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Gastroprotective Properties of Manganese Chloride on Acetic Acid Induced Ulcer in Wistar Rats

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ABSTRACT

Drugs with multiple mechanisms of protective action may be effective in minimizing tissue injury during diseases. Manganese has shown varied positive biological properties in reverting diseased conditions. There is dearth of information regarding its effects on gastrointestinal integrity, hence the aim of this study. Seventy male Wistar rats used in this study were randomly assigned into 7 groups viz: Groups 1 – control, 2 – ulcer untreated rats, 3,4,5,6 and 7 received 50mg/kg, 100mg/kg Manganese, 40mg/kg Cimetidine, 1mg/kg Mistoprotol and 30mg/kg Omeprazol respectively. Two weeks oral treatment (in groups 3-7) began 3 days after laparotomy of which chronic gastric ulcer was induced using acetic acid. On days 7 and 14, gastric acid secretion was performed on animals (fasted for 24 hours) from each group and their stomachs were removed, weighed and scored for ulcer before histological evaluation. Data were analyzed using ANOVA & Student t-test and significant at $p \leq 0.05$. Results revealed that Manganese had dose and treatment duration dependent effect on healing of ulcerated stomach. Ulcer index in Manganese (50 and 100mg/kg) treated groups significantly reduced on days 7 and 14 (77.5% and 94.1%) and (93.8% and 100%) respectively compared with ulcer untreated group. Anti-secretory property was more prominent in animals treated with Omeprazole while Cimetidine treated animals showed similar trends with Manganese (100mg/kg). These results were further buttressed by histological findings that revealed no ulcer in Manganese treated groups. Findings of this study suggests that manganese might possess gastro-protective and anti-secretory activities.

Key words: Manganese Chloride, Acetic acid, Ulcer, Rat

INTRODUCTION

Peptic ulcer is a common disease throughout the world (Elegbe *et al*., 1976, Odaibo, 1988, Eastwood, 1997; Kang et al, 2002 and Owoyele *et al.*, 2001). It represents one of the major health problems, both in terms of morbidity and mortality (Bhattacharya *et al.*, 2003). The worldwide ulcer prevalence differs, with duodenal ulcers dominating the Western populations while gastric ulcer is more frequent in Asia, especially Japan (Sonnenberg, 1985; Sonnenberg and Everhart, 1996). The true prevalence rate of peptic ulcer in the Nigerian populace is not certain although over three decades ago Nigeria was listed as an area of high peptic ulcer disease prevalence, perforation of the stomach being the most

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frequent indication for surgery (Ndububa and Adeyemi, 2008).

The gastric mucosa is continuously exposed to potentially aggressive agents such as acid, pepsin, bile acids, food ingredients, bacterial products (*Helicobacter pylori*) and non-steroidal inflammatory drugs (Peskar and Maricic, 1998). Even though a number of other factors causes ulcer, gastric acid secretion still remains an important factor in the pathogenesis of inflammatory disorders of the GIT especially peptic ulceration. This is evidenced by the action of many anti-ulcerogenic agents which reduce the acid secretion (Schmassmann, 1998). Gastric acid plays an important physiological role but acid hyper secretion can also cause problems such as peptic ulcer and reflux esophagitis (Waldum *et al*., 1993).

According to Okabe *et al.*, 1972 and Jainu *et al.*, 2006, acetic acid induces gastric ulcer by stimulating gastric acid hyper secretion. Gastric ulcer produced by acetic acid is due to the release of histamine, which increases the capillary permeability and back diffusion of Hydrochloric acid (Umamaheswari *et al.*, 2007). In addition, the sub mucosal injection of acetic acid also damages the muscle layer so that even an advanced tumor infiltrating the muscle layer could be necrotized (Wang *et al.*, 2000 and Okabe *et al.*, 2010)

Manganese is a trace element essential for the proper functioning of both humans and animals; it plays a role in bone mineralization, protein and energy metabolism, metabolic regulation and cellular protection from damaging free radical species (Aschner *et al.*, 2005). A deficiency of manganese causes skeletal deformation in animals thereby inhibiting the production of collagen in wound healing (Keen *et al.*, 1996). Many nutritionists attribute joint pain, inflammation, arthritis, dermatitis and many diseases including osteoporosis, schizophrenia, diabetes, and epilepsy to manganese deficiency. Testicular degeneration has been reported in Manganese deficient rats, mice, and rabbits (Leach and Harris, 1997).

It is however not known if manganese offer any beneficial effect on gastric integrity, hence the thrust of this study.

MATERIALS AND METHODS

Experimental Animals

Seventy healthy male Wistar strain rats (140 – 170g) obtained from the Central Animal House, Department of Physiology, College of Medicine, University of Ibadan, Nigeria were used for this study. They were acclimatized for a period of 3 weeks and housed in cages at standard laboratory condition of room temperature (23 ±2ºC), humidity (55 ± 15%) with 12 hours light and dark cycle. They were allowed free access to water and standard commercial rat pellets (Ladokun Feeds Nigeria Limited, Ibadan, Nigeria). The rats were handled according to the ethics of animal handling in compliance with the institution's guideline and criteria for human care (National institute of Health Guidelines for the care and Use of Laboratory Animals) and were randomly divided into 7 groups of 10 animals each.

Group I (Normal control)
Group II (Ulcer Untreated control)
Group III (ulcer+50mg/kg bw $MnCl_2$
Group IV (ulcer + 100mg/kg b.w of $MnCl_2$
Group V (ulcer + 40mg/kg bw Cimetidine)
Group VI (ulcer + 1mg/kg bw Misoprostol)
Group VII (ulcer + 30mg/kg bw Omeprazole)

Test and Standard drugs

Manganese chloride *(Qualikems Fine Chemicals Pvt. Ltd, 15b/4, Near Old Rajinder Nagar, New Delhi)* was administered through oral gavage at prescribed doses, (50mg/kg and 100mg/kg of Manganese chloride).

Cimetidine capsule *(manufactured by Laborate Pharmaceutical (India) E-11,Ind. Area, Panipat – 132103),*

Mistoprotol tablets *(manufactured by JRP Co., Ltd. 34-40, Jeyakgongdan 2-gil, Hyangnam-eup, Hwaseong-si,Gyeonggi-do, Korea for Zolon healthcare limited, Isolo, lagos , Nigeria* and

Omeprazol tablets *manufactured by Vee Excel Drugs and Pharmaceuticals Private Limited, Delhi, Ghaziabad No 703, Devika Tower, Ghaziabad – 201011, Uttar* were administered at the various doses 40mg/kg b.w, 1mg/kg b.w and 30mg/kg b.w respectively.

Induction of ulcer

Gastric ulcer was induced by acetic acid. According to Jainu *et al.*, 2006 and Okabe *et al.*, 1972 and 2010, acetic acid induces gastric ulcer by stimulating gastric acid hyper secretion i.e due to the release of histamine, which increases the capillary permeability and back diffusion of HCl (Umamaheswari *et al.*, 2007). Under ketamine and xylazine anesthetization, a laparotomy was done through a midline epigastric incision. After exposing the stomach, it was clamped with an eye forceps of a known internal diameter. 60% acetic acid solution was injected into the clamped portion and withdrawn after 60 seconds. The stomach was bathed with normal saline before the abdomen was then sutured and animals were allowed to recover before been returned to their cages having free access to food and water.

Gastric acid secretion

Administration of drugs began three days after laparotomy (because well-defined deep ulcer develops three to five days after induction) and lasted for fourteen (14) days. By the 7th day of treatment, gastric secretions (acididty and pH) were measured (using the continuous perfusion method of Ghosh and Schild, 1958, modified by Amure and Ginsburg, 1964) as well as ulcer scoring on five rats from each groups before they were sacrificed. This same procedure was repeated on the 14th day. Food was withdrawn from all the groups for 24 hours but allowed free access to water before gastric acid secretion experiment.

Ulcer score

The degree of ulceration was assessed by carrying out a microscopic and macroscopic examination with 2X magnification hand lens. The stomach were opened along the greater curvature, bathed in normal saline, spread out with pins on a cork board, and then measured. The ulcerated area in (cm^2) was calculated according to the collection of guiding principles of Drug administration of Ministry of Health Beijing, 1993, using the equation:

$$S = \pi (d_1/2) \times (d_2/2),$$

Where **S** represents the ulcerated area (cm^2), $\mathbf{d_1}$ represent the longest longitudinal diameter of the ulcer, $\mathbf{d_2}$ represents the longest transverse diameter of the ulcer

The percentage of ulcer protection was obtained according to Samuel *et al*., 2010 using the follsowing formula:

$$\text{Percentage (\%) Protection} = \frac{U_C - U_X}{U_C} \times 100$$

U is the percentage of animals in the group with ulcer $\mathbf{U_C}$ is the Control mean ulcer index, $\mathbf{U_X}$ is the Test mean ulcer index

The stomach of each animal was also weighed and fixed in 10% formalin in order to prevent autolysis before histological analysis was carried out on the excised stomach. The weight of the rat was measured on daily basis after surgery and during administration.

Statistical analysis: The results were analysed using one way ANOVA and Student's T test, values were expressed as Mean ± SEM. The statistical difference was taken to be significant at $p<0.05$.

RESULTS

Effect of Manganese on basal gastric secretion and pH of acetic acid induced Ulcerated rats after treatment by Days 7 and 14: In Table 1, there was significant decrease in the basal secretions of all the treatment groups [except manganese (50mg/kg b.w) group (by day 7 alone)] compared with ulcer untreated group both by days 7 and 14.

Table 1:
Effect of Manganese on basal gastric secretion and pH of acetic acid induced Ulcer after treatment by Days 7 and 14

GROUPS	Basal Acid Output(ml/10mins)		Acidity ($\times 10^4$ mmol)		pH	
	Day 7	**Day 14**	**Day 7**	**Day 14**	**Day 7**	**Day 14**
Control (no ulcer)	0.65 ± 0.02	0.53 ± 0.01	1.64 ± 0.40	1.32 ± 0.28	3.79 ± 0.01	3.88 ± 0.01
Ulcer untreated (distilled H_20)	1.22 ± 0.04[a]	1.18 ± 0.02[a]	3.06 ± 0.87[a]	2.91 ± 0.34[a]	3.51 ± 0.01[a]	3.53 ± 0.01[a]
Manganese (50mg/kg b.w)	1.10 ± 0.08[a,c,d]	1.02 ± 0.01[a,b,c,d,e,f]	2.76 ± 0.21[a,c,d]	2.56 ± 0.24[a,b,c,d,e,f]	3.57 ± 0.03 [a,c,d]	3.59 ± 0.02[a,b,c,d,e]
Manganese (100mg/kg b.w)	0.95 ± 0.05[a,b,c]	0.97 ± 0.01[a,b,c,d,e]	2.38 ± 0.12[a,b,c]	2.42 ± 0.18 [a,b,c,d,e]	3.63 ± 0.02 [a,b,c]	3.61 ± 0.02[a,b,c,d,e]
Cimetidine (40mg/kg b.w)	0.96 ± 0.01[a,b,c]	0.67 ± 0.01 [a,b,c,d]	2.39 ± 0.24 [a,b,c]	1.67 ± 0.17 [a,b,c,d]	3.62 ± 0.01[a,b,c]	3.78 ± 0.01 [a,b,c,d]
Misprostol (1mg/kg b.w)	0.86 ± 0.01[a,b,c]	0.91 ± 0.01 [a,b,c]	2.16 ± 0.37 [a,b,c]	2.27 ± 0.12[a,b,c]	3.67 ± 0.01 [a,b,c]	3.65 ± 0.01 [a,b,c]
Omeprazole (30mg/kg b.w)	0.42 ± 0.01[a,b]	0.41 ± 0.01 [a,b,]	1.06 ± 0.29 [a,b,]	1.02 ± 0.12[a,b]	3.98 ± 0.01 [a,b]	3.99 ± 0.01[a,b]

Values are expressed as Mean ± SEM. Values are significant when $p < 0.05$.
Keys for significance; [a]- compared with control, [b]- compared with ulcer untreated control, [c]- compared with Omeprazole , [d]- compared with Misoprostol and [e]- compared with Cimetidine, [f]- compared with Manganese (100mg/kg b.w).

Table 2:
Effect of manganese on acetic acid-induced ulcers after treatment by day 7 and 14

GROUPS	Ulcer Index (cm^2) (Mean ± SEM)		% Protection $\frac{U_C - U_X}{U_C} \times 100$	
	Day 7	**Day 14**	**Day 7**	**Day 14**
Control (no ulcer)	0.00 ± 0.00	0.00 ± 0.00	-	-
Ulcer alone(distilled H_20)	9.78 ± 0.89[a]	2.39 ± 0.50[a]	-	-
Manganese (50mg/kg b.w)	2.20± 0.22[a,b,c,d]	0.14 ±0.09[b]	77.5[a,b,c,d]	94.1[b]
Manganese (100mg/kg b.w)	0.61 ±0.37[b]	HEALED[b]	93.8[b]	100[b]
Cimetidine (40mg/kg b.w)	0.93 ± 0.57[b]	HEALED[b]	90.4[b]	100[b]
Misoprostol (1mg/kg b.w)	HEALED[b]	HEALED[b]	100[b]	100[b]
Omeprazole (30mg/kg b.w)	HEALED[b]	HEALED[b]	100[b]	100[b]

Values are expressed as Mean ± SEM. Values are significant when $p < 0.05$. [a]$p < 0.05$ when compared with control, [b]$p < 0.05$ when compared with ulcer untreated control, [c]$p < 0.05$ when compared with Omeprazole, [d]$p < 0.05$ when compared with Misoprostol

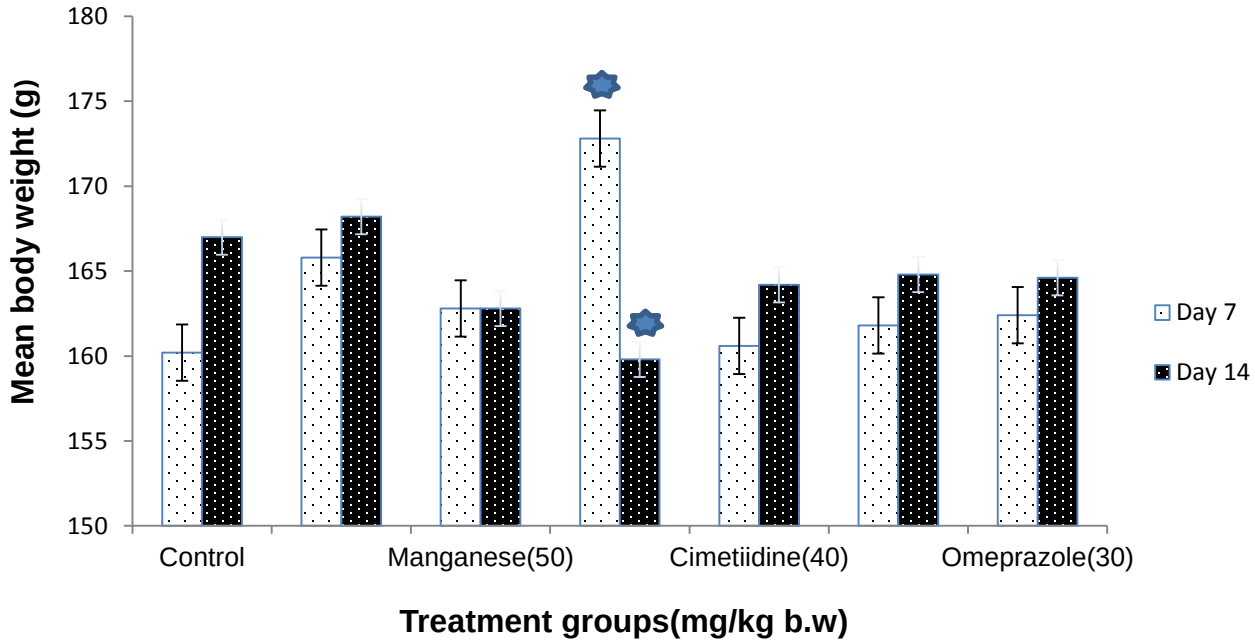

Figure 1:
Effect of Manganese on body weight of acetic acid-induced ulcers after treatment by days 7 and 14. *Each vertical bar represents Mean ± SEM of five rats per group. Values are significant when $p < 0.05$.*

The animals treated with 100mg/kg b.w of Manganese and 40mg/kg b.w of Cimetidine showed the same trend when compared with ulcer untreated group. By day 7, there was significant increase in the basal secretions of Manganese (50mg and 100mg/kg b.w) treatment groups compared with Omeprazole (30mg/kg b.w) as well as Manganese (50mg/kg b.w) treatment group when compared with Misoprostol (1mg/kg b.w).

Manganese treatment groups (50mg and100mg/kg b.w) were significantly different ($p<0.05$) when compared with all the standard drug groups by day 14.

The pH of all the treatment groups compared with the ulcer alone, normal and standard drug groups both by days 7 and 14 followed the same trend as basal secretion.

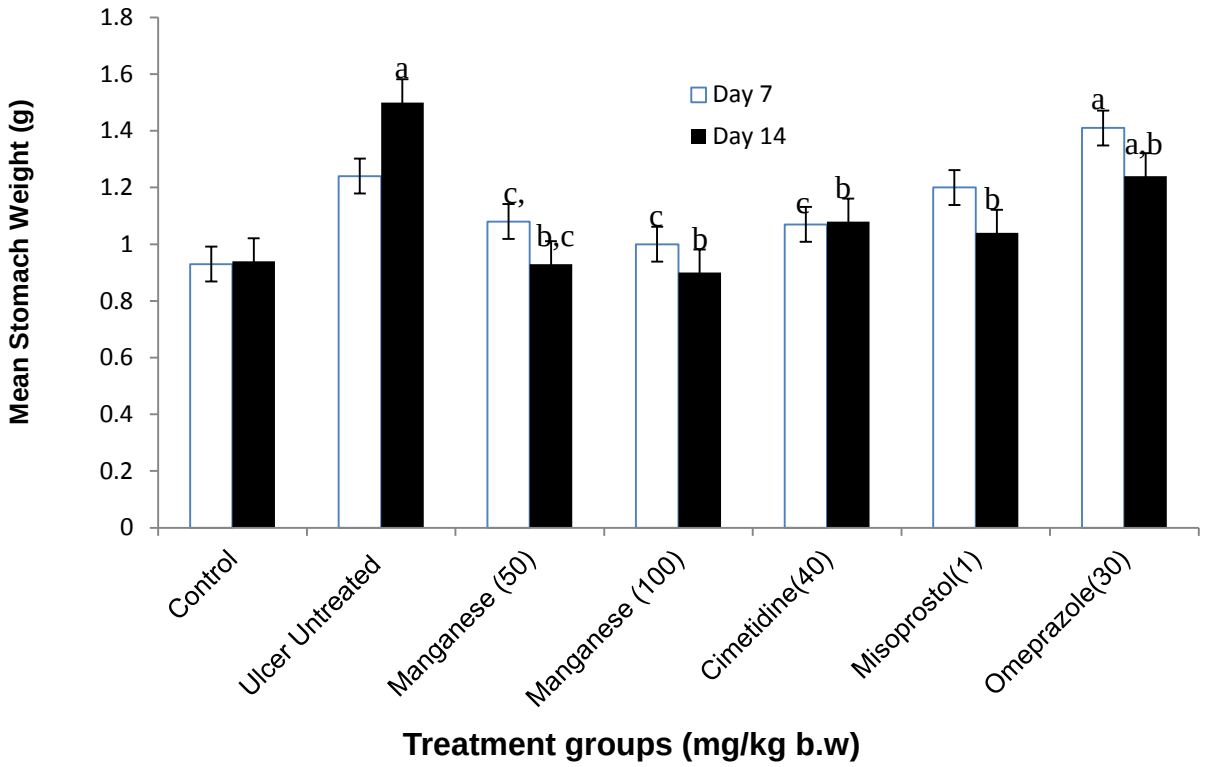

Figure 2:
Effect of manganese on stomach weight of acetic acid-induced ulcers after treatment by days 7 and 14.
Each vertical bar represents Mean ± SEM of five rats per group. [a]p < 0.05 when compared with control, [b]p < 0.05 when compared with ulcer untreated control, [c]p < 0.05 when compared with Omeprazole.

Effect of Manganese on acetic acid-induced ulcers after treatment by day 7 and 14

By day 7 and 14, repeated doses of all treatment groups significantly reduced the ulcer index of acetic acid-induced ulcers compared with ulcer untreated group (Pable 1.2). There was significant increase ($p<0.05$) in the ulcer index of Manganese (50mg/kg b.w) treated group when compared with Omeprazole (30 mg/kg) and misoprostol (1m/kg b.w) group by day 7 only. The animals treated with 100mg/kg b.w of Manganese and 40mg/kg b.w of Cimetidine showed the same trend when compared with ulcer untreated group (Table 2).

Effect of manganese on mean body and stomach weight of acetic acid induced ulcer after treatment by days 7 and 14.

There was no significant increase in the mean body weight of the animals in the treated groups [except in manganese (100mg/kg b.w) group which reduced from 172.80 ± 5.33(day 7) to 159.80± 2.85(day 14)] when compared with control and ulcer untreated group both by days 7 and 14 (Figure 1).

There was significant decrease ($p<0.05$) in weight of the stomach from animals in all treatment groups [except in Omeprazole (30 mg/kg b.w) with significant increase] compared with ulcer untreated group by day 14 only (figure 2).

DISCUSSION

Peptic ulcer is a common disease throughout the world that represents one of the major health problems both in terms of morbidity and mortality. There is substantial evidence that oxygen derived free radicals plays an important role in the pathogenesis of various diseases, including peptic ulcer disease, with antioxidants reported to play a significant role in the protection of the gastric mucosa against various necrotic agents (Dursun *et al.*, 2009).

The goals of treating peptic ulcer disease are to relieve pain, heal the ulcer and prevent ulcer recurrence. Currently there is no cost-effective treatment that meets all these goals. This has been the rationale for the development of new antiulcer drugs and the search for novel molecule has been extended to antioxidants. Salim, 1994 investigated the influence of free radical scavengers on the healing of gastric and duodenal ulcers resistant to therapy and found that anti oxidative therapy stimulates the healing of therapy resistant ulcers. Drugs with multiple mechanisms of protective action, including antioxidant activity, may be highly effective in minimizing tissue injury in human diseases (Umamaheswari *et al.*, 2007).

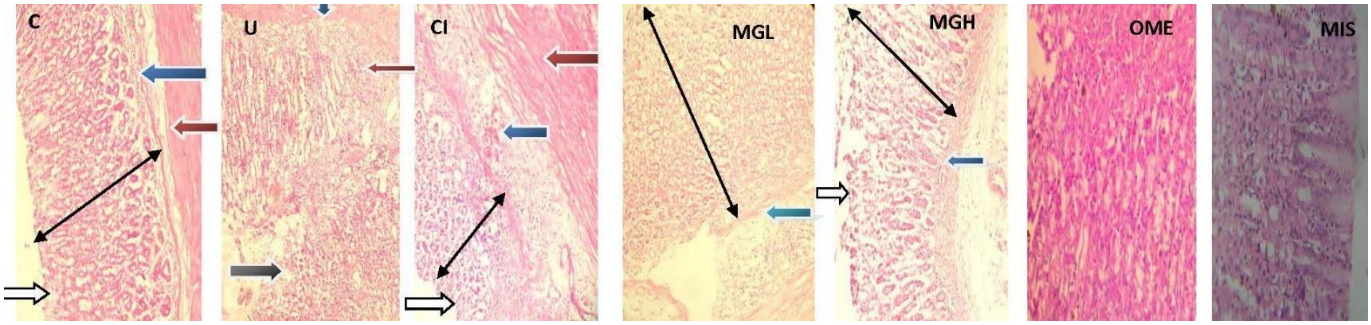

Plate 1:
Photomicrograph of A Stomach Sections (Mag X 100) By Day 7 showing **C (Control)**:- normal mucosa surface epithelial layer (white arrow). The mucosa layer (spanned) shows no infiltration of inflammatory cells.the gastric gland and lamina propria appear normal. The parietal cells appear normal (slender arrow). The circular muscle appears normal (red arrow); **U (ulcer alone)**:- mucosa layer with mild ulcer (black arrow), the mucosa layer (spanned) shows severe infiltration of inflammatory cells.the gastric gland and lamina propria shows severe gastritis with severe infiltration (red arrow). The parietal cells appear normal but depleted. The submucosa layer shows moderate infiltration (blue arrow); **CI (40mg/kg b.w Cimetidine)**:- showing moderately preserved mucosa epithelial layer (white arrow), the mucosa layer (spanned) shows mild infiltration of inflammatory cells.the gastric gland and lamina propria shows moderate gastritis with mild infiltration (red arrow). There is no ulcer seen. The submucosa layer shows mild infiltration (blue arrow); **MGL(50mg/kg b.w Maganesse)**:- mildly preserved mucosa surface epithelium (white arrow) and normal mucosal layer (spanned) showing the gastric gland and lamina propria without infiltration. The eosinophilic parietal cells appear normal. There is no ulcer, no haemorrhage seen. The submucosa layer shows mild inflammatory cells (blue arrow). **MGH (100mg/kg b.w Manganesse)**:- well preserved mucosa surface epithelium and normal mucosal layer (spanned) showing the gastric gland and lamina propria without infiltration of inflammatory cells. The eosinophilic parietal cells (slender arrow) appear normal. There is no ulcer, no haemorrhage seen. The submucosa layer (blue arrow) shows no inflammatory cells (slender arrow). The circular muscle layer appear normal. **OME (30mg/kg b.w Omeprazole)**:- widespread moderate erosion of the upper part of surface epithelium (slender black arrow), disrupted glands (☆), intact Lamina muscularis mucosa and widespread accumulation of neutrophils. **MIS (1mg/kg b.w Mistoprotol)**:- intact surface epithelium, lamina muscularis mucosa, submucosa and muscularis externa

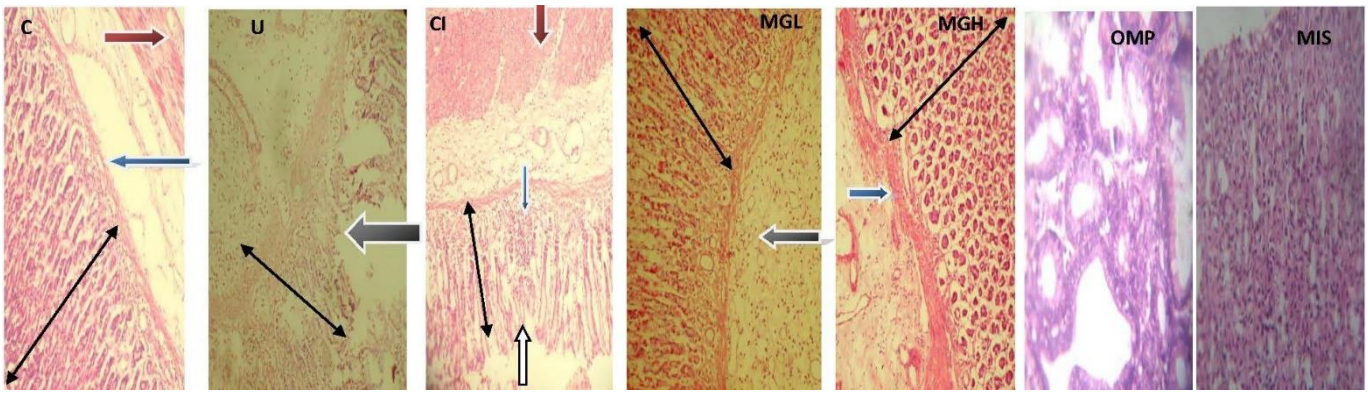

Plate 2:
Photomicrograph Of A Stomach Sections (Mag X 100) By Day 14 Showing **C (Control):-** normal mucosa surface epithelial layer (white arrow). The mucosa layer (spanned) shows no infiltration of inflammatory cells.the gastric gland and lamina propria appear normal. The parietal cells appear normal. The circular muscle appears normal (red arrow). **U (Ulcer alone):-** mucosa layer with moderate ulcer (black arrow), the mucosa layer (spanned) shows severe infiltration of inflammatory cells.the gastric gland and lamina propria shows severe gastritis with moderate infiltration (slender arrow).. The parietal cells appear normal but depleted. The submucosa layer shows moderate infiltration (blue arrow). **CI (40mg/kg b.w Cimetidine):-** moderately preserved mucosa surface epithelium (white arrow) and normal mucosal layer (spanned) showing the gastric gland and lamina propria without infiltration. The eosinophilic parietal cells appear normal. There is no ulcer, no haemorrhage seen. The submucosa layer shows moderate inflammatory cells (blue arrow). **MGL (50mg/kg b.w Maganesse):-** poorly preserved surface epithelium and normal mucosal layer (spanned) showing the gastric gland and lamina propria without infiltration of inflammatory cells. The eosinophilic parietal cells (slender arrow) appear normal. There is no ulcer, no haemorrhage seen. The submucosa layer (blue arrow) shows mild inflammatory cells (slender arrow). The circular muscle layer appear normal; **MGH (100mg/kg b.w Maganesse) :-** well preserved mucosa surface epithelium and normal mucosal layer (spanned) showing the gastric gland and lamina propria without infiltration of inflammatory cells. The eosinophilic parietal cells (slender arrow) appear normal. There is no ulcer, no haemorrhage seen. The submucosa layer (blue arrow) shows no inflammatory cells (slender arrow). The circular muscle layer appear normal. **OME (30mg/kg b.w Omeprazole)**:- Mild atrophy of the muscle wall thickness, minimal inflammation. **MIS (1mg/kg b.w Mistoprotol)**:- fairly normal surface epithelium, moderatly congested blood vessel in the lamina propia with moderate amount of neutrophils. The submucosa is expanded with very loose connective tissue

Manganese is an essential nutrient required in trace amounts for human health and important for normal processes in the body. Manganese (Mn) has been proven to be a chain dose breaking antioxidant in biological system (Schmassmann, 1998). Tajaddini *et al.*, 2013 showed that Manganese inhibits oxidative stress damage and may improve or protect mice epididymal sperm parameters as well as testis structure.

Overall, the mean body weight of the animals treated with Maganese increased but was not significant compared with normal control and ulcer untreated group. A study found that when fed a manganese-supplemented diet, iron-deficient pups absorbed more manganese and experienced greater weight loss than iron-sufficient controls (U.S. Centers for Disease Control ASTDR, 2000). Probably the reduction in body weight of ulcerated animals treated with manganese (100mg/kg b.w) might be through similar mechanism though it was not significant. Careful regulation of the amount of manganese delivered in children's parenteral nutrition was found to be important for their long term health (Arnaud and Favier, 1995).

The results from this study showed that Manganese had a dose and duration dependent effect on the healing of ulcerated rat. Manganese (100mg/kg bw) showed result that resemble that of Cimetidine (40mg/kg bw) both on days 7 and 14. This result is in agreement with Umamaheswari *et al*., 2007 that drugs with multiple mechanisms of protective action, including antioxidant activity, may be highly effective in minimizing tissue injury in human diseases. It has been demonstrated that many drugs and formulations possess potent antioxidant action and are effective in healing experimentally induced gastric ulcers (Salim, 1994 and Dhuley, 1999).

It may be due to the fact that antioxidant enzyme superoxide dismutase (SOD), with high manganese content being a major component, was significantly produced and thus helped neutralize, reduce or prevent some damages caused by free radicals. Manganese is required for the activation of prolidase, an enzyme that functions to provide the amino acid, proline, for collagen formation in human skin cells (Shetlar and Shetlar, 1994, Keen, 1996 and Muszynska *et al.*, 2000). It might also be that in this experiment, Manganese would have caused wound healing by collagen formation at the site of ulceration.

Etiology of acetic acid-induced ulcers mimics human gastric and duodenal ulcers in location, chronicity and severity (Okabe and Amagase, 2005), being accepted as the best model for studying effects of treatments on the healing process (Okabe *et al.*, 1972 and Jainu *et al.*, 2006). This study showed consistency with other data that acetic acid-induced ulcer was decreased by Omeprazole, Misoprostol and Cimetidine, (Brown and Wilson, 1999 and Okabe and Amagase, 2000) thus validating the use of this model. Chronic ulcers induced by acetic acid are mainly due to an increased volume of acid output, subsequent pyloric obstruction and mucosal necrosis. It is logical, therefore, that anti secretory substances, like Omeprazole, Misoprostol and Cimetidine accelerate the healing of these ulcers.

Though several factors causes ulcer, gastric acid secretion still remains an important factor in the pathogenesis of inflammatory disorders of the gastrointestinal tract (GIT) especially peptic ulceration (Schmassmann, 1998). Group treated with 100mg/kg b.w of Manganese showed significant reduction in gastric secretion both on days 7 and 14 compared with ulcer alone group while 50mg/kg b.w of Manganese group showed significant decrease only on day 14. This is evidenced by the action of many anti-ulcerogenic agents which reduced the acid secretion (Schmassmann, 1998). Omeprazole showed the highest inhibition on gastric secretion both on days 7 and 14 supporting the work of Sach, 1997 that omeprazole inhibits last stage of secretion when compared to ulcer untreated and control group than Cimetidine and Misoprostol group.

In general, the superiority of the proton pump inhibitor (Omeprazole) over histamine receptor antagonistic (Cimetidine) and mucosa protective agent (Misoprostol), in preventing and healing peptic ulcers has been documented (Wiklund, 1999). The significant antiulcer protection of Manganese (50 and 100mg/kg b.w) and gastric anti-secretory property compared with ulcer untreated group reveals its efficacy in ameliorating chronic ulcer. Manganese 100mg/kg b.w showed results that resemble that of Cimetidine both on days 7 and 14.

The histological analysis further buttressed these above obtained results. It revealed that ulcer untreated rats exhibited the characteristic histological pattern of acetic acid induced gastric ulcers, showing damaged mucosal epithelium, distortion of glands, severe inflammatory infiltrate, proliferation of fibroblasts and cellular debris in the ulcerated wall of stomach while the normal control rats did not exhibit such pathological changes. In contrast, the stomach rats of all treated groups showed healing signs, such as significant reduction of ulcer sizes and inflammatory infiltrates, with some extent of mucosal regeneration.

CONCLUSION

This study demonstrates and suggests that treatment with 100mg/kg/b.w of Manganese has antiulcer and anti-secretory properties which are comparable to standard drug Cimetidine (40mg/kg/b.w). The reduction in gastric volume and ulcer index revealed anti secretory and anti-

ulcer potential of manganese. Further studies are ongoing in understanding the mechanism behind the gastro protective property of manganese.

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