few people taking the drug (Fisher and Le Couteur, 2001). Most liver reactions are mild and reversible; but extensive liver damage has occurred in individuals undergoing ranitidine therapy (Ribeiro *et al.*, 2000). Thus, confirming the adverse effects earlier alluded to. Nevertheless, with the onset of scientific research in medicinal herbs, it is becoming clearer that medicinal herbs have potentials of great importance in this regard (Kurekci *et al.*, 2012).

Indeed, there has been growing interest in alternative therapies and the use of natural products, especially those derived from plants (Schmeda-Hirschmann and Yesilada, 2005). Studies on the treatment of gastrointestinal disorder have focused on the potential role of natural medicine due to their availability, better protection, lower cost, and lower toxicity (Bansal and Goel, 2012). Plant extracts are some of the most attractive sources of new drugs and have been shown to produce promising results for the treatment of gastric ulcers (Jung *et al.*, 2019; Morufu *et al.*, 2014). One of such plants that has been extensively studied and reported to have great potential is *Telfairia occidentalis* –the plant on focus in this study.

*Telfairia occidentalis* commonly called fluted pumpkin occurs in the forest zone of West and Central Africa, most frequently in Benin, Nigeria and Cameroon. It is a popular vegetable all over Nigeria. It has been suggested that it originated from South-East Nigeria, and distributed by the

Igbo who have cultivated it crop since time immemorial (Kayode and Kayode, 2011). It is a vigorous perennial vine, growing to 10m or more in length. The stems have branching tendrils and the leaves are divided into 3– 5 leaflets. The fruits are pale green, 3 – 10 kg in weight, strongly ribbed at maturity and up to 25cm in diameter. The seeds are 3– 5cm in diameter (FAO 1989). The leaf is consumed in different parts of the country because of the numerous nutritional and medicinal attributes ascribed to it. *Telfairia occidentalis* seeds serve as a high quality and low cost plant protein source for animal feed formulations (Kuku *et al.*, 2014). It has different traditional names: “Ugu” in Igbo, “Iroko” or Aporoko in Yoruba, Ubong in Efik, Umee in Urhobo and Umeke in Edo (Akoroda, 1990). Young succulent shoots and leaves are used as vegetables in the eastern part of Nigeria. Apart from its nutritional value, the plant also has agricultural and industrial importance (Oboh, 2005).

Medicinally, the herbal preparation of the plant has been employed in the treatment of sudden attack of convulsion, gastrointestinal disorders, malaria and anaemia (Akindele *et al.*, 2013; Gbile, 1986). Quite a number of researchers in the field of medical sciences have observed free radical scavenging ability and antioxidant property in *Telfairia occidentalis*. The darkish green leafy vegetable of *Telfairia occidentalis*, and its extracts (such as aqueous and ethanol extracts), have been found to suppress or prevent the production of free radical and/or scavenge already produced free radicals, lower lipid peroxidation status and elevate antioxidant enzymes (such as superoxide dismutase and Catalase) both in vitro and in vivo (Kayode *et al.*, 2010; 2009; Oboh *et al.*, 2006; Oboh and Akindahunsi, 2004). Studies have also shown that the leaves of *Telfairia occidentalis* are rich in antioxidants such as ascorbic acid and phenols (Oboh, 2005; Oboh and Akindahunsi, 2004). Toyin *et al.* (2013) and Adisa *et al.* (2018) had also reported the blood glucose-lowering effects of *Telfairia occidentalis* and its potentials in the management blood glucose levels.

Before the discovery of *H pylori* it was known that patients with duodenal ulcers secrete about twice as much acid as controls because they have twice as many parietal cells (Calam and Baron, 2001). Patients with gastric ulcer and those with functional dyspepsia have normal acid output and parietal cell count (Calam and Baron, 2001). Thus, there was good evidence that acid played a major role in ulcer formation (Calam and Baron, 2001).

Although several studies have been conducted on the medicinal potentials of *Telfairia occidentalis*, its pharmacological effects on gastrointestinal system is yet to be adequately explored. Adisa *et al.* (2019), reported ameliorative effect of *Telfairia occidentalis* on induced gastric ulcer; worrisome however, is that its ingestion may increase gastric acidity and hence this research to investigate further; the effect of *Telfairia occidentalis* leave extract on indomethacin induced gastric ulcer in rats.

## MATERIALS AND METHODS

**Materials (Plant, drugs and feed):** *Telfairia occidentalis* leaves commonly called pumpkin leaves were obtained from a local market in Ekpoma, Edo State and taken to the herbarium unit of the Department of Botany of Ambrose Alli University, Ekpoma for identification.

Indomethacin (B.P. 25mg; Manufacture by Fabrique Par, Yangzhou Pharmaceutical Co. LTD. Yiling-Jiangdu, China) was purchased from a pharmacy in Ekpoma, Edo State, Nigeria. the animal feed (grower’s mash; Grower palletised produced by Grand Cereals Ltd, a subsidiary of UAO Nigeria PLC, Jos, Plateau State) was purchased from an open shop in Ekpoma, Edo State Nigeria.

All other chemicals (sodium bicarbonate used to dissolve indomethacin) were obtained from a chemical store in Ekpoma and the solution needed prepared in the physiology laboratory where the experiment was conducted and all other chemicals were of analytical grade.

The instruments (dissecting set, magnifying lens, weighing balance and centrifuge) used in this study were obtained from the Department of Physiology, Faculty of Basic Medical Sciences, College of Medicine, Ambrose Alli University, Ekpoma, Edo State-Nigeria. Others such as plastic basket, Wattman No. 1 filter paper, orogastric cannula, plates for food and water, syringes, centrifuge bottles and hand gloves were obtained from a local store in and around Edo State, Nigeria.

**Preparation of extract:** The *Telfairia occidentalis* leaves were washed several times under running tap water. The fresh leaves were then blended and the grinded paste was mixed with some quantity of water and filtered. The filtrate was then allowed to sediment and the sedimented extract was left to dry in a water bath. This way, a powdery product was obtained from which aqueous extract was formed by dissolving appropriate grams in equal ml of distilled water to form the plant extract. This procedure is as previously described by Adisa *et al.*, (2014).

**Experimental animals:** Male rats (N=30) weighing between 200±250g were procured from Animal Farm. The animals were fed standard diet (Grower’s mash) and water given ad libitum. They were housed in six well-ventilated cages (each with a dimension of 45cm x 45cm x 45cm) under standard environmental conditions in a well-ventilated room under a 12/12 hours light/dark cycle and allowed two weeks of acclimatization.

**Experimental grouping:** After allowed two weeks (14 days) of acclimatization to the new environment, the animals were divided into groups as follows;

- i. Group A (n = 5) serves as the control and received no treatment or ulcer induction.
- ii. Group B serves as the test control 1 (n = 5). Ulcer was induced in this group with single oral administration of 40mg/kg indomethacin without treatment and scarified after four hours.
- iii. Group C serves as the test control 2 (n = 5). Ulcer was induced in this group with single oral administration of 40mg/kg indomethacin without treatment for four hours and fed normal rat chow afterward and scarified after 72 hours (three days).
- iv. Group D serves as the test (n = 5). The animals in this group received 100mg/kg of the aqueous leave extract of *Telfairia occidentalis* for 7 days without ulcer induction.
- v. Group E serves as pre-treated test group (n = 5 rats). In this group of animals, ulcer was induced with 40mg/kg indomethacin after pre-treating the animal with 100mg/kg aqueous leave extract of *Telfairia occidentalis* daily for 7 days. Four hours after the induction of ulcer the animals were scarified.
- vi. Group F serves as post-treated test (n = 5 rats). In this group of animals’ ulcer was induced with 40mg/kg indomethacin and then four hours later was treated with 100mg/kg aqueous leave extract of *Telfairia occidentalis* daily for 7 days.

**Experimental Procedure:** Following two weeks of acclimatization, animals in each group received their corresponding treatments.

The doses chosen for indomethacin and aqueous leaf extract of *Telfairia occidentalis* were based on previous findings by Akpamu (2014) and Adisa *et al.* (2014) respectively. Indomethacin solutions was prepared by mixing indomethacin in required ml of sodium bicarbonate while aqueous leave extract of *Telfairia occidentalis* was prepared daily by mixing 1gm of the plant extract in 10ml of distilled water and the required quantity given to each rat per kg body weight. All suspension was given orally according to their body weight by oro-gastric iron cannula and was prepared within 15 to 30minutes before use.

**Sample Collection:** At the end of the treatments, animals were mildly anaesthetized with chloroform and the stomach harvested following standard laboratory procedures (Akpamu, 2014). The stomachs were obtained for the determination of ulcer indices and macroscopic evaluation.

### Sample Analysis

**a. Determination of gastric ulcer severity/ulcer score:** Gross gastric lesions severity were measured as described by Wilhelmi and Menasse-Gdynia (1972) using the 0 to 5 scoring system. Severity factor 1 = 1 or 2 minutes, sporadic, punctuate lesion; 2 = several small lesion; 3 = one extensive lesion or multiple moderate sized lesions; 4 = several large lesions; 5 = several large lesions with stomach perforation.

The lesions score/ ulcer index (UI) for each rat was calculated as the number of lesions in the rat multiplied by their respective severity factor. The UI for each group was taken as the mean lesion score of all the rats in that group.

**b. Determination of percentage ulcer inhibition:** The percentage ulcer inhibition (%UI) of a given drug was calculated by the equation of Hano *et al.* (1976).

$$\% \text{ UI} = \frac{(\text{UI of ulcer control} - \text{UI of treated})}{(\text{UI of ulcer control})} \times 100\%$$

**c. Determination of marker of oxidative stress:** The stomach was harvested and devoid of fat and accessory tissues. They were then patted dry with tissue paper and weighed and placed in a plain bottle containing homogenize buffer solution (phosphate buffer 1:10 w/v). The stomach was homogenized (grind using homogenizer machine) and the content (homogenate) centrifuged at 3000 rpm for 10 minutes to obtain the supernatant and stored at minus 20°C. This was used for the determination oxidative stress.

The protein concentration of the homogenate samples was determined by means of the Biuret method as described by Gornal *et al.*, (1949). 5.0ml of blank Biuret reagent was prepared by dissolving CuSO<sub>4</sub>.5H<sub>2</sub>O crystals in 500mls of distilled water added to sample blank. These was mixed well and allowed to stand for 20 minutes at room temperature 25-27°C. Absorbance was read for test and standard against a

blank at 540nm. The concentration of protein was calculated using:

$$\frac{\text{optical density for standard} \times \text{concentration of standard}}{\text{optical density for test sample}}$$

MDA (an index of lipid peroxidation) was determined using the method of Buege and Aust (1978). 1.0ml of the supernatant was added to 2ml of the Tricarboxylic acid-Thiobarbituric acid-Hydrochloric acid reagent. (TCA - TBA-HCL) reagent boiled at 100oC for 15 minutes and allowed to cool. Flocculent materials were removed by centrifuging at 3000rpm for 10 minutes. The supernatant was removed and the absorbance read at 532nm against a blank. MDA was then calculated using the molar extinction coefficient for MDA – TBA — Complex of 1.56 x 10<sup>5</sup>M<sup>-1</sup> CM<sup>-1</sup>.

**e. Macroscopic (Gross) evaluation of gastric lesions:** The stomachs were washed with saline water and examined for macroscopical mucosal lesions using magnifying lens. Ulcers of the gastric mucosa appear as inflammation and as elongated bands of hemorrhagic lesions parallel to the long axis of the stomach rugus.

**Macroscopic (Gross) Presentations:** Macroscopic observations of the gastric mucosa were represented in pictures.

**Statistical Analysis:** The Statistical Package for Social Sciences (SPSS version 20) was used for data analysis. The one-way analysis of variance (ANOVA) was employed for data analysis and where applicable LSD was determined and confidential interval of  $p \leq 0.05$  considered statistically significant. Results were presented as mean  $\pm$  Standard deviation using suitable tables and charts.

## RESULTS

### Effect of aqueous leave extract of *Telfairia occidentalis* on ulcer indices in indomethacin induced gastric ulcers:

Table 1 shows the effect of aqueous leave extract of *Telfairia occidentalis* on ulcer indices (ulcer severity, ulcer score and percentage ulcer inhibition potentials) in indomethacin induced gastric ulcers. It was the finding of this study that ulcer severity by indomethacin was highest in post-treatment with aqueous leave extract of *Telfairia occidentalis* (group F; 2.51 $\pm$ 0.72) compared to pre-treatment (group E; 0.81 $\pm$ 0.46) and this was followed by group B (2.26 $\pm$ 0.97) and group C (2.01 $\pm$ 0.01). The lowest ulcer severity was observed in the control and this was followed by pre-treatment with extract and then 7 days extract ingestion without ulcer induction (group D; 1.21 $\pm$ 0.46). Compared to the control (Group A; 0.34 $\pm$ 0.59), ulcer severity was significantly high ( $p < 0.05$ ) in groups B, C and F. Compared to group B, ulcer severity was significantly low ( $p < 0.05$ ) in groups A and E

**Table 1.**

The effect of aqueous leave extract of *Telfairia occidentalis* on ulcer indices in indomethacin induced gastric ulcers

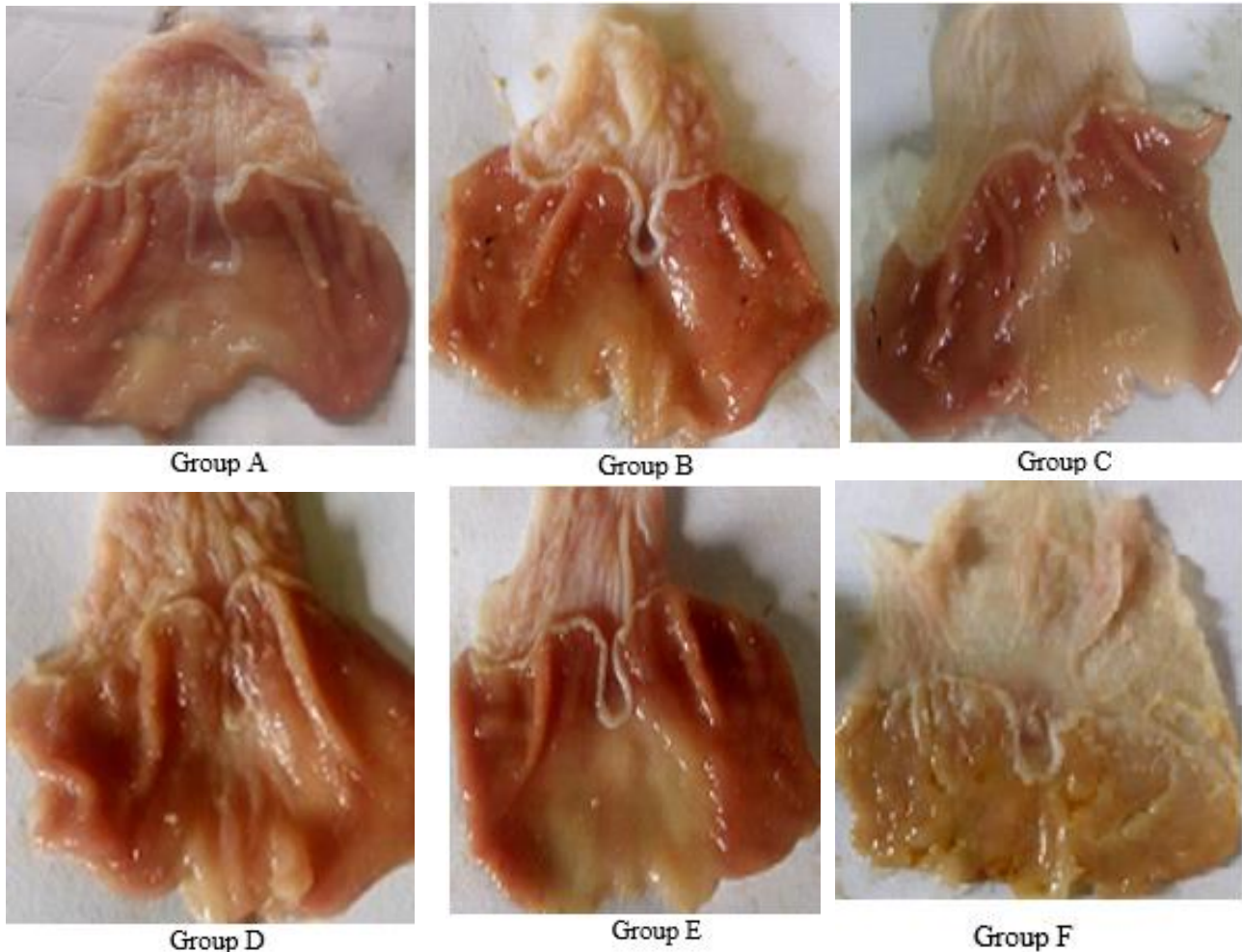
Ulcer indices	Group A	Group B	Group C	Group D	Group E	Group F
Ulcer severity	0.34 $\pm$ 0.59 <sup>+</sup>	2.26 $\pm$ 0.97*	2.01 $\pm$ 0.01*	1.21 $\pm$ 0.46	0.81 $\pm$ 0.46 <sup>+</sup>	2.51 $\pm$ 0.72*
Ulcer score	0.34 $\pm$ 0.39 <sup>+</sup>	10.26 $\pm$ 4.06*	7.01 $\pm$ 1.42*	3.01 $\pm$ 1.88 <sup>+</sup>	1.01 $\pm$ 0.72 <sup>+</sup>	10.01 $\pm$ 2.82*
%UIP	0.00%	0.00%	32.72%	0.00%	91.25%	3.45%

values are mean  $\pm$  standard deviation; n = 5; \* significant different at  $p < 0.05$  compared with control (group A); + significant different at  $p < 0.05$  compared with group B; Group A = Control; Group B = 4 hours ulcer induction without treatment; Group C = 72 hours ulcer induction without treatment; Group D = 7 days ingestion of extract without ulcer induction; Group E = 7 days pre-treatment with extract before 4hours ulcer induction; Group F = 7 days post-treatment with extract after 4 hours ulcer induction.

**Table 2.**The potential of aqueous leave extract of *Telfairia occidentalis* on indomethacin- induced oxidative stress.

Ulcer indices	Group A	Group B	Group C	Group D	Group E	Group F
Proteins	3.86±0.60 <sup>+</sup>	0.84±0.13 <sup>*</sup>	1.79±0.61 <sup>**</sup>	1.68±0.58 <sup>**</sup>	2.28±0.75 <sup>**</sup>	1.27±0.01 <sup>*</sup>
MDA	0.55±0.07 <sup>+</sup>	4.45±0.86 <sup>*</sup>	1.92±0.10 <sup>+</sup>	2.55±1.50	2.18±2.01 <sup>+</sup>	1.78±0.44 <sup>+</sup>

values are mean ± standard deviation; n = 5; \* significant different at  $p < 0.05$  compared with control (group A); + significant different at  $p < 0.05$  compared with group B; Group A = Control; Group B = 4 hours ulcer induction without treatment; Group C = 72 hours ulcer induction without treatment; Group D = 7 days ingestion of extract without ulcer induction; Group E = 7 days pre-treatment with extract before 4 hours ulcer induction; Group F = 7 days post-treatment with extract after 4 hours ulcer induction

**Plate 1.**

Stomach macroscopic observation of the effect of the extract on indomethacin-induced gastric ulcers. (Group A = Control; Group B = 4 hours ulcer induction without treatment; Group C = 72 hours ulcer induction without treatment; Group D = 7 days ingestion of extract without ulcer induction; Group E = 7 days pre-treatment with extract before 4 hours ulcer induction; Group F = 7 days post-treatment with extract after 4 hours ulcer induction).

Ulcer score was highest in group B (10.26±4.06) and this was followed by group F (10.00±2.83) and then group C (7.00±1.41) and these were significant ( $p < 0.05$ ) compared to the control (group A; 0.34±0.39). Pre-treatment with the extract before ulcer induction (1.01±0.72) resulted in a significant lower ( $p < 0.05$ ) ulcer score compared to post-treatment (10.01±2.84). Ingestion of the extract without ulcer induction was observed to induced minimal ulcer score (3.01±1.88) that was not significantly higher ( $p > 0.05$ ) than the control (0.34±0.39).

The ulcer inhibition potential of aqueous leave extract of *Telfairia occidentalis* on indomethacin induced gastric ulcers as presented showed that pre-treatment with the extract resulted in a 91.25% protection potential. Whereas, the post-treatment resulted in a 3.45% healing capacity.

Interestingly, there was a 32.72% self-healing capacity when indomethacin induced ulcer is left untreated for 72 hours (3 days).

**The potential of aqueous leave extract of *Telfairia occidentalis* on indomethacin-induced oxidative stress (MDA and protein):** Table 2 shows the impact of aqueous leave extract of *Telfairia occidentalis* on indomethacin-induced oxidative stress. Compared to the control (3.86±0.60), protein concentration was significantly reduced in all other groups. However, compared to group B (0.84±0.13), protein concentration was significantly higher in groups A (3.86±0.60), C (1.79±0.61), D (1.68±0.58) and E (2.28±0.75).

MDA concentration was highest in group B ( $4.45 \pm 0.86$ ) and this was followed by group D ( $2.55 \pm 1.50$ ) and then Group E ( $2.18 \pm 2.01$ ). On the other hand, MDA concentration was lowest in the control (Group A;  $0.55 \pm 0.07$ ) and this was followed by group F ( $1.78 \pm 0.44$ ) and the group C ( $1.92 \pm 0.10$ ). Statistically, MDA was significantly higher ( $p < 0.05$ ) in groups B ( $4.45 \pm 0.86$ ) compared to control ( $0.55 \pm 0.07$ ) but significantly lower ( $p < 0.05$ ) in group A ( $0.55 \pm 0.07$ ), C ( $1.92 \pm 0.10$ ), E ( $2.18 \pm 2.01$ ) and F ( $1.78 \pm 0.44$ ) compared to group B ( $4.45 \pm 0.86$ ).

**Gastric macroscopic effect of treatments with aqueous leave extract of *Telfairia occidentalis* on indomethacin-induced gastric ulcers:** Plate 1 indicate the macroscopic observations of the protective and healing potentials of aqueous leave extract of *Telfairia occidentalis* on indomethacin-induced gastric ulcers. Note the mild reduced mucus in group A. Group B presented thick mucosal with several perforated mucosa and mildly spread mucosa inflammation. Group C presented several elongated mucosa perforations with thick mucosa. Group D presented thick mucosal with mildly localized inflammations. Pre-treatment with extract (group E) presented widely spread severe hemorrhagic inflammation with thin mucosa, while the post-treated, Group F presented several perforated ulcerations that are healing with thick mucosa.

## DISCUSSION

The use of non-steroidal anti-inflammatory drugs (NSAIDs) is considered to be the major risk factor in gastric ulcers. In fact, the deleterious effects of Indomethacin on different diseases are well known and it induces gastric ulcers both in humans and experimental animals (Ilahi *et al.*, 2006). This study also confirmed the ulcerogenic potential of indomethacin on gastric mucosa as observed in group B. The mechanisms suggested for the gastric damage caused by NSAIDs are inhibition of prostaglandin synthesis and inhibition of epithelial cell proliferation in the ulcer margin, which is critical for the reepithelization of the ulcer crater (Levi *et al.* 1990).

There has been a considerable interest in finding natural antioxidants from plant materials to replace synthetic ones for effective management of therapeutic drug toxicity such as peptic ulcer (Pratt, 1992). In the present study, indomethacin caused damage on the glandular mucosa with a high ulcer index (see table 1), increased MDA level (table 2), alterations of macroscopic structure of gastric mucosa (figure 1). In contrast to this observed effect of indomethacin, pre-treatment with aqueous leave extract of *Telfairia occidentalis* at the dose of 100 mg/kg body weights (see group E) significantly decreased ( $P < .05$ ) the ulcer index (table 1), MDA level (table 2) and restored the gastric mucosa architecture (figure 1) with indomethacin-induced ulcer inhibition potential of 91.25%. On the other hand, although post-treatment with aqueous leave extract of *Telfairia occidentalis* at the dose of 100 mg/kg body weight (group F) reduced gastric MDA level (table 2), there were distorted macroscopic damage in the mucosa and a weak ulcer inhibition of 3.45% (table 1). This indicates therefore that aqueous leave extract of *Telfairia occidentalis* at the dose of 100 mg/kg body weights may slow ulcer healing considering the 31.71% ulcer healing potential of group C;

that was untreated for 72 hour. The finding of this study is consistent with that of Airaodion *et al.*, (2019), that *Telfairia occidentalis* was able to remedy the effect of ethanol by regulating the oxidative stress biomarkers, thus possesses therapeutic effect against ethanol-induced oxidative stress and can protect the body against free radicals arising from oxidative stress. This also appeared to be in line with the finding of Oboh (2005), while Adejuwon *et al.*, (2014) reported that *Telfairia occidentalis* at lower doses could significantly improve oxidative stress related pathological changes in brain of irradiated rats.

Although the protective mechanism of aqueous leave extract of *Telfairia occidentalis* against indomethacin induced gastric damage was not investigated in this study, it is however believed to be associated with the components of the extract. This assertion is based on the fact that *Telfairia occidentalis* is rich in minerals, antioxidants, vitamins and essential oils (Oboh *et al.*, 2004, 2006; Nwanna and Oboh, 2007; Adaramoye *et al.*, 2007; Emeka and Obidoa, 2009; Kayode *et al.*, 2009; Kayode *et al.*, 2010). Thus, the gastro protective effect with pre-treatment may be linked to its antioxidants and vitamins component. This may explain the reduced MDA levels in groups D, E and F compared to group B. Vitamins; for example vitamin C has been reported by Akpamu (2014) to attenuates the deleterious effect of indomethacin on ulcer and this was said to be due to its anti-oxidant activity by mechanism involving preservation of gastric microcirculation, attenuation of lipid peroxidation and release of pro-inflammatory cytokines (Konturek *et al.*, 2006). Administration of both indomethacin and vitamin C induce less gastric mucosal damage due to the increase in expression and activity of hemeoxygenase-1(HO-1). HO-1 plays an important role in gastric protection against indomethacin, by making cells more resistant to apoptotic death (Zhu *et al.*, 2000). Therefore, the observed ulcer preventive and weak ulcer curative activity of the aqueous leave extract of *Telfairia occidentalis* may be partially due to its relative antioxidant activity and its phyto-chemical constituents. The assertion of its phyto-constituents is based on the fact that phyto-constituents like flavonoids, tannins, terpenoids, and Saponin have been reported in several anti-ulcer literatures as possible gastro protective agents (Pandian *et al.* (2000).

In conclusion, the analyses of ulcer indices and macroscopic examinations showed that indomethacin is ulcerogenic and that aqueous leave extract of *Telfairia occidentalis* increased gastric protein level, reduced MDA level and restored the macroscopic structure of gastric mucosa. The best results were observed in rats pre-treated with aqueous leave extract of *Telfairia occidentalis* where, ulcer indices and stomach injury were almost restored to the pre-ulceration states. This indicates therefore that aqueous leave extract of *Telfairia occidentalis* possesses more of a protective effect than a healing potential.

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## REFERENCES

- Adaramoye, O.A., J. Achem, O.O. Akintayo and Fafunso, (2007). Hypolipidemic effect of *Telfairia occidentalis* (fluted pumpkin) in rats fed a cholesterol-rich diet. J. Med. Food; 10: 330-336.

- Adejuwon S. A., Imosemi I.O., Ebokaiwe P.A., Omirinde J.O. and Adenipekun A.A., 2014. Protective role of *Telfairia occidentalis* in irradiation-induced oxidative stress in rat brain. *Int. J. Biol. Chem. Sci.* 8(3): 843-853.
- Adisa, W.A., Nwankwo, A.A., Eidangbe, A.P., Uwuigbe, M., Olugbenga, M.A. Gastro-protective effects of aqueous extract of *Telfairia occidentalis* in indomethacin induced gastric ulcer. *International Journal of Herbs and Pharmacological Research*, 2019, 8(1): 9- 19.
- Adisa W.A., Olugbenga M.A., Bankole J.K., Uwuigbe M., Eidangbe A.P. (2018). Protective and therapeutic potential of *Telfairia occidentalis* on blood glucose level in alloxane induced diabetes mellitus in adult male rats. *International Journal of Herbs and Pharmacological Research*; 7(1): 31-39.
- Adisa W.A., Okhiai O., Bankole J.K., Iyamu O.A., Aigbe O. (2014). Testicular Damage in *Telfairia occidentalis* Extract Treated Wistar Rats. *American Journal of Medical and Biological Research*; 2(2): 37-45.
- Akindele A.J., Ajao M.Y., Aigbe F.R., Enumah U.S. (2013). Effects of *Telfairia occidentalis* (fluted pumpkin; Cucurbitaceae) in mouse models of convulsion, muscle relaxation, and depression. *J Med Food*; 16 (9): 810-816.
- Airaodionl A.I., Ogbuagu E.O., Ekenjoku J.A., Ogbuagu U., and Airaodion E.O. (2019). Therapeutic Effect of Methanolic Extract of *Telfairia occidentalis* Leaves against Acute Ethanol-Induced Oxidative Stress in Wistar Rats. *International Journal of Bio-Science and Bio-Technology (IJBSBT)*; 11(7): 179-189.
- Akoroda, M.O. (1990). Ethnobotany of *Telfairia occidentalis* (cucurbitaceae) among Igbos of Nigeria. *Econ. Bot*; 44: 2939.
- Akoroda, M.O., 1990. Seed production and breeding potential of the fluted pumpkin, *Telfairia occidentalis*. *Euphytica*; 49: 25-32.
- Akpamu, U. (2014). Combined effect of testosterone and vitamin C on indomethacin induced peptic ulcers in female Sprague Dawley rats. A project submitted to the Department of Human Physiology, Faculty of Basic Medical Sciences, Ambrose Alli University, Ekpoma, in partial fulfillment for the award of a Master of Science Degree in Human Physiology, 2014.
- Bansala V. K., Goel R.K. (2012). Gastroprotective effect of *Acacia nilotica* young seedless pod extract: Role of polyphenolic constituents. *Asian Pacific Journal of Tropical Medicine*; 5 (7):523-528.
- Bourdet, L. David, J. B., Pritchard, D. and Thakker, R. (2005). Differential substrate and inhibitory activities of ranitidine and famotidine toward human organic cation transporter 1 (hOCT1; SLC22A1), hOCT2 (SLC22A2), and hOCT3 (SLC22A3). *Journal of pharmacology and experimental therapeutics*; 315(3):1288-1297.
- Bagchi, M., Milnes, M., Williams, C., Balmoori, J., Ye, X., Stohs, S. and Bagchi, D. (1999). Acute and chronic stress-induced oxidative gastrointestinal injury in rats and the protective ability of a novel grape seed proanthocyanidic extract. *Nutr. Res.*; 19: 1189.
- Calam O. and Baron J.H. (2001). Pathophysiology of duodenal and gastric ulcer and gastric cancer. *BMJ*; 323:980.
- Chaturvedi, A., Kumar, M., Hawani, G., Chaturvedi, H. and Goel, R.K. (2007). Effect of ethanolic extract of *Eugenia jambolana* seeds on gastric ulceration and secretion in rats. *Indian J. Physiol. Pharmacol*; 51: 131-140.
- Emeka, E.J.I. and Obidoa, O. (2009). Some biochemical, haematological and histological responses to a long term consumption of *Telfairia occidentalis*-supplemented diet in rats. *Pak. J. Nutr*; 8: 1199-1203.
- FAO (1989). Some medicinal plants of Africa and Latin America. FAO Forestry Paper, 67.
- Fisher A.A. and Le Couteur D.G. (2012). Nephrotoxicity and Hepatotoxicity of Histamine H2 Receptor Antagonists. Springer Link.
- Gbile, Z.O. (1986). Ethnobotany, Taxonomy and Conservation of Medicinal Plants. In: *The State of Medicinal Plants Research in Nigeria*, Sofowora, A. (Ed.). University of Ibadan Press, Ibadan, Nigeria.
- Gornal AG, Bardwil GS, David MM. 1949. Determination of serum proteins by the means of Biuret reactions. *J Biol Chem.* 177:751-766.
- Hano, J., Bugajski, J. and Danek, L. (1976). Effect of adrenergic blockade on gastric secretion altered by catecholamine's in rats. *Arch. Immunol. Ther. Exp. (Warsz)*, 24(4):507- 524.
- Ilahi, M, Khan, J, Inayat, Q., Abidi, T.S. (2006). Histological changes in parts of foregut of rat after indomethacin administration. *J Ayub Med Coll Abbottabad*; 18(3): 29-32.
- Kayode, A.A.A. and Kayode, O.T. (2011). Some Medicinal Values of *Telfairia occidentalis*: A Review. *American Journal of Biochemistry and Molecular Biology*; 1: 30-38.
- Kayode, A.A.A., Kayode, O.T. and Odetola, A.A. (2010). *Telfairia occidentalis* ameliorates oxidative brain damage in malnourished rats. *Int. J. Biol. Chem*; 4: 10-18.
- Kayode, O.T., Kayode, A.A. and Odetola, A.A. (2009). Therapeutic effect of *Telfairia occidentalis* on protein energy malnutrition-induced liver damage. *Res. J. Med. Plant*; 3: 80-92.
- Jung, U.P., JiHoon, K., Aziz, A., Ahtesham, H., Jin Sook, C. and Young, I. L. (2019). Gastroprotective effects of Plants Extracts on Gastric Mucosal Injury in Experimental Sprague-Dawley Rats. *BioMed Research International*; Article ID 8759708 11 pages.
- Kim, J.W. (2008). NSAID-induced gastroenteropathy. *Korean J. Gastroenterol.*; 52(3):134-141.
- Konturek, C.P., Kania, J., Hahn, G.E. and Konturek, W.J. (2006). Ascorbic acid attenuates aspirin-induced gastric damage: role of inducible nitric oxide synthase. *Journal of Physiology and Pharmacology*; 57(5): 125 – 136.
- Kurekci, C., Bishop-Hurley, S.L., Vercoe, P.E., Durmic, Z., Al Jassim, R.A., McSweeney, C.S. (2012). Screening of Australian plants for antimicrobial activity against *Campylobacter jejuni*. *Phytother Res*; 26:186-90.
- Kuku, A., Etti, U. and Ibronke, I.S. (2014). Processing of fluted pumpkin seeds, *Telfairia occidentalis* (hook f) as it affects growth performance and nutrient metabolism in rats. *African journal of food agriculture nutrition and development*; 14 (5).
- Lanas, A, Carrera-Lasfuentes, P, Garcia Rodriguez, L.A., et al. (2015). Outcomes of peptic ulcer bleeding following treatment with proton pump inhibitors in routine clinical practice: 935 patients with high- or low-risk stigmata. *Scand J Gastroenterol*; 49: 1181-90.
- Lanas, A. and Chan, F.K. (2017). Peptic ulcer disease. *Lancet*; 390:613-24

- Leontiadis, G.I., Molloy-Bland, M., Moayyedi, P., Howden, C.W. (2013). Effect of co-morbidity on mortality in patients with peptic ulcer bleeding: systematic review and meta-analysis. *Am J Gastroenterol*; 108: 331–45.
- Levi, S., Goodlad, R.A. and Lee, C.Y. (1990). Inhibitory effect of NSAIDs on mucosal cell proliferation associated with gastric ulcer healing. *Lancet* 336(8719):840-843.
- Miami, H., Kautianen, H., Virta, L.J. and Farkkila, M.A. (2016). Increased short- and long-term mortality in 8146 hospitalised peptic ulcer patients. *Alimentary Pharmacology and Therapeutics*; 44:234.
- Malysenko, O.S., E.I. Beloborodova, A.M. Vavilov, G.V. Lomivorotova and V.I. Kasperskaia, 2005. Impact of age and type of behavior on the course of ulcer disease. *Ter. Arkh*; 77: 28-31.
- Morufu E. B., Nwachukwu, D., Onwe, P.E., and Folawiyo, M.A. (2014). Gastric acid anti-secretory effects of aqueous leaf extract of *Nauclealatifolia* (Rubiaceae) in rats. *The Journal of Phytopharmacology*; 3(6): 389-394.
- Nwanna, E.E. and Oboh, G (2007). Antioxidant and hepatoprotective properties of polyphenol extracts from *Telfairia occidentalis* (Fluted Pumpkin) leaves on acetaminophen induced liver damage. *Pak. J. Biol. Sci*; 10: 2682-2687.
- Oboh, G. and Akindahunsi, A.A. (2004). Change in the Ascorbic Acid, Total Phenol and Antioxidant Activity of Some Sun-Dried Green Leafy Vegetables in Nigeria. *Nutrition and Health*; 18: 29-36.
- Oboh, G., 2005. Hepatoprotective property of ethanolic and aqueous extracts of fluted pumpkin (*Telfairia occidentalis*) leaves against garlic-induced oxidative stress. *J. Med. Food*; 8: 560-563.
- Oboh, G., Nwanna, E.E. and , C.A. (2006). Antioxidant and antimicrobial properties of *Telfairia occidentalis* (Fluted pumpkin) leaf extracts. *J. Pharmacol. Toxicol.*, 1: 167-175.
- Pandian RS, Anuradha CV, Viswanathan P. (2002).Gastroprotective effect of fenugreek seeds (*Trigonellafoenumgraecum*) on experimental gastric ulcer in rats. *J Ethnopharmacol.*81:393–7.
- Pohle, T., Brzozowski, T., Becker, J.C., Van Der Voort, I.R., Markman, A. and Konturek, S.J. (2001). Role of reactive oxygen metabolites in aspirin-induced gastric damage in humans: gastroprotection by vitamin C. *Aliment Pharmacol. Ther.*; 15: 677–687.
- RibeiroFilho, E. ; Paiva, P. C. de A. ; Barcelos, A. F. ; Rezende, C. A. P. ; Cardoso, R. M. ; Banyas, V. L., 2000. The effect of coffee hulls on the performance of Holstein-zebu steers during the growing period. *Ciencia e Agrotecnologia*; 24 (1): 225-232.
- Rates, S.M.K. (2001). Plants as source of drugs. *Toxicon*, 39(5): 603-613.
- Repetto, M.G.I. and Llesuy, S.F. (2002). Antioxidant properties of natural compounds used in popular medicine for gastric ulcers. *Braz J Med Biol Res*; 35(5):523-34.
- Schmeda-Hirschmanna G. and Yesiladab E. (2005). Traditional medicine and gastroprotective crude drugs. *Journal of Ethnopharmacology*; 100(1–2): 61-66.
- Tortora, G.J. and Grabowski, S.R. (2003). *Principles of Anatomy and Physiology*. 10th ed. John Wiley & Sons, Inc, NJ, p.889.
- Toyin, M. S., Isiaka, A. A., Sikiru, A. B., Olusegun, A.A., Opeyemi, K. O., Olanrewaju, A.A.(2013). Blood glucoselowering effect of *Telfairia occidentalis*: A preliminary study on the underlying mechanism and responses. *Biokemistri An International Journal of the Nigerian Society for Experimental Biology*; 25 (3): 133–139.
- Wedemeyer, R.-S., and Blume, H. (2014). Pharmacokinetic drug interaction profiles of proton pump inhibitors: an update. *Drug Safety*; 37(4): 201–211.
- Whittle J. R.B. (2003). Gastrointestinal effects of nonsteroidal anti- inflammatory drugs. *Fundamental & Clinical Pharmacology*; 17(3): 301-313.
- Wilhelmi, G. and Menasse- Gdynia, R. (1972). *Pharmacology*; 8: 321-328. In: Sadik, S.A.E. (1984).
- Zhu GH, Wong BC, Slosberg ED, Eggo MC, Ching CK, Yuen ST, Lai KC, Soh JW, and Weinstein IB, Lam SK. (2000): Overexpression suppresses indomethacin-induced apoptosis in gastric epithelial cells. *Gastroenterology*. 118: 507-514.