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Protective Effects of Glycine against Cadmium Chloride-Induced Gastric Toxicity in Wistar Rats

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ABSTRACT

Background: Heavy metal poisoning poses significant health risk to both human and animal subjects. Increased human activities and industrialization have led to increased exposure to these heavy metals. This study investigated the potential of glycine in ameliorating cadmium chlorinde-induced toxicity on gastric tissues of Wistar rats.

Methods: Thirty adult male Wistar rats weighing between 150 and 170g were randomly assigned into six groups of five rats per group and received 1 ml of distilled water (control), 10 mg/kg body weight of Cadmium chloride, 500 mg/kg body weight of Glycine, 1000 mg/kg body weight of Glycine, 10 mg/kg body weight of Cadmium chloride and 500 mg/kg body weight of Glycine, 10 mg/kg body weight of Cadmium chloride and 1000 mg/kg body weight of Glycine respectively. Cadmium and Glycine were administered orally for 14 days. Rats stomach were harvested and analyzed for Malondialdehyde(MDA), Superoxide Dismutase(SOD), Catalase(CAT), Glutathione Peroxidase(GPx) and histological examination.

Results: The mean body weight and the SOD level in rats treated with cadmium chloride were significantly decreased ($p < 0.05$). The MDA level was significantly increased with cadmium chloride but significantly reduced with Glycine treatment ($p < 0.05$). The CAT and GPx levels were significantly increased with Glycine treatment. Histological examination of rats stomach revealed evidence of Glycine mitigation in Cadmium chloride-induced gastric damage in Wistar rats.

Conclusion: Glycine possesses anti-inflammatory, antioxidant and ameliorative potentials against cadmium chloride-induced gastric damage in Wistar rats.

Keywords: Cadmium chloride; Glycine; Oxidative stress; Anti-oxidant; Anti-inflammatory; Heavy metal toxicity

INTRODUCTION

The ramifications of heavy metal poisoning on human health have been documented extensively, with industrialization and human activities significantly contributing to heightened heavy metal exposure (1). Heavy metals such as cadmium, lead, and mercury, among others, pose significant risks to global populations through contaminated water, food, and environments (2). These metals interact with biological systems, leading to a range of health issues from gastrointestinal problems to nervous system disorders due to accumulation in cells and tissues of the body thus exacerbating these disorders (1).

Glycine, an amino acid crucial for protein synthesis, plays diverse roles in biological processes. It is a non-essential amino acid with many function and effects. It binds to specific receptors and transporters that are expressed in many cell types throughout the organism to exert it effects (3). Dysfunction in glycine release, as seen in conditions like Clostridium tetani infection, can result in severe consequences such as spastic paralysis (4).

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An understanding of the anatomy of the human stomach sheds light on its vital role in digestion. Positioned between the esophagus and duodenum, the stomach comprises distinct regions like the cardia, fundus, body, and pylorus (5). The cardia may not be anatomically distinct but it represent a transition region between the esophagus and stomach (6). Sphincters at the junctions with the esophagus and duodenum regulate food passage (7).

Although little is known about the activities of cadmium on gastric tissues, substantial evidence suggests that cadmium toxicity in the liver, kidneys, testicles, and brain, is associated with a decrease in several antioxidants levels (8,9,10). There is a dearth of information on the antioxidant potential of glycine on cadmium activities in gastric tissues. Hence this study seeks to investigate the antioxidant potential of glycine on oxidative stress parameters associated with cadmium chloride toxicity in gastric tissues

MATERIALS AND METHODS

Experimental rats and design

Thirty adult male Wistar rats weighing between 150g and 170g were used. The rats were purchased from the animal house

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of the Department of Anatomy, School of Basic Medical Sciences, University of Benin, Benin City, Nigeria. They were kept in plastic cages, at room temperature with good ventilation. The normal day and night light cycles were maintained. The rats were given two weeks acclimatization period before the administration began. They were given free access to conventional rat feed and portable water.

The rats were randomly assigned into six (6) groups of five (5) rats per group and cadmium chloride was used to induce gastric damage as stated in the below.

Cadmium chloride and Glycine were purchased from a licensed vendor in Benin City, Pyrex Lg Scientific Supply Company Nigeria and they were both products of a reputable company in the United States; Sigma-Aldrich Ltd

Table 1. Animal groupings and dosage of drugs administered

GROUPS	DOSAGE
Group A	Served as control and received 1ml of distilled water daily throughout the study.
Group B	Received 10 mg/kg body weight of cadmium chloride daily for 14 days.
Group C	Received 500 mg/kg body weight of glycine daily for 14 days.
Group D	Received 1000 mg/kg body weight of glycine daily for 14 days.
Group E	Received 10 mg/kg body weight of cadmium chloride daily for 14 days and thereafter 500 mg/kg body weight of glycine daily for 14 days
Group F	Received 10 mg/kg body weight of cadmium chloride daily for 14 days and thereafter 1000 mg/kg body weight of glycine daily for 14 days

All administrations were done by gavage using orogastric tube and lasted for fourteen (14) and twenty-eight (28) days respectively. All animals received rat feed and portable water ad libitum.

Tissue collection, processing and staining for histology

The rats were euthanized via cervical dislocation according to approved guidelines of the ethics committee of the College of Medical Sciences, University of Benin and gastric tissues were harvested at the end of the 14 days and 28 days study. Gastric tissues were preserved in physiological saline in sterile bottle and immediately taken to Chemical Pathology Laboratory of the University of Benin Teaching Hospital for analysis of tissue MDA, SOD, CAT and GPx. The stomach tissues were preserved for 72 hours in 10% buffered formalin before histologically processed and stained with Haematoxylin and Eosin (H & E) using standard procedures (11). The sections obtained were examined and photomicrographs were taken using a Leica DM750 research microscope with an attached digital camera (Leica CC50). The tissues were photographed digitally at magnifications of 100x.

Statistical analysis

Results obtained were expressed as Mean ± SEM (standard error of mean). Differences between the means were determined by one-way analysis of variance (ANOVA). Values were considered statistically significant if P value was less than 0.05 ($p < 0.05$). LSD Post Hoc test was used to determine where the statistical significance lay across the groups. Statistical package Graph Pad Prism Version 9.0 for Windows (GraphPad Software Inc.) was used to analyze the data obtained in this study.

RESULTS

Effects of cadmium chloride and Glycine on body weight changes of rats

There was significant decrease ($p<0.05$) in the mean change in body weight of rats exposed to cadmium chloride and significant increase ($p<0.05$) in the mean change in body weight of rats treated with 500 mg/kg body weight of Glycine. There was no significant difference ($p>0.05$) in the mean change in body weight in Glycine treated rats following cadmium chloride exposure (Fig. 1)

Effects of cadmium and Glycine on oxidative stress parameters of Gastric tissues of rats

There was significant decrease ($p<0.05$) in SOD level in cadmium chloride exposed rats compared to control (Fig. 2) and a significant decrease ($p<0.05$) in Glycine treated groups compared to cadmium chloride treated group

There was significant increase ($p<0.05$) in MDA level in cadmium treated rats (Fig. 3) compared to control and a significant decrease ($p<0.05$) in Glycine treated groups following exposure to cadmium

There was significant increase in CAT in Glycine treated group (Fig. 4)

There was significant increase ($p<0.05$) in GPx of rats treated with 500 mg/kg body weight of Glycine when compared to control but no significant difference ($p>0.05$) in cadmium exposed rats.

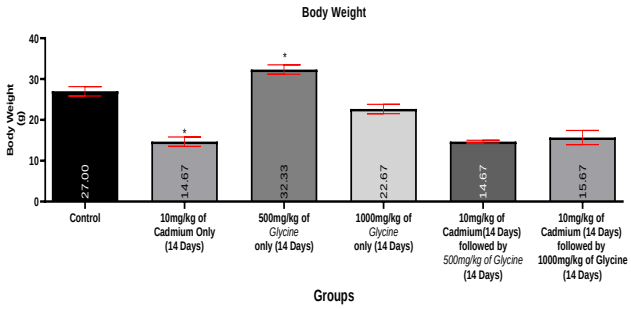


Fig 1. Mean Change in Body Weight
*Represent statistically significant difference ($p<0.05$) Compared with Control

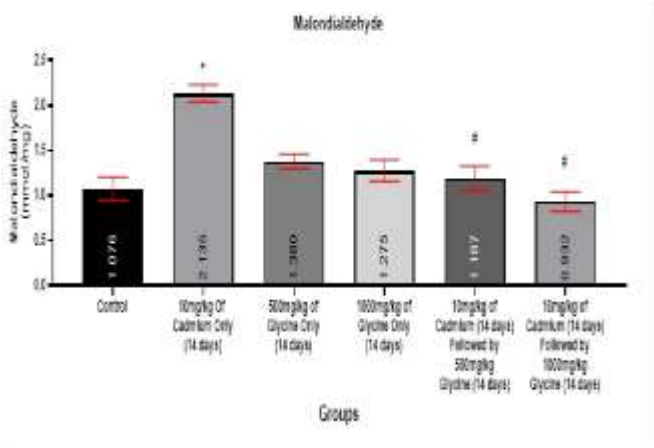


Fig 2. Stomach Malondialdehyde (MDA)
*Represent statistically significant difference ($p<0.05$) Compared with Control
#Represent Statistically significant difference ($p<0.05$) Compared with Cadmium only.

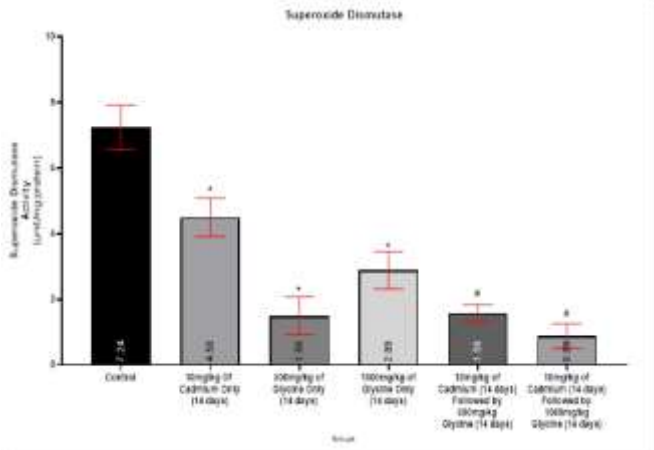


Fig 3. Stomach Superoxide Dismutase Activities
*Represent Statistically significant difference ($p<0.05$) Compared with Control
#Represent Statistically significant difference ($p<0.05$) Compared with Cadmium chloride only

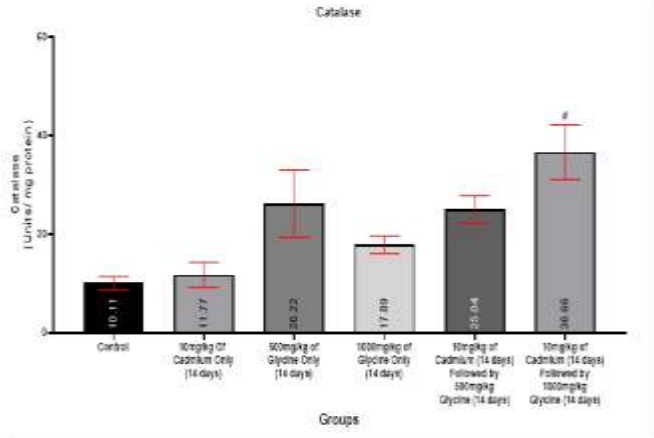


Fig 4. Stomach Catalase Activities
#Represent Statistically significant difference ($p<0.05$) Compared with Cadmium only

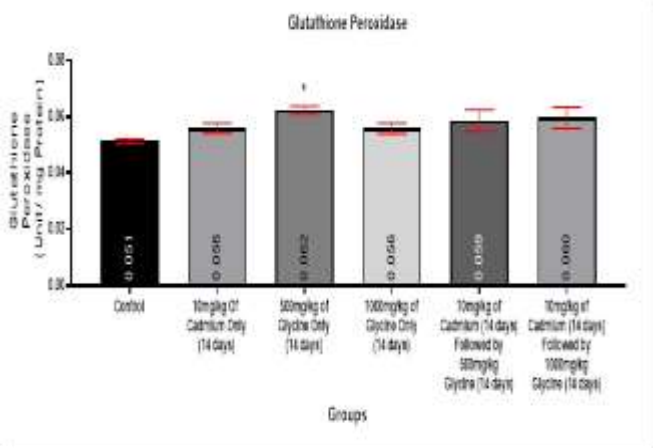


Fig 5. Stomach Glutathione Peroxidase Activities.
*Represent Statistically significant difference ($p<0.05$) Compared with Control

Histological findings

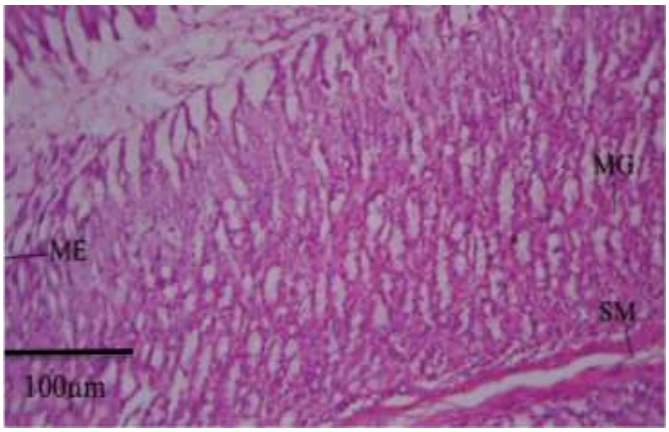


Plate 1. Rat stomach. Control. Composed of normal tissue architecture: mucosal epithelial lining indented by pits (ME), mucosal glands (MG), submucosa (SM), muscularis propria (MP): H & E 100x

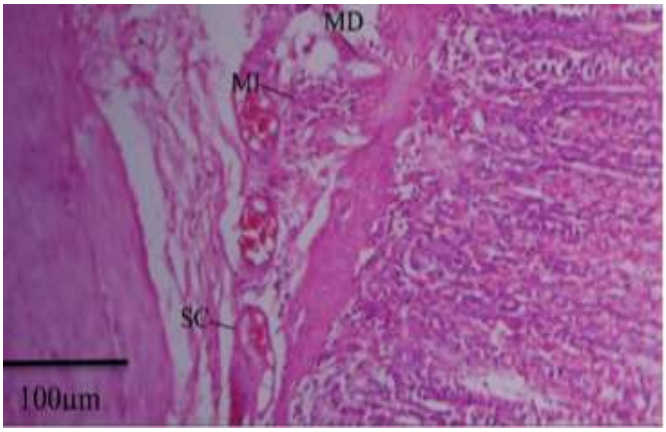


Plate 2. Rat stomach given 10 mg/kg body weight of Cadmium chloride only showing: mucosal and submucosal infiltrates of

inflammatory cells (MI), muscle degeneration (MD), submucosal congestion (SC): H& E 100x

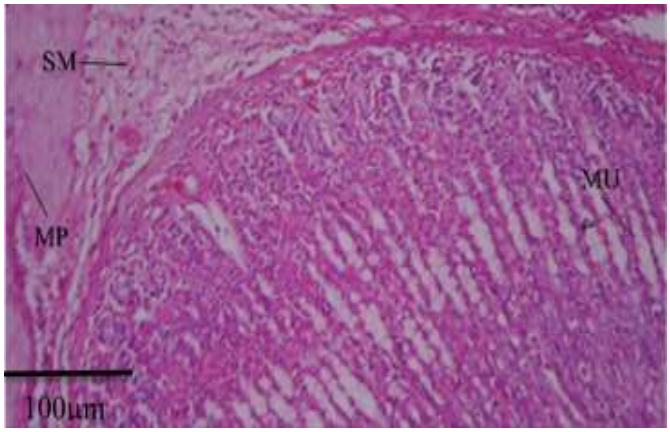


Plate 3. Rat stomach 500 mg/kg body weight of Glycine only showing normal architecture: mucosa (MU), submucosa (SM), muscularis propria (MP): H & E 100x

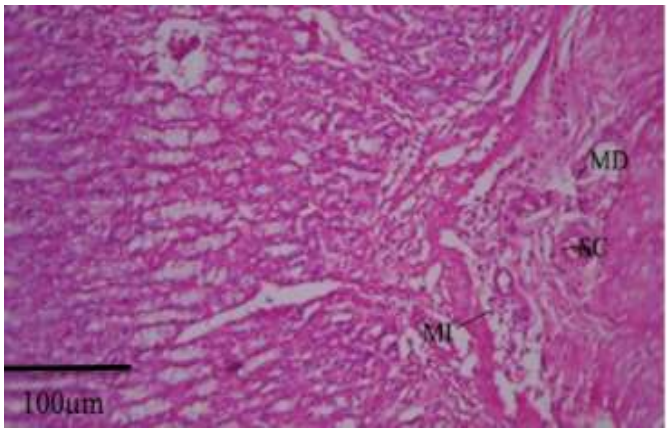


Plate 4. Rat stomach given 1000 mg/kg body weight of Glycine only showing normal architecture: mucosa (MU), submucosa (SM), muscularis propria (MP): H & E 100x

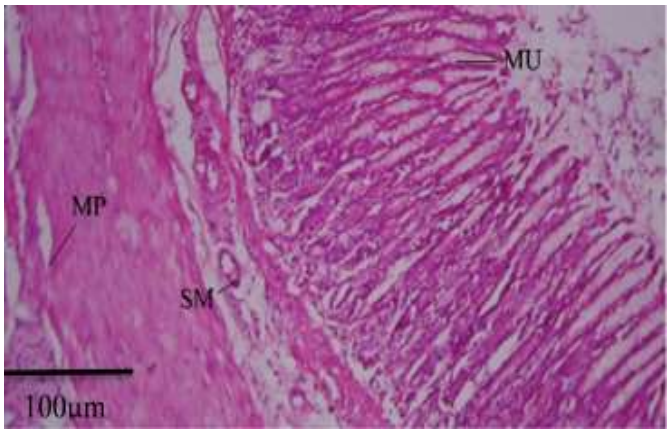


Plate 5. Rat stomach given Cadmium chloride + 500 mg/kg body weight of Glycine showing normal architecture: mucosa (MU), submucosa (SM), muscularis propria (MP): H & E 100x

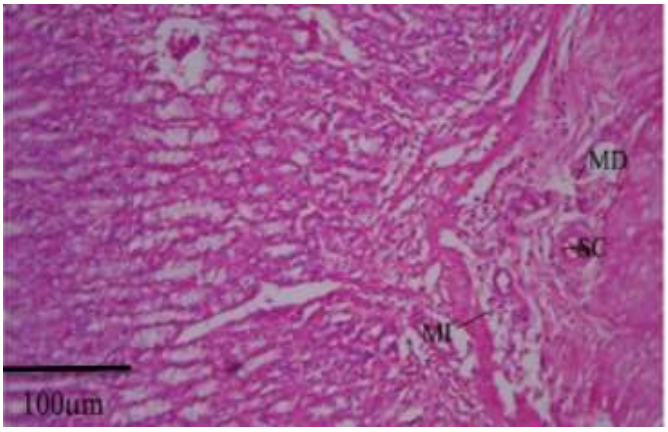


Plate 6. Rat stomach given Cadmium chloride + 1000 mg/kg body weight of Glycine showing: mucosal and submucosal infiltrates of inflammatory cells (MI), submucosal congestion (SC), muscle degeneration (MD): H & E 100x

DISCUSSION

Cadmium, a toxic heavy metal, poses significant health risks to the body. Upon exposure, it can induce oxidative stress within cells, leading to damage of essential molecules (12). Long-term exposure to cadmium is linked to increased risk of cancer and other disease conditions in the body such as heart disease and osteoporosis indicating its systemic impact on health (13,14,15,16).

In this study there was significant decrease in the mean weight of cadmium chloride treated rats. (Fig 1). This weight reduction in cadmium treated rats has also been reported in previous studies (17) where the weight of experimental animals was significantly reduced following cadmium chloride treatment. This weight reduction in cadmium treated rats could be due to reduction in food intake induced by cadmium toxicity. Glycine administration significantly increased the mean body weight of rats but did not reverse the weight loss in cadmium chloride treated rats (Fig 1).

Cadmium chloride significantly increased the level of stomach Malondialdehyde (MDA) when compare with the untreated control (Fig 2). This increase in MDA indicates oxidative stress within the gastric tissues, resulting from lipid peroxidation of cellular component induced by reactive oxygen species (18). Cadmium chloride produces oxidative stress by disturbing the prooxidant-antioxidant balance (19). Glycine was able to reverse the increase in stomach Malondialdehyde levels caused by cadmium chloride treatment (Fig 2).

The stomach Superoxide Dismutase (SOD) was significantly reduced in cadmium chloride treated rats (Fig 3). This reduction signifies a compromised antioxidant defence mechanisms, leading to increased oxidative stress and potential negative consequences on cellular health and overall well-being. Glycine treatment did not potentiate the anti-

oxidant activities of SOD but rather it was observed that glycine induced a significant decrease in stomach SOD (Fig 3). Previous study has reported possible interference of glycine with the body's antioxidant system. Study by researchers (20) showed that Glycine could potentially interfere with the cellular redox balance or antioxidant systems, indirectly affecting SOD activities. It was also reported that excessive glycine might lead to imbalances that affect cellular metabolism, which could in turn impact the efficiency of antioxidant enzymes like SOD (21).

The activities of stomach catalase showed no significant change with cadmium chloride treatment when compared with untreated control in this study (Fig 4). However treatment with glycine potentiated the antioxidant activities of catalase by slight-to-significant increase in the stomach catalase activities. An increase in catalase activity is generally considered beneficial because it enhances the cell's antioxidant defences, reduces oxidative stress, and helps maintain cellular health (22). However, as with any biological process, the level of catalase activity should remain within a balanced range to avoid potential imbalances or unintended effects (22).

There was no significant change in stomach Glutathione peroxidase activities when compared with untreated control (Fig 5). Glutathione peroxidase is a free radical scavenger and provides oxidative stress protection by detoxifying hydrogen peroxide radical into alcohols or water. It has been reported that lipid peroxidation increases significantly by inhibiting GPX activities (23). Stomach Glutathione Peroxidase was significantly increased following treatment with 500 mg/kg body weight of glycine when compared with untreated control. An increase in glutathione peroxidase activity is generally considered beneficial because it enhances the cell's ability to counteract oxidative stress, protect cellular component (24). A similar report from previous study showed that an increase in GPx enhances the cell's ability to combat oxidative stress, detoxify harmful compounds, repair damage, and maintain overall cellular health (25).

Histological findings showed normal stomach architecture in untreated rats and glycine only treated groups (Plate 1, 3 and 4). However treatment with cadmium chloride showed features of altered stomach histology (Plate 2). This is evident by the presence of inflammatory cells in the mucosal and submucosal layers, muscular degeneration and submucosal vascular congestion of the stomach. Previous studies have shown that cadmium has potential to induce inflammation. Previous study (26) also showed that cadmium's toxicity is partly due to its ability to induce oxidative stress, inflammation, and apoptosis in cells. This process is often observed in response to inflammation, infections, autoimmune conditions, or other immune responses affecting the stomach (27). However, these effects of cadmium chloride were reversed following administration of glycine particularly the 500 mg/kg of glycine (Plate 5). Glycine exerts its protective effects through several mechanisms, including antioxidant actions, modulation of inflammatory pathways, and stabilization of cellular membranes (28). Treatment with 1000 mg/kg body weight of glycine following cadmium chloride pretreatment did not reverse the structural damage induced by cadmium chloride in the stomach tissue (Plate 6). Rather features of inflammation and muscular damage was seen in this tissues.

Limitations of Study

This study has some limitations that should be acknowledged. First, the sample size was relatively small, which may limit the generalizability of the findings. Second, only adult male Wistar rats were used; therefore, sex-related differences in response to cadmium chloride toxicity and glycine treatment were not evaluated. Furthermore, the study focused primarily on oxidative stress biomarkers and histological assessment without evaluating inflammatory cytokines or molecular pathways associated with cadmium chloride-induced gastric toxicity and glycine-mediated protection. In addition, the duration of exposure and treatment was limited to the experimental period, and thus the long-term effects of glycine administration following cadmium-induced gastric injury were not assessed. Future studies involving larger sample sizes, both sexes, extended treatment periods, and molecular analyses are recommended to further elucidate the protective mechanisms of glycine against cadmium chloride-induced gastric toxicity.

Conclusion

Glycine has antioxidant, anti-inflammatory and ameliorative potentials against cadmium chloride-induced gastric tissue damage. The 500 mg/kg body weight dose of glycine has more positive outcomes than the 1000 mg/kg body weight dose.

DECLARATIONS

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Conflict of interest
The authors declare that there are no competing interests regarding the publication of this manuscript.

Authors Contribution
E.O. conceptualized and designed the study. E.O., M.O.O., R.J.E., S.M.N., and E.Y.O. participated in data collection, laboratory procedures, and analysis. R.J.E. contributed to data interpretation and manuscript preparation. All authors reviewed, edited, and approved the final version of the manuscript.

Ethical Approval

All experimental procedures involving animals were conducted in accordance with institutional guidelines for the care and use of laboratory animals and in compliance with the ARRIVE 2.0 guidelines for reporting animal research. Ethical approval for the study was obtained from the Research Ethics Committee of the College of Medical Sciences, University of Benin, Nigeria (Approval No. CMS/REC/2026/9011; approved on 7 February, 2026).

Availability of Data

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Consent for publication

Not applicable.

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