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Research Article

Pro-ulcerogenic activity of sodium arsenite in the gastric mucosa of male wistar rats

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ABSTRACT

Background: The gastrointestinal tract is constantly exposed to various protective and aggressive factors from food and the environment. Recent studies have shown that environmental factors, including heavy metal exposure and diet may alter gastrointestinal mucosal integrity. Arsenic (extensively available in the form of oxides or sulfides or as a salt of iron, sodium, calcium, copper, etc) is a major contaminant of soil, air as well as various water sources used for human and industrial activities, making it a huge public health burden. The present study was designed to characterize gastrointestinal alterations induced by sodium arsenite (SA) exposure. **Methods:** Sixty-four male Wistar rats were divided into four groups (n = 16) in two separate studies. Groups I and 2 received distilled water and indomethacin (40mg/kg, p.o) respectively while groups 3 and 4 animals received 5mg/kg and 10mg/kg SA respectively for two weeks prior to administration of indomethacin. In the first study, gastric acid secretion (GAS) was studied using the continuous perfusion technique. In the second study, animals were sacrificed after indomethacin administration. Ulcer was assessed based on macroscopic appearance of the stomach using an ulcer score scale. Each excised stomach was thoroughly cleaned and small sections were taken for histological analysis. Data were analysed using one-way ANOVA and differences considered significant at $p<0.05$. **Results:** Basal GAS was 0.08 ± 0.004 mEq/L in control rats. Indomethacin increased GAS significantly (0.14 mEq/L). The effect of indomethacin was augmented in rats with prior exposure to SA in a dose-dependent manner (0.17±0.01 and 0.26±0.02 mEq/L respectively). In the second study, SA significantly increased mean ulcer score, parietal and mucous cell counts when compared with the unexposed groups. Moderate epithelial erosion with infiltration of inflammatory cells as well as decreased intraglandular mucin and mucous secreting cells were observed in the stomach tissues of sodium arsenite treated rats. **Conclusion:** It is suggested that sodium arsenite potentiates gastric ulceration during indomethacin induced ulceration by increasing basal gastric acid secretion, increased parietal cell counts with extensive damage to the mucous secreting cells thereby distrupting the cyto-protecting ability of the stomach.

INTRODUCTION

Normal gastrointestinal homeostasis is maintained by an interplay of aggressive (acid, pepsin, *Helicobacter pylori*) and defensive (mucous and bicarbonate) forces. A reduced defense or increased aggression leads to a compromise in the integrity of the mucosal epithelial lining.

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Peptic ulcers are disruptions in the protective mucosal lining caused primarily such an imbalance. (Grossman, 2009; Lawande *et al.*, 2012). It is a prevalent and fairly heterogeneous disease with worldwide distribution (Laurette *et al.*, 2015). Several factors have been implicated in the etiology of peptic ulcer, including lifestyle and nutritional deficiency (caused by alteration in the mucosal blood flow and prostaglandin production), use of NSAID (which causes local irritation, back diffusion of acid in the gastric mucosa and damage to tissue inhibition of COX and

prostaglandin), involvement of pathogen such as *Helicobacter pylori* (which produces urease and caused ulceration by hydrolysis of urea due to generation of cytotoxic ammonia) (Nash *et al.,* 1994; Basil and Howard,1995).

There has been an increase in global incidence and prevalence of peptic ulcer disease (Elegbe and Bamgbose, 1976; Sato et al, 1985; Bello *et al*, 2018). Moreover, psychological stress has been reported to increase peptic ulcer disease irrespective of *H. pylori* infection or Non-steroidal anti-inflammatory drugs (Levenstein et al, 2015). In recent times, the involvement of trace elements in food and other dietary intakes have been highlighted. Thus, Lead and Cadmium have been reported to be ulcerogenic in several studies (Miniayan *et al*.,2006; Olaleye *et al*., 2006, 2007; Ma and Navarrete, 2011; Adegoke et al, 2017).

Arsenic is a semi-metallic element which occupies the twentieth position in the abundance of elements. Its inorganic forms such as arsenite and arsenate compounds are lethal to the environment and living creatures. Humans may encounter arsenic and its inorganic compounds through oral (via consumption of contaminated water) or inhalation (via exposure to non-ferrous ore, smelting semiconductors, glass manufacturing, and power generation by burning contaminated coal etc), and such exposure can be lifelong (Liu *et al*., 200; Bates *et al.,* 1992, Pott *et al.,* 2001). In Nigeria, areas such as Northern Kaduna senatorial district have high percentage of arsenic compound in the well water and bore hole which exceeds the maximum concentration limit of 0.01 mg/L set by WHO thus subjecting the people in the environment to arsenicolysis (Garba et al., 2012). According to Musa *et al.,* (2008), Zaria, Getso, Gwarzo local area of Kano state recorded high levels of arsenic compound, due to disposal of arsenic containing materials, burning of solid wastes, natural processes and human activities (Garba et al., 2008, Musa et al, 2008). The Biu volcanic province in the North-Eastern Nigeria (also contain high levels of arsenic compound concentration as observed in the surface water and obvious symptoms of its poisonous effect on the inhabitant of the area. Other areas (Usman and Lar, 2013), with recorded and reported high levels of arsenic acid in their water includes Ogun state (Kayode et al., 2011) and the south west of Ibadan (Egbinola and Amanambu in 2014).

Studies have shown that acute arsenic exposure may cause gastrointestinal tract disorder (Goebi *et al*., 1990) such as vomiting, abdominal pain, bloody diarrhea (which is the most common) (ATSDR, 2007a). However, chronic exposure may exert degenerative inflammatory and neoplastic changes of respiratory, hematopoietic, cardiovascular and nervous system (NRC 1999, 2001; Abernathy *et al.,* 2003; Watanabe *et al.,* 2003; Wasserman *et al*., 2004, Kim and Kim,2015). The effect of both acute exposure and chronic exposure of arsenic compounds as well as its mechanism of action on gastrointestinal tract is not yet established. Its use as herbicides, insecticides rodenticides, food preservatives and by- product of used fossil fuel cannot be over emphasized (Flora *et al*., 1995, Nickson *et al.,* 1998, Jana *et al.,* 2006). It was reported from several other systemic studies that the mechanism of toxicity of arsenic acid is by generation of reactive oxygen species, induction of multiple biological effects such as DNA damage, apoptotic cell death and DNA hypomethylation (Liu *et al.,* 2001, Kirkpatrick *et al*., 2003, Kitchin and Ahmad; 2003, Chen *et al.,* 2004, Jiang *et al*., 2009).

Gastric ulceration by non-steroidal anti-inflammatory drugs (NSAIDs), has been researched to be by disruption of the cyclooxygenase pathway in the gastric tissue (Scarpignato and Hunt, 2010). Other pathways involved are impaired mucosal blood flow and platelet aggregation, reduced mucus secretion, bicarbonate secretion, impaired platelet aggregation, impaired angiogenesis, increased leukotriene adherence (local responses such as ROS release) and acid back diffusion (which increases the gastric acid secretion) (Repetto & Llesuy, 2002, Wallace, 2008). In this study, the effect of acute or chronic sodium arsenite exposure in indomethacin induced gastric ulcer was investigated.

MATERIALS AND METHODS

Chemicals

Indomethacin was purchased from Medrel pharmaceuticals (India) while sodium arsenite was purchased Sigma Chemical Co., Germany. Sodium arsenite (1000 mg) was dissolved in 200 mLs of distilled water to make 5 mg/mLs stock solution. Xylazine and ketamine (were purchased from Hoge Mauw 900-B- 2370 Arendonk, Belgium and Rotex. Med. ICA, Trittau, Germany). All other reagent such as Sodium hydroxide (NaOH), phenothalein, Sodium chloride (NaCl), 10% formalin and distilled water was obtained from the Department of Physiology, University of Ibadan.

Animals

Sixty-four male Wistar rats (176 ± 20g) obtained from the Central Animal House, College of Medicine, University of Ibadan, Nigeria were used for the studies. The animals were housed under standard laboratory conditions with free access to standard food and water *ad libitum*. They were randomly divided into four

groups as follows: Group 1 and 2 animals, which served as controls (positive and negative) were given distilled water (p.o) throughout the study. Animals in groups 3 and 4 received 5mg/kg and 10mg/kg SA respectively. After two weeks of exposure, a known Non-steroidal anti-inflammatory drug, indomethacin (40mg/kg) was given to animals in groups 2, 3 and 4. Eight animals were used for two separate studies as described below.

Measurement of Gastric Acid Secretion

Gastric acid secretion was studied in normal rats and those with acetic acid induced ulcers using the continuous perfusion technique described originally by Ghosh and Schild (1958) via a modified Langerdoff perfusion apparatus. Animals were anesthetized with a mixture of xylazine (0.0005ml/g b.w) and ketamine (0.0015ml/g b.w). The animal was then placed on the dissecting board and the limbs tied to the board. The trachea was located and isolated around the neck; it was cannulated and slightly opened to aid breathing. The stomach was located and a cannula placed in it from the duodenal end of the stomach as previously described. Normal saline was then passed to the stomach from the mouth through the aid of a cannula. The gastric content of the stomach was collected after every 10 minutes. This was for the basal recording of gastric acid. After about three different recordings, histamine was injected into the animal's system via the hepatic portal vein. The gastric content was also collected after every 10 minutes and three readings were collected for the stimulated acid secretion.

The acidity of each 10 minutes effluent collected was assayed by titration. Sodium hydroxide was titrated against 10mls of gastric collection after every 10 minutes with phenolphthalein as indicator.

Assessment of Gastric Ulcer Score

Indomethacin was suspended in 1% carboxyl methylcellulose in water and administered by gavage at the dose of 40 mg/kg body weight (Elegbe and Bamgbose, 1976; Ozbakis-Dengiz et al., 2012). Sixteen hours after the induction of gastric ulcer with indomethacin (40mg/kg), animals were sacrificed with an overdose of a mixture of ketamine (120mg/kg) and xylazine (10mg/kg). After sacrifice of rats in this study, the abdomen was incised and irrigated with normal saline (Elegbe *et al.*, 1978, Olaleye and Farombi, 2006). Subsequently, the stomach was excised along the greater curvature and then washed gently in running tap water. Ulcers were independently assessed and scored by two observers using the method described by Pihan et al., [1987] according to the following scale: 0 = normal gray coloured stomach, 0.5 = pink to red coloration of stomach, 1 = spot ulcer, 1.5 = hemorrhagic streak, 2 = number of ulcers <5, 3 = number of ulcers >5, 4 = ulcers with bleeding.

Histological Analysis

Small cut tissues from cleaned excised stomachs were fixed in 10% formalin overnight and processed for routine paraffin embedding. The stomach was sectioned in to 5µm, mounted on the slide, de-parafinised, rehydrated, stained with Hematoxylin and eosin (H&E) for assessment of inflammatory/other pathologic changes including infiltration of cells, necrosis or damage to nucleus or tissue structures. Another section of the same stomach was stained with periodic acid Schiff stain (PAS) for assessment of glandular Mucin and estimation of mucous cell count. The H&E sections of the stomach were viewed under Olympus light microscope at magnification of 100 while the PAS stained slide was viewed at magnification of 400.

Determination of Parietal Cell Counts

The prepared H and E stained slide was viewed under light of microscope at magnification of 100. Parietal cell counts were evaluated as number of cells per field as described by Perraso *et al*., 1991. Five counts were made from randomly selected fields and the average count per unit area were calculated for each stomach.

Assessment of glandular Mucin and estimation of mucous cell count

PAS stained was viewed under microscope at magnification of 400 and the number of mucous cells was estimated. The secretion of glandular mucin was assessed under light microscope and classified as either minimum secretion (+, representing weak positivity for mucin) or maximum secretion (++ representing strong positivity for mucin) (Gad, 1969, Tock and Tan, 1969, Taib et al, 1998, Nikumph et al., 2012).

Statistical Analysis

Data are presented as Mean ± SEM and analyzed using one-way ANOVA. Significant difference was tested by Newman –keuls *post hoc* test. Statistical significance was considered at $P<0.05$.

RESULTS

Effect of Sodium Arsenite (Na_2AsO_3) on body weight.

There was a significant decrease in the body weight of groups III (159.3± 6.5g) and IV (176.6 ± 0.9g) exposed animals compared with groups I (196.0 ± 1.6g) and II (190.3 ± 0.3g); (Figure 1).

Effect of Sodium Arsenite On Basal and Stimulated Gastric Acid Secretion

The basal gastric acid output was significantly increased in the groups III (0.17 ± 0.010 mEq/l and IV

(0.26 ± 0.023 mEq/l) exposed animals compared with control (0.08 ± 0.004 mEq/l) and group II (0.14 ± 0.003 mEq/l); (Table 1).

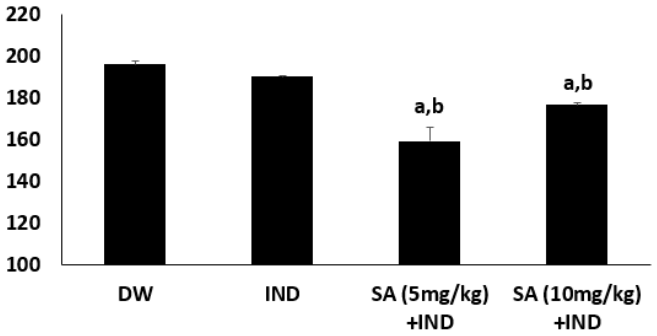


Fig. 1: Effect of sodium arsenite on body weight of animals exposed to distilled water (DW), Indomethacin (IND), 5mg/kg sodium arsenite (SA, 5mg/kg+IND) and 10mg/kg sodium arsenite(SA, 10mg/kg+IND). Each bar represents Mean ± SEM of 16 animals per group, $p<0.05$. [a]significant when compared with group I, [b]significant when compared with group II.

On stimulation with histamine, the gastric acid secretion was significantly increase in group III (0.235 ± 0.141 mEq/l) while a significant reduction was observed in group IV (0.112 ± 0.058 mEq/l) exposed animals; (Table 1).

Table 1: Effect of Sodium arsenite on Basal and Histamine stimulated gastric acid secretion.

Group	Treatment	Basal acid output (mEq/L)	Peak responses to Histamine (mEq/L)
I	Distilled water	0.08 ± 0.004	0.092 ± 0.003
II	IND (40mg/kg)	0.14 ± 0.003[a]	0.098 ± 0.004
III	SA (5 mg/kg) + IND (40mg/kg)	0.17 ± 0.010[a,b]	0. 235 ± 0.141a
IV	SA (10 mg/kg) + IND (40mg/kg)	0.26 ± 0.023[a,b]	0.112 ± 0.058

Each value represents the Mean + SEM of 8 rats per group at $p<0.05$. [a]significant compared with group I, [b]significant compared with group II.

Effect of Sodium Arsenite On Indomethacin-Induced Gastric Ulcer

There was a significant increase in the ulcer score of groups III (10.00±0.875) and IV (14.33±1.579) exposed animals compared with group II (7.83± 0.542); (Table 2).

Histological assessment

Table 2 also shows the effect of sodium arsenite exposure on gastric mucosa in indomethacin induced ulcer. In group I, there was intact gastric mucosal layer. Induction of ulcer with indomethacin caused mucosal ulceration with infiltration of inflammatory cells in group II treated animals compared with the group I. On inducing gastric ulcer to sodium arsenite-exposed animals, severe gastric mucosal ulceration which extended in to the submucosa and muscularis was observed. There was also hemorrhage and edema, with marked infiltration of inflammatory cells in groups III and IV (sodium arsenite exposed) as compared with the groups 1 and 2.

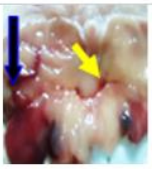
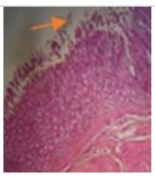
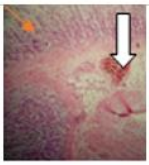
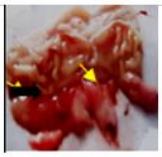
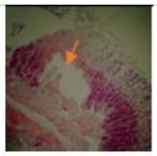
DISCUSSION

Arsenic is a ubiquitous metalloid present in various compounds throughout the Earth's crust, with its toxicity reported in several studies. Reports are available in literature of its effects on the liver, brain and cancers of the skin, bladder, kidney and lungs (Eisler, 1994), with relative paucity on its biological effects on the gastrointestinal tract. This study described the effect of Sodium arsenite on indomethacin-induced experimental gastrointestinal injury in rats. Two groups of rats were given sodium arsenite orally while and two other groups served as controls. After 14 days, indomethacin was given orally to all but one group. Sixteen hours later, gastric acid secretion was studied in one experiment and the extent of gastric ulceration processes observed in a second experiment.

The total body weights of rats treated with sodium arsenite significantly decreased after two weeks of exposure when compared with the control groups. This is in tandem with previous reports of decreased body weight in SA exposed animals (Sarker *et al*, 2012; Kim and Kim, 2015). It has been reported that the weights of some vital organs such as liver and lungs are compromised after exposure to sodium arsenite attributable to arsenic toxicity in the liver and increased hepatic metabolism to eliminate it (Sharma et al, 2009; Roy et al, 2009, Owumi et al, 2013).

Indomethacin, a known inhibitor of prostaglandin synthesis, has been shown in several studies to increase gastric acid secretion in humans (Feldman and Colturi,1984) and experimental animals (Arai et al, 1987). Since endogenous prostaglandins have long been implicated in the inhibitory regulation of gastric acid secretion (Befrits et al, 1984), it is deducible that the inhibition of prostaglandin synthesis by indomethacin may be responsible for the increased basal gastric acid secretory output observed in all the animals given indomethacin when compared with the untreated control. In addition to the reported findings, our study showed a potentiation of the effects of

Table 2:
Ulcer scores, gross and microscopic features of stomach sections in rats pre-treated with and Sodium arsenite .

Group	Treatment	Ulcer score	Gross picture	Histology	Observations
I	Distilled water	0			Intact mucosa
II	IND (40mg/kg)	7.83 ± 0.54[ad]			Hemorrhagic gastric ulcers, (blue arrow) and ulceration of the mucosal layer (orange arrow) with infiltration of inflammatory cells.
III	SA(5 mg/kg) + IND (40mg/kg)	10.00 ±0.88[ad]			Deep ulceration in the gastric mucosa, (yellow arrow; marked infiltration of inflammatory cells in the mucosal, with focal hemorrhage, there was extensive ulceration of the mucosal layers extending to the submucosal layers of the stomach, (orange arrow); white arrow indicates focal hemorrhage).
IV	SA (10 mg/kg) + IND (40mg/kg)	14.33 ±1.5[abc]			Deep ulceration on the gastric mucosa, (yellow arrow) and there was increased infiltration of inflammatory cells with hemorrhage, extensive mucosal erosion extending to muscular externa, (orange arrow).

Values are represented as Mean ± SEM, a-significant as compared with group I, b-significant as compared with group II, c-significant as compared with the group III, d- as significant as compared with group IV.

indomethacin by both doses of AS used in this study. However, the mechanism of this potentiation is yet to be investigated. Like AS in this study, some other heavy metals have been documented to potentiate gastric acid secretion, including Lead (Olaleye *et al*., 2006) and Cadmium (Trujano and Navarrete, 2011).

In addition to the potentiation of gastric acid secretion, AS was observed to increase the severity of indomethacin-induced ulcers as evidenced by increased macroscopic ulcer scores in the gross appearance of the stomach samples. In addition, microscopic observations of the prepared histological slides revealed that indomethacin caused severe haemorrhagic gastric ulcers in the stomach mucosa which is in line with previous reports (Seo *et al.*,2012,Sabiu *et al.*,2015), thus laying credence to previous reports that acute exposure to sodium arsenite caused gastrointestinal tract disorder in humans (Goebi *et al*., 1990) such as vomiting, abdominal pain, bloody diarrhoea (which is the most common) and other GIT effects like inflammation in the pharynx and the oesophagus.

Effect of sodium arsenite on mucin secretion and goblets cell in the mucosa in indomethacin induced ulceration.

In the control group without indomethacin treatment (group 1), there were intact goblet cells with maximum secretion of intraglandular mucin in the stomach mucosa. In control group treated with indomethacin, there was minimal secretion of intraglandular mucin and constriction of the mucous gland lumen compared with group 1. In the 5mg/kg SA treated group, , the intraglandular mucin secretion was minimal with necrosis/ degeneration of mucous secreting cells observed compared with groups 1 and 2. In group IV, there was no intraglandular mucin secretion though there was infiltration of inflammatory cell with severe necrosis in the gastric mucosa compared with the other groups (Plate 1).

Effect of Sodium Arsenite (Na_2AsO_3) on parietal cells and mucus cell count

The parietal cell counts of groups 3 (297.2 ± 3.440) and 4 (323.8±8.603) exposed animals significantly

increased compared with group 1 (207±2.061); (Table 3). Significant increases were observed in the mucous cell count of groups 3 (452.0 ± 4.986 cells/field) and 4 (443.8 ± 3.690 cells/field) compared with group 1 (384.2 ± 3.787 cells/field), as shown in table 3.

Table 3:
Effect of sodium arsenite on parietal cell count, mucous cell count and in indomethacin induced gastric ulcer

Group	Treatment	Parietal cell counts (cells/field)	Mucous cell count (cells/field)
1	Distilled water	207± 2.061	384.2± 3.787
2	IND (40mg/kg)	284.4± 1.426[a]	420.8± .014[a]
3	SA (5 mg/kg) + IND (40mg/kg)	297.2± 3.440[a]	452.0± 986[a,b]
4	SA (10 mg/kg)+IND (40mg/kg)	323.0± 8.603[a,b]	443.8± .690[a,b]

Values represent Mean ± SEM, $p < 0.05$.[a]- significant as compared with group 1, [b]- significant as compared with group 2

DISCUSSION

Arsenic is a ubiquitous metalloid present in various compounds throughout the Earth's crust, with its toxicity reported in several studies. Reports are available in literature of its effects on the liver, brain and cancers of the skin, bladder, kidney and lungs (Eisler, 1994), with relative paucity on its biological effects on the gastrointestinal tract. This study described the effect of Sodium arsenite on indomethacin-induced experimental gastrointestinal injury in rats. Two groups of rats were given sodium arsenite orally while and two other groups served as controls. After 14 days, indomethacin was given orally to all but one group. Sixteen hours later, gastric acid secretion was studied in one experiment and the extent of gastric ulceration processes observed in a second experiment.

The total body weights of rats treated with sodium arsenite significantly decreased after two weeks of exposure when compared with the control groups. This is in tandem with previous reports of decreased body weight in SA exposed animals (Sarker *et al*, 2012; Kim and Kim, 2015). It has been reported that the weights of some vital organs such as liver and lungs are compromised after exposure to sodium arsenite attributable to arsenic toxicity in the liver and increased hepatic metabolism to eliminate it (Sharma et al, 2009; Roy et al, 2009, Owumi et al, 2013).

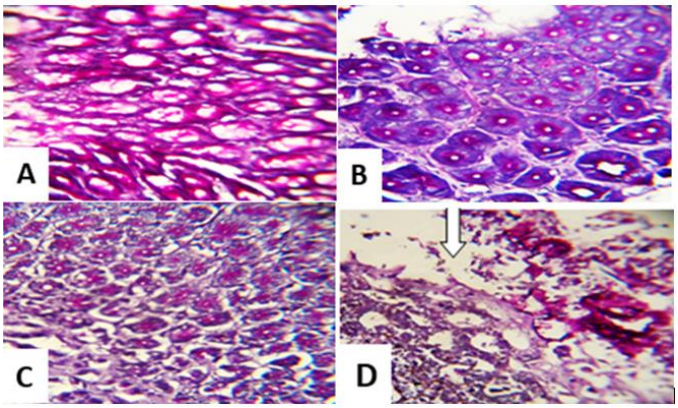


Plate 1: Photomicrograph of gastric mucosa section using PAS staining, X400: showing expression interglandular mucin: **A.** (Control): Intact surface goblet cells with maximum secretion of intraglandular mucin and surface mucous secretion) **B**. (indomethacin alone): Decrease in the goblet cells with minimum intraglandular mucin secretion and constriction of the lumen. **C** - (5mg/kg of Na_2AsO_3 + indomethacin): Minimum intraglandular mucin secretion,necrosis/degeneration of goblet cells, significant reduction in the mucus cell size. **D** - (10mg/kg of Na_2AsO_3 + indomethacin): No secretion, hyperplasia of goblets cells and necrosis of goblet cells, white arrow indicate eroded goblet cells

Indomethacin, a known inhibitor of prostaglandin synthesis, has been shown in several studies to increase gastric acid secretion in humans (Feldman and Colturi,1984) and experimental animals (Arai et al, 1987). Since endogenous prostaglandins have long been implicated in the inhibitory regulation of gastric acid secretion (Befrits et al, 1984), it is deducible that the inhibition of prostaglandin synthesis by indomethacin may be responsible for the increased basal gastric acid secretory output observed in all the animals given indomethacin when compared with the untreated control. In addition to the reported findings, our study showed a potentiation of the effects of indomethacin by both doses of AS used in this study. However, the mechanism of this potentiation is yet to be investigated. Like AS in this study, some other heavy metals have been documented to potentiate

gastric acid secretion, including Lead (Olaleye *et al*., 2006) and Cadmium (Trujano and Navarrete, 2011).

In addition to the potentiation of gastric acid secretion, AS was observed to increase the severity of indomethacin-induced ulcers as evidenced by increased macroscopic ulcer scores in the gross appearance of the stomach samples. In addition, microscopic observations of the prepared histological slides revealed that indomethacin caused severe haemorrhagic gastric ulcers in the stomach mucosa which is in line with previous reports (Seo *et al.*,2012,Sabiu *et al.*,2015), thus laying credence to previous reports that acute exposure to sodium arsenite caused gastrointestinal tract disorder in humans (Goebi *et al*., 1990) such as vomiting, abdominal pain, bloody diarrhoea (which is the most common) and other GIT effects like inflammation in the pharynx and the oesophagus (ATSDR, 2007a). In addition, acute inflammation and haemorrhage was seen in the intestine of rhesus monkey exposed to arsenic after 28 days (Heywood and Sortwell, 1979). In our study, the histological evaluation of the gastric tissue in the sodium arsenitetreated groups revealed marked infiltration of inflammatory cells with focal haemorrhage, hyperplasia of parietal cells, decrease in the intraglandular mucin and necrosis with gastric erosion extending into the sub-mucosa and *muscularis* compared with indomethacin treated groups. The exact mechanism of the potentiation of ulceration by AS is not clear and further studies may be required to throw light in this area. The parietal cells were increased in the sodium arsenite treated groups particularly the 10mg/kg. Increased activity of parietal cells has been reported to enhance gastric acid secretion, it could probably be a contributing effect to the earlier observed increased gastric acid secretion. Brunton *et al*., 2005 had earlier reported that there is a linear relationship between gastric acid secretion and parietal cell count. There was observed hyperplasia of the gastric mucous cell in this study, it could probably be a defence mechanism exerted by (the rats') body system to suppress the adverse effect of increased parietal cell and gastric acid secretion.

In conclusion, the present study further established the toxic nature of sodium arsenite on the gastrointestinal tract, specifically increasing the rate of gastric acid secretion and aggravating ulcer formation in the presence of a known ulcerogen, indomethacin.

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