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Healing potentials of aqueous extract of irish potato tubers on indomethacin-induced peptic ulcer in albino rats

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Abstract
The healing potential of aqueous extract of Irish potato tubers (IPT) on indomethacin-induced peptic ulcer was investigated. Freshly harvested and dried IPT were milled into fine powder and extracted using water. Forty albino rats weighing 165.00 ± 21.21g were fasted overnight and ulcer induced with a single oral dose of indomethacin (30 mg/kg body weight). After confirmation of ulceration, 35 animals were randomly divided into 5 groups. Groups 1, 2 and 3 ulcer-induced animals were treated with 400 and 800 mg/kg of IPT extracts and omeprazole (20 mg/kg) respectively. Groups 4 and 5 animals served as the indomethacin ulcer-induced but untreated, and normal control animals respectively. All drug treatments were done once daily via oral route for 21 days. Thereafter animals were anaesthetized, their stomach excised and ulcer index and gastric acid output determined using standard methods. The stomach tissues of 5 animals per group were homogenized and assayed for superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and pepsin activities as well as malondialdehyde (MDA) and reduced glutathione (GSH) concentrations. The remaining 2 stomach tissues per group were processed for histological analysis. The results showed that treatment with 400 and 800 mg/kg IPT extracts significantly ($p<0.05$) elicited high percentage ulcer inhibitory effects comparable to omeprazole. Treatment with extracts also significantly ($p<0.05$) increased the pH but reduced gastric acid output of the stomachs to values within the range of the normal control group. There were significantly ($p<0.05$) higher SOD, CAT and GPx but reduced pepsin activities in the stomach tissues of extracts and omeprazole treated animals compared to the indomethacin group. Similarly, treatment with both IPT extracts significantly ($p<0.05$) reduced MDA but increased GSH concentrations. Treatment with the IPT extracts also appreciably corrected the stomach tissue necrotic changes and inflammatory infiltrations elicited by indomethacin. The study concluded that aqueous extract of IPT reversed perturbations caused by indomethacin-induced ulcer, thus confirming the folkloric use of the plant extract in the treatment of peptic ulcer.

Keywords: peptic ulcer, irish potato, *Solanum tuberosum*, antioxidant enzymes, ulcer index

Introduction

Peptic ulcer is a pathological condition that affects the gastrointestinal tract (GIT). The GIT is continuously exposed to potentially injurious agents such as acid, pepsin, bile acids, food ingredients, bacteria and drugs such as non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs are a group of drugs that reduce pain, decrease fever and in higher doses, decrease inflammation. NSAID-induced peptic ulcer is one of the most serious complications of any synthetic drug therapy. It is now well-recognized that ulceration induced by NSAIDs is mediated by suppression of the cyclooxygenase (COX)-dependent pathway and subsequent blocking of the synthesis of prostaglandins (PG) [1].

Irish potato (*Solanum tuberosum* L.) belongs to the solanaceae family. It is a native of Western Hemisphere and is believed to have originated somewhere between Mexico and Chile, possibly in Andes highlands of Bolivia and Peru. It later spread to other places like England and Ireland. The planting stock was believed to have been received from Ireland, hence the name Irish potato. Irish potato was introduced into Nigeria in the later part of the 19th century or early 20th century by the Europeans notably the tin miners in the Jos Plateau. Irish potato is grown for food as well as a commercial crop. It is a major source of income among the rural farmers in many African communities [2]. Potatoes are one of the most common and important food sources on the planet. They contain a wealth of health benefits that make them essential as a staple dietary item for the world's population. These health benefits include their ability to improve digestion, reduce cholesterol levels, boost heart health, protect from polyps, prevent cancer, manage diabetes, strengthen the immune system, reduce signs of aging, protect the skin, increase circulation, reduce blood pressure, maintain fluid balance, reduce insomnia, and boost eye health [3].

Fig 1: Irish potato tubers

Potatoes have anti-inflammatory properties. This is primarily due to the presence of beta-carotene, vitamin-C and magnesium. It is equally effective in curing internal and external inflammation. It's content of vitamin-C, iron and other nutrients help to cure bronchitis. Potatoes are believed to be capable of warming up the body, possibly due to the sweetness and other nutrients that impact body temperature. This property is also beneficial for people suffering from bronchitis, along with its powerful effect on congestion [1]. Potatoes have a soothing effect on the stomach and the intestines. Its B-complex vitamins, vitamin C, beta-carotene, potassium and calcium content have been associated with treatment of stomach ulcers. Moreover, the roughage in potatoes prevents constipation and the resultant acid formation, thereby reducing the chances of ulcers. The anti-inflammatory and soothing properties of potatoes also reduce the pain and inflammation associated with ulcers [4]. Furthermore, the fiber or roughage present in potatoes helps the body retain water. This maintains water balance in the body, keeping the body hydrated and the cells functioning efficiently including the mucus producing cells of the stomach [5]. This study evaluated the healing potential of aqueous extract of Irish potato tubers on indomethacin induced peptic ulcerated rats.

Materials and Methods

1. Collection and extraction of plant materials

Freshly harvested Irish potato tubers were purchased from Aba grocery market, Abia State, Nigeria. They were identified by Prof. Obiefuna of Department of Crop Science, Federal University of Technology Owerri, Nigeria. The potatoes were thoroughly washed in running water, peeled, sliced and dried in an oven at 60 ^{o}C to constant weight. The dried potatoes were milled into fine powder (flour). Exactly 100 g of the flour was weighed into a 100 ml conical flask and made up with distilled water. This was mixed with magnetic stirrer and allowed to stand for 24 hours at room temperature with intermittent stirring. The extract was filtered through Whatman No. 2 filter paper and residue discarded. The filtrate was evaporated in a rotary evaporator at 35^{o}C with a yield of 20 % extract, which was preserved for further analysis.

2. Acute toxicity test (LD_{50})

This was carried out in 2 phases using the modified Lorke's method [6]. Briefly, in phase 1, 9 mice which were divided into 3 groups containing 3 mice each was used. Each group of animals were administered different doses (10, 100 and 1000 mg/kg) of the extract. The animals were placed under observation for 24 h to monitor their behavior as well as to see if mortality would occur.

Phase 2 also used 9 mice which were divided into 3 groups of 3 mice each. The mice were administered higher doses of 2500, 5000 and 10000 mg/kg of the extract respectively and were observed for 24 hours for changes in behavior or mortality. The LD_{50} which is the square root of the highest dose with no mortality multiplied by the lowest dose with mortality could not be calculated since none of the doses elicited death of the animals.

3. Experimental animals

Forty albino rats with average weight of 165.00 ± 21.21g were used for the study. They were maintained in standard conditions in the small animal center of the Department of Biochemistry, Federal University of Technology Owerri, Nigeria.

4. Induction of ulceration

The rats were administered a single oral dose of indomethacin (30 mg/kg body weight). They were deprived of food but had free access to water 24 hours prior to ulcer induction. Various degrees of ulceration manifested after 8 hours of indomethacin administration. This was determined using the fecal occult blood test for ulceration and further confirmed by extracting the stomach of randomly selected animals from each group to check for ulceration using the procedure outlined by Szabo and Hollander [7].

5. Experimental design

The remaining thirty-five albino rats were randomly divided into five groups of seven rats each and treated as follows:

Group 1 (low dose group) received 400 mg/kg body weight of aqueous Irish potato extract after 8 hours of induction of ulcer.

Group 2 (high dose group) received 800 mg/kg body weight of aqueous extract of Irish potato extract after 8 hours of induction of ulcer.

Group 3 (standard control group) received standard drug (omeprazole 20 mg/kg body weight) after 8 hours of induction of ulcer.

Group 4 (negative or ulcer control group) were not treated after ulcer induction.

Group 5 served as normal control group (received only food and water) without ulcer induction.

The administration was done once daily via oral route for 21 days, while all the animals were provided water *ad libitum*. At the end of the administration period, the animals were anaesthetized using dichloromethane and their stomach and duodenum were harvested. Stomach tissues from 5 animals per group were later homogenized (after gastric acid output determination) in ice cold 0.1 M phosphate buffer (pH 7.4) in a ratio of 4:1, and centrifuged at 12,000×g for 20 min at 4^{o}C. The supernatant was collected and preserved at 4^{o}C for further analysis.

6. Determination of gastric acid output

The gastric content of the extracted stomach was drained into a centrifuge tube and diluted with 1ml of distilled water. The pH of the solution was measured using a pH meter. Distilled water (4ml) was added to the tubes and centrifuged at 2000 g for 5mins. The gastric acid output was determined in the supernatant (2 ml) by titration with 0.01N NaOH using phenol red as indicator.

7. Determination of biochemical parameters

Activity of superoxide dismutase (SOD) was assayed according to the procedure of Das and Roy [8]. Catalase (CAT) and glutathione peroxidase (GPx) activities were determined by the methods described by Sinhn *et al.* [9] and Retruck *et al.* [10] respectively. Pepsin activity was assayed according to the method of Debnath [11], while lipid peroxidation was determined spectrophotometrically by measuring the concentration of thiobarbituric acid reactive substances (TBARS) as described by Liu and Ma [12]. Concentration of reduced glutathione (GSH) was assessed according to the method of Jollow *et al.* [13].

8. Histological studies of tissues

The method described by Slaoul and Fiette [14] was used with minor modifications. Briefly, the stomach and intestinal tissues of two animals per group were fixed in a large quantity of 10% neutral buffered formalin. The tissues were dehydrated by passing them through grades of alcohol and then immersed in xylene for 3 hours. The tissues were later transferred from the clearing agent (xylene) to a bath of molten paraffin wax in an embedding oven. From the oven, the tissues were gently transferred with the aid of a pair of warmed blunt-nosed forceps into Leuckhart embedding boxes of molten paraffin wax. The molds were transferred into a container of cold water and left for 30 min until the wax hardens. The hardened blocks were trimmed and the tissues sectioned with a rotary microtome. The sections were then attached to grease-free slides, dewaxed, dehydrated and stained with haematoxylin and eosin. The stained sections were mounted with dibutylpthalate polystyrene xylene (DPX) and examined under high resolution microscope (x 400) with photographic facility and photomicrographs were taken.

9. Statistical analysis

The data obtained were analyzed using one way analysis of variance (ANOVA) with the aid of computer-based GraphPad Prism 5.3 software (GraphPad Inc., USA). Values for $p<0.05$ were considered statistically significant.

Results

Administration of aqueous extract of Irish potato tubers to mice at doses of up to 10000 mg/kg body weight did not lead to any mortality, and hence the lethal (LD50) dose was indeterminate.

There were no significant ($p>0.05$) differences in the baseline ulcer index of the animals obtained after 8 hours of indomethacin administration (Figures 2A). The values ranged from 43.89 ± 0.89 through 44.28 ± 1.21 and 44.65 ± 0.62 to 45.10 ± 0.77 (unit of measurement) for the indomethacin, omeprazole, 400 mg/kg extract and 800 mg/kg extract groups respectively. Figure 2B showed significant ($p<0.05$) reductions in the ulcer index of the omeprazole (1.40 ± 0.20), 400 mg/kg extract (1.58 ± 0.26) and 800 mg/kg extract (1.21 ± 0.19) treatment groups when compared with the ulcer-induced but untreated indomethacin group (5.08 ± 0.72). The percentage ulcer inhibitory effects of the extracts and omeprazole were calculated to be 68.90 ± 4.07%, 70.86 ± 4.13 and 74.28 ± 3.82% for 400 mg/kg extract, omeprazole, and 800 mg/kg extract respectively (Figure 2C).

Figure 3A shows the pH values of the gastric content of the albino rats. It showed that the pH values of the Indomethacin (3.58 ± 0.17), omeprazole (4.25 ± 0.76) and 400 mg/kg extract (4.20 ± 0.61) groups were significantly ($p<0.05$) lower than those of the 800 mg/kg extract (5.60 ± 0.74) and normal control (6.13 ± 0.28) animals. On the other hand, the gastric acid output of the 800 mg/kg extract (25.00 ± 1.97 mEq/L) and normal control (25.50 ± 2.65 mEq/L) groups were significantly ($p<0.05$) lower than those of the Indomethacin (32.35 ± 1.96 mEq/L), omeprazole (28.50 ± 1.29 mEq/L) and 400 mg/kg extract (30.00 ± 1.92 mEq/L) groups.

Treatment of the indomethacin ulcer-induced animals with 400 and 800 mg/kg of Irish potato tuber extracts significantly ($p<0.05$) increased the stomach tissue SOD activity from 1.57 ± 0.02 IU for the Indomethacin group to values of 1.77 ± 0.01 and 1.78 ± 0.01 IU respectively. These were non-significantly ($p>0.05$) comparable to that of the normal control animals (1.78 ± 0.02 IU) but significantly ($p<0.05$) lower than the SOD activity of the omeprazole group (1.84 ± 0.02 IU) (Figure 4A). Similarly, while induction of ulcer with indomethacin reduced stomach tissue catalase activity to 0.67 ± 0.04 µmol H_2O_2/min, treatment with 800 mg/kg extract and omeprazole significantly ($p<0.05$) improved its activity to 0.96 ± 0.05 and 1.09 ± 0.08 µmol H_2O_2/min, which are values comparable with that of the normal control group (0.93 ± 0.011 µmol H_2O_2/min) (Figure 4B). The highest catalase activity was observed with the 400 mg/kg extract treatment group at 1.16 ± 0.08 µmol H_2O_2/min. Figure 4C showed that the glutathione peroxidase (GPx) activity of the ulcer-induced but treated groups were significantly ($p<0.05$) higher than those the indomethacin (8.17 ± 2.08 µmol GSH/min/g protein) and normal control (16.90 ± 21.28 µmol GSH/min/g protein) untreated groups. The GPx activities of the omeprazole, 400 mg/kg and 800 mg/kg extracts treated groups were 22.97 ± 2.75, 22.66 ± 3.41 and 19.99 ± 2.02 µmol GSH/min/g protein respectively. The pepsin activities (Figure 4D) of the indomethacin (37.12 ± 2.64 µmol/L) and 400 mg/kg extract (35.97 ± 4.59 µmol/L) groups were significantly ($p<0.05$) higher than those of the 800 mg/kg extract (25.81 ± 3.33 µmol/L) and omeprazole (28.08 ± 3.96 µmol/L) treated groups as well as the normal animal group (26.24 ± 3.93 µmol/L).

Figure 5 showed that induction of ulcer with indomethacin elicited a significant ($p<0.05$) increase in malondialdehyde (MDA) concentration (4.78 ± 0.52 nmol/L) when compared with that of the normal control (3.07 ± 0.32 nmol/L) group. Treatment of indomethacin-induced ulcer with 400 and 800 mg/kg extracts of Irish potato as well as with omeprazole significantly ($p<0.05$) reduced the MDA concentrations to 3.65 ± 0.12, 3.63 ± 0.69 and 1.73 ± 0.19 nmol/L respectively, which comparable to that of the normal control animals. On the other hand, treatment of the indomethacin-ulcerated animals with 400 and 800 mg/kg of Irish potato extracts and omeprazole significantly ($p<0.05$) improved reduced glutathione (GSH) concentrations to 0.35 ± 0.03, 0.33 ± 0.03 and 0.32 ± 0.07 mmol/L respectively in comparison with that of the indomethacin-ulcer-induced but untreated group (0.22 ± 0.03 mmol/L).

Figure 6 shows the histological photomicrographs of the stomach tissues of indomethacin-ulcer-induced animals treated with Irish potato tuber extracts. The micrograph of the normal control animals showed normal tissue architecture which indomethacin treatment distorted eliciting presence of necrotic changes and inflammatory infiltrations. Treatment with 400 mg/kg and 800 mg/kg of Irish potato extracts apparently corrected the observed damages, although mild congestion of blood vessels and inflammatory infiltrations were still observable, when compared with the microphotographs of the omeprazole treated and normal control groups.

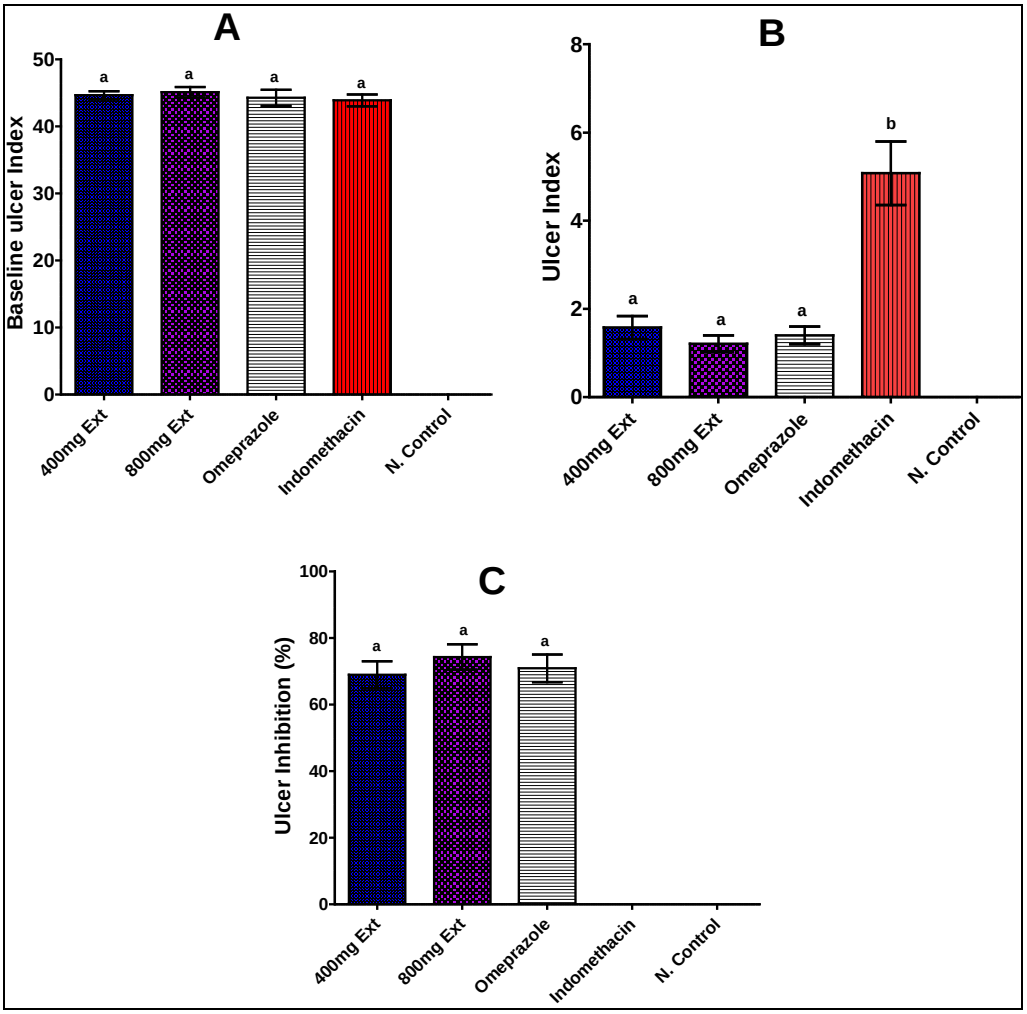

Fig 2: Baseline ulcer index (A; after 8 hours of indomethacin ulcer induction), ulcer index (B) and percentage ulcer inhibition (C) after 21 days of treatment with aqueous extract of Irish potato. Bars are mean ± standard deviation. Bars with different alphabets are statistically significant ($p<0.05$)

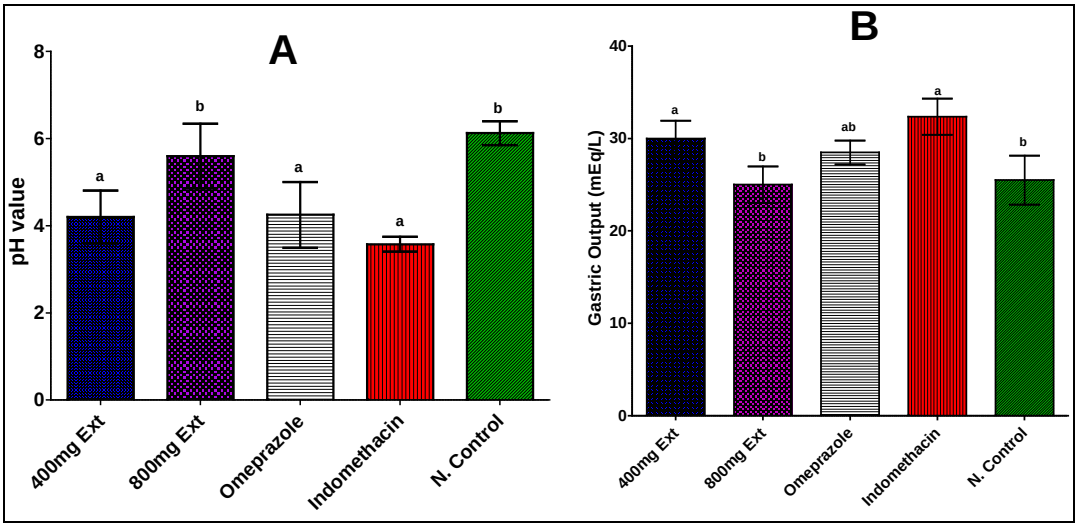

Fig 3: pH value (A) and gastric acid output (B; mEq/L) of the stomach content of albino rats exposed to indomethacin and treated with aqueous extract of Irish potato. Bars are mean ± standard deviation. Bars with different alphabet letters are statistically significant ($p<0.05$)

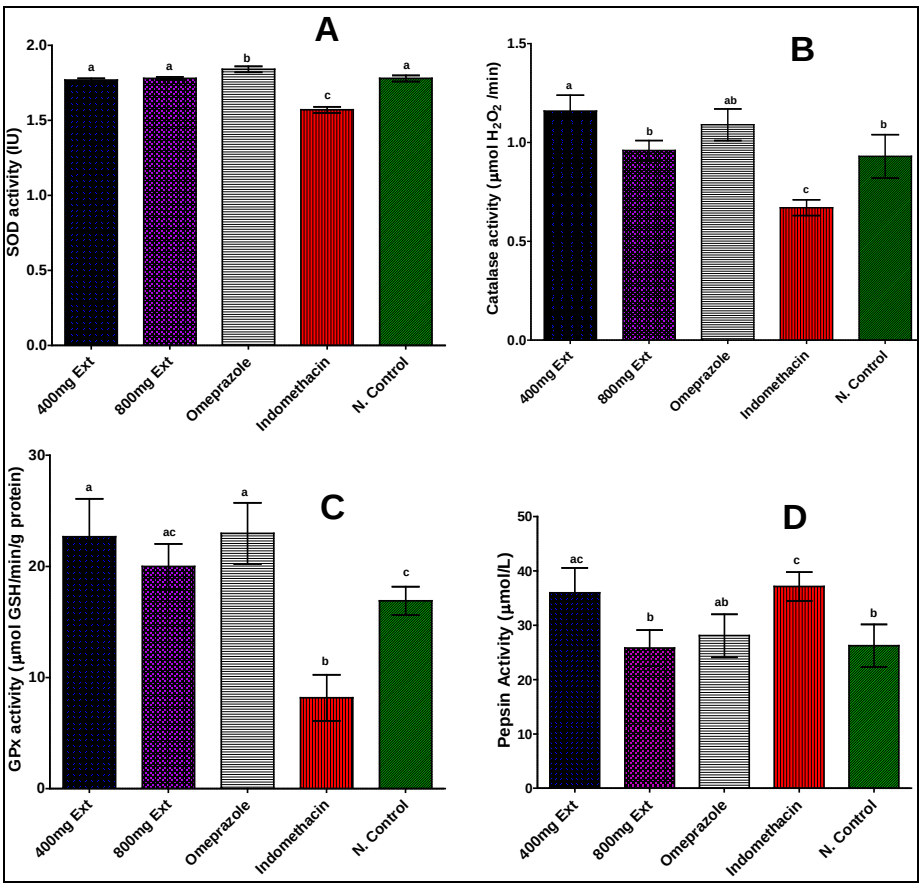

Fig 4: Superoxide dismutase (A; IU), catalase (B; µmol H_2O_2/min), glutathione peroxidase (C; µmol GSH/min/g protein) and pepsin (D; µmol/L) activities of albino rats exposed to indomethacin and treated with aqueous extract of Irish potato. Bars are mean ± standard deviation. Bars with different alphabet letters are statistically significant ($p<0.05$). SOD, superoxide dismutase; GPx, glutathione peroxidase.

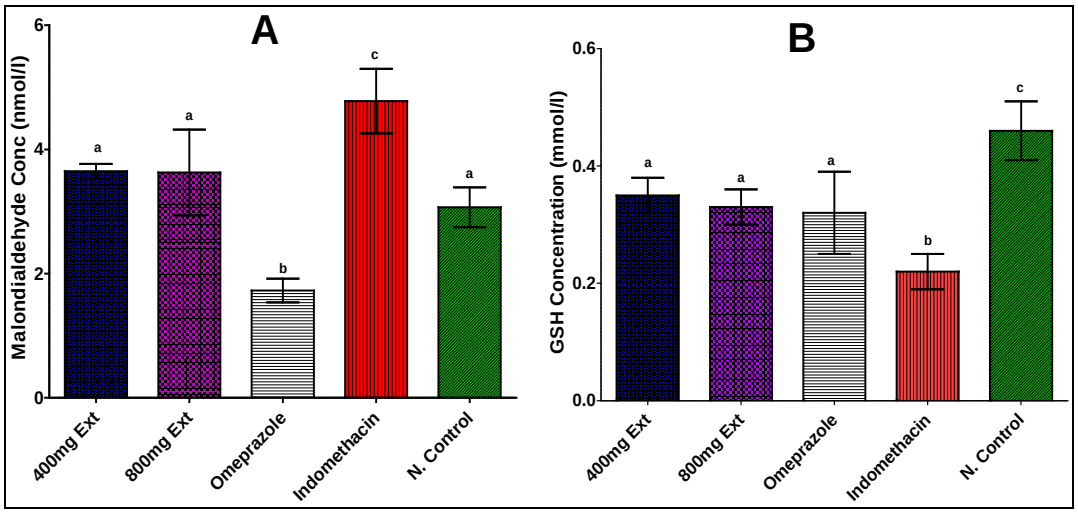

Fig 5: Malondialdehyde (A; nmol/L) and reduced glutathione (B; mmol/L) concentrations of albino rats exposed to indomethacin and treated with aqueous extract of Irish potato. Bars are mean ± standard deviation. Bars bearing different alphabet letters are statistically significant ($p<0.05$). GSH, reduced glutathione

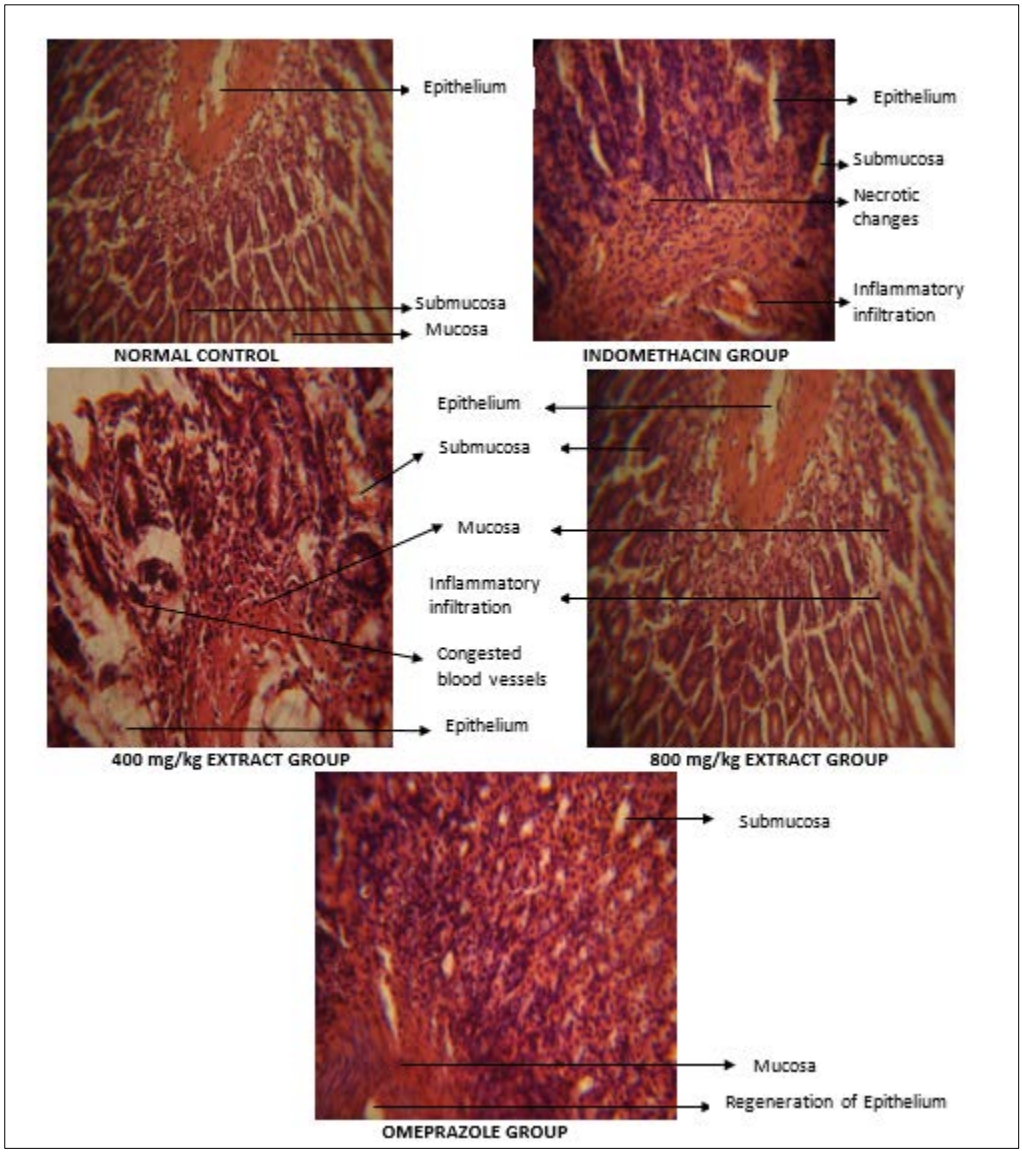

Fig 6: Cross section of albino rats exposed to indomethacin and treated with aqueous extract of Irish potato (Hematoxylin and Eosin × 400).

Discussion

Peptic ulcer is a widespread disease of global importance and is not restricted to any particular sex or age group [15]. The predisposing factors are common which includes stress, alcohol, NSAIDS, *H. pylori* infection, etc. Much effort has been made to find treatment for peptic ulcer. The diversity of factors implicated in the etiology of peptic ulcer coupled with the different mechanisms of action of the currently available drugs indicate that all is not yet known about peptic ulcer treatment. The etiology of peptic ulcer is incidental in most cases. However, it is generally accepted that the ulcer results from an imbalance between aggressive factors and maintenance of mucosal integrity through the endogenous mechanism [16]. To equilibrate this balance, different therapeutic agents are used to obstruct gastric acid secretion, boost the mucosal defense mechanisms by increasing mucosal production and stabilize the surface epithelial cells or interfere with prostaglandin synthesis [17]. Some of these therapeutic agents include plants that have been traditionally used for ulcer treatment such as Irish potato, pawpaw, *Zingiber officinale*, etc.

The result of acute toxicity test (LD_{50}) of aqueous extract of Irish potato tubers showed that at both low and high doses of extract administration no mortality was recorded. This implies that the extract was apparently non-toxic and is expected as the tuber is a staple food for humans.

Results of ulcer index study of the animals after 8 hours of ulcer induction with indomethacin and after 21 days of treatment with Irish potato extracts are presented in Figures 2A-B. Induction of ulcer with indomethacin produced typical lesions in the gastric mucosa resulting in substantial ulceration after 8 hours. The observed high ulcer index following oral administration of indomethacin in the ulcer-induced rats may be attributed to either free radical formation or inhibition of prostaglandin synthesis, which in turn inhibits the release of mucus, a defensive factor against gastrointestinal damage [15]. Decreased prostaglandin level has been associated with impaired gastro-protection and increased gastric acid secretion, which are important events in the etiology of mucosal ulceration. This is in tandem with the reports that indomethacin cause alteration in gastric secretions of experimental animals [15, 16]. Treatment with Irish potato extract

for 21 days significantly reduced the ulcer index of the animals when compared with the ulcer-induced but untreated animals.

The percentage ulcer inhibitory potentials of the extracts after 21 days of treatment as shown in Figure 2C is the level of protection offered by the aqueous Irish potato extract against indomethacin induced ulceration in the gastric mucosa. Interestingly, no significant difference was observed between the ulcer inhibitory effects of both doses of the extracts and omeprazole, the standard ulcer drug used. The protective potential of the extract against ulceration may be linked to the reported array of beneficial antioxidant nutrients and phytochemical constituents of the plant [18]. These have been associated with ability to scavenge free radical and regulate mucosal membrane permeability thereby countering the effect of indomethacin on the gastric acid secretion. This is in agreement with the reports of Airaodion *et al*. [19] where gastro-protective potentials of *Curcuma longa* and *Moringa oleifera* extracts against indomethacin ulcerated rats were associated with the phenolic compounds, flavonoids and various other bioactive principles of the studied plants.

In the present study, treatment of ulcerated animals with omeprazole and 400 mg/kg of aqueous Irish potato extract did not significantly ($p>0.05$) affect the pH values and gastric acid outputs of the animals' stomach content. However, treatment with 800 mg/kg of aqueous Irish potato extract significantly ($p<0.05$) increased the pH but reduced gastric acid output when compared with the indomethacin ulcer-induced but untreated animals (Figure 3). This could be an indication that Irish potato at high doses could reduce the high acidic and gastric output level of the stomach gastric content. The pH of gastric juice gives an idea of the level of acidity of gastric secretions. Lower pH value is an indication of increased hydrogen ion concentration in gastric juice, which has been linked to pathogenesis of ulcer and gastric damage in experimental animals [19]. The observed effect of 800 mg/kg of aqueous Irish potato extract help to restore the gastric pH to values comparable to those of the normal control animals.

Results of our study also showed that administration of Irish potato extract perturbed the activities of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) when compared with normal control animals (Figure 4A-C). SOD, CAT and GPx are the key antioxidant enzymes of cellular defense system against reactive oxygen species [20, 21]. SOD catalyzes the conversion of superoxide (O_2) to hydrogen peroxide (H_2O_2) and thus it is a major defense system for aerobic cells in combating the toxic effects of superoxide radicals. The product of SOD catalysis, H_2O_2 is a harmful by-product in many metabolic processes. To prevent H_2O_2 based damage to cells and tissues, it must be quickly converted into less toxic substances. CAT is used by cells to rapidly catalyze the decomposition of H_2O_2 into less reactive gaseous oxygen and water molecules [22]. GPx is an important intracellular enzyme that breaks down hydrogen peroxides (H_2O_2) to water and lipid peroxides to their corresponding alcohol mainly in the mitochondria and sometimes in the cytosol. GPx plays crucial role of inhibiting lipid peroxidation process and therefore protects cells from oxidative stress [22, 23].

The SOD, CAT and GPx activities of the animals treated with Irish potato extract were significantly higher than that of the indomethacin group. The decrease in SOD, CAT and GPx activities in the indomethacin ulcerated rats when compared with normal control is a manifestation of enhanced lipid peroxidation, increased production of free radicals and mucosal damage. Free radicals thwart antioxidant enzymes activities and initiate lipid peroxidation which is an important event in the toxicity mechanism of indomethacin [15]. Indomethacin has previously been reported to decrease antioxidant enzymes (SOD, CAT and GPx) activity in rat stomach thereby inducing gastric ulceration [15, 19].

Increase in pepsin activity of indomethacin ulcerated rats observed in this study is an indication of altered hydrophobicity and reduced ability of the mucosal membrane against hemorrhagic lesion [24]. As present in Figure 4D, treatment with Irish potato extract and omeprazole reversed the effect of indomethacin on pepsin activity. Pepsin, a member of the peptidase A_1 family, is a predominant digestive protease in the gastric juice. The observed reduction in pepsin activity as a result of treatment with Irish potato extracts is in consonance with the earlier observed reduction in gastric juice output, which is the immediate medium of pepsin activity. Pepsin-induced damage is characterized by focal areas of discontinuity in the adherent mucus gel layer, localized hemorrhagic punctuated ulcers with bleeding into the lumen, and no evidence of re-epithelization or mucoid cap formation [25].

The observed significant ($p<0.05$) increase in tissue MDA concentration of the indomethacin treated animals is an indication of oxidative stress in the ulcerated animals. MDA is a product of lipid peroxidation of polyunsaturated fatty acids and thus has been applied in the estimation of degree of peroxidation in tissues [26]. Lipid peroxidation involves the formation and propagation of lipid radicals, the uptake of oxygen, a rearrangement of double bonds in unsaturated lipids and the eventual destruction of membrane lipids with the production of a variety of breakdown products, including alcohols, ketones, alkanes, aldehydes and ethers [15, 22]. Figure 5A shows that administration of Irish potato extract at both 400 and 800 mg/kg bodyweight significantly reduced the observed oxidative toxicity induced by indomethacin. Thus, the observed reduction in the MDA concentrations of the animals treated with aqueous Irish potato extracts might be an indication of the anti-peroxidation and anti-oxidative potential of the extract.

In the present study, reduced glutathione (GSH) concentration was significantly ($p<0.05$) depleted in indomethacin ulcer-induced animals when compared with normal control group. GSH protects cells against free radicals, peroxides and toxic compounds. It is a tripeptide that is composed of L-glutamate, L-cysteine and L-glycine. GSH is an important metabolic antioxidant that plays key role in the biological antioxidant system. GSH and H_2O_2 are twin substrates for glutathione peroxidase. It is generated from the oxidized glutathione (GS-SG) through the participation of glutathione reductase and NADPH [21]. Endogenous GSH plays an important role in sustenance of gastric mucosal integrity [15, 20]. Depletion of gastric mucosal GSH in indomethacin treated animals may have resulted in the accumulation of free radicals that initiated membrane damage by lipid peroxidation. This effect was apparently annulled by Irish potato extract administration for 21 days due probably to its content of rich array of antioxidant molecules and phytochemicals [18].

Histological analyses of the stomach tissues of the indomethacin ulcer-induced but untreated animals, when compared with the normal control group, showed extensive gastric mucosal erosions

in the glandular part of the stomach, sloughing of gastric glands and exfoliated cells appearing in the lumen (Figure 6). There were also observed exposed muscularis mucosa, submucosal edema and congestion of blood vessels. In areas with no erosion, vacuolated cytoplasm and pyknotic nuclei of the gastric mucosal epithelium were detected denoting necrotic changes. Observation of the control animals' tissues revealed features of intact mucosa with regular glands and normal submucosa with no observable microscopic pathologic lesion. Microphotographic results of the haematoxylin and eosin stained stomach tissues of rats treated with 400 mg/kg Irish potato extract showed restoration of gastric mucosal cells. However, inflammatory infiltration and congestion of blood vessels were detected. Similarly, histological sections of the animals treated with 800 mg/kg extract elicited apparent preservation of gastric mucosal architecture and gastric mucosa comparable to that of normal control animals, except for presence of mild inflammatory infiltration observed. In the group treated with omeprazole, regeneration of epithelium over the gastric mucosal surface, thickening of the submucosa and inflammatory infiltrations were also observed (Figure 6). The observed healing potential of Irish potato extracts against indomethacin induced ulceration may be linked to their rich content of antioxidant vitamin and phytochemical constituents [18]. Presence of such constituents have been directly associated with ability to scavenge free radicals and heal mucosal lesions, thereby countering the ulcerative effect of indomethacin.

Conclusion

The results of this study indicate that indomethacin induces ulceration in rats, which significantly affects oxidative stress biomarkers adversely. Treatment with aqueous Irish potato extracts for 21 days significantly reversed the oxidative stress associated effects, stomach tissue necrotic changes and inflammatory infiltrations induced by indomethacin. The study concluded that aqueous extract of IPT can reverse perturbations caused by indomethacin-induced ulcer, thus confirming the folkloric use of the plant extract in the treatment of peptic ulcer.

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