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Magnesium glycinate attenuates cyclophosphamide-induced neurotoxicity by modulating brain neurotransmitters, inflammatory markers, and hippocampal synaptophysin immunoreactivity

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Abstract

The usage of cyclophosphamide (CYP) in cancer treatment is associated with organ toxicity, cellular degeneration, and myelosuppression, which result in treatment discontinuation. Its debilitating impact has increased the quest to search for novel substances or measures that will alleviate the adverse effects, while its therapeutic efficiency remains intact. This study evaluated the effects of Magnesium glycinate on cyclophosphamide-induced neurotoxicity in Wistar rats.

Forty-eight Wistar rats (eight weeks old) were allocated into four experimental groups (n = 8), as the normal control (A), oral Magnesium glycinate at 22.8 mg/kg (B) and 32.8mg/kg (C), 150mg/kg of CYP (D), CYP/oral magnesium glycinate at 22.8 mg/kg (E) and CYP/oral magnesium glycinate 32.8mg/kg (F). The animal's body weight was measured weekly. Following the spatial working memory evaluation using the Y-maze. Animals were sacrificed by cervical dislocation, brain tissues excised, followed by the homogenization of the right hemisphere. The supernatant of the homogenates was used to assess the neurotransmitter activities and the levels of brain-derived neurotrophic factor, interleukin 1beta, interleukin 10, and Tumour Necrosis Factor alpha. Furthermore, the left hemisphere was processed for histological evaluation (H&E and Cresyl fast violet stain) and synaptophysin immunoreactivity.

Cyclophosphamide induces weight loss, dysregulation of neurotransmitter and modulator activities, and inflammatory marker levels, as well as neurodegeneration and decreased hippocampal synaptophysin immunoreactivity. However, Magnesium glycinate, particularly at 32.8mg, reversed the stated adverse effects.

Mg. Glycinate possesses potential therapeutic properties as a supplement in the management of cancer, particularly in alleviating the adverse effects of Cyclophosphamide.

Introduction

Cancer, a malignant disease defined by dysregulated cellular expansion, resistance to apoptosis, persistent neovascularization, and invasive dissemination capacity, has recently emerged as a global burden [1], constituting the second leading cause of mortality worldwide [2]. Chemotherapeutic agents such as cyclophosphamide show promising effects in reducing the death rate in some cancer patients [3]. Despite the significant positive impact of the chemotherapeutic agents in some cancer management, the debilitating effects, such as organ toxicity, cellular degeneration, and myelosuppression, often result in treatment discontinuation. Notably, cyclophosphamide usage is usually associated with neurotoxicity, loss of hair (alopecia), immunosuppression, haemorrhagic cystitis, and cardiotoxicity, particularly at high dosage [4].

Induction of inflammatory processes and reactive oxygen species (ROS) are its known pharmacological mechanisms of action that result in neurotoxicity [5]. Moreover, associated with the oxidative and inflammatory processes are the depleted levels of brain magnesium, which further result in intracellular depletion that exacerbates neuronal damage through N-methyl-D-aspartate receptor NMDA receptor

hyper-excitability [6]. The inability of most chemotherapeutic drugs to discriminate between the cancerous cells and the healthy body cells is mostly a documented reason for their toxic adverse effects [7]. The debilitating effects of these drugs have further necessitated and increased our quest to search for novel substances or means that would not only mitigate the adverse effects but would also enhance chemotherapeutic efficiency in a functional biological system in the absence of cancer.

Studies have continued to support the effects of magnesium on brain health through its neuroprotective impact and synaptic functions [8]. A study done by Li et al. (2014) showed an increased level of brain magnesium in mouse models of Alzheimer's disease (APPswe/PS1dE9), reduced amyloid plaques by 36%, prevented synapse loss through NMDAR, signaling preservation, and also reversed memory deficits even at late stages of disease [9]. Subsequently, Chen et al. (2024), in their systematic review of RCTs, corroborate magnesium's role in brain health and cognition, with elevated levels of brain magnesium reducing neuroinflammation and enhancing learning and memory through NMDA modulation [10]. However, this study examined the therapeutic role of magnesium glycinate at varying dosages on the neurotoxicity induced by cyclophosphamide by evaluating levels of some brain neurotransmitters, markers of inflammation, memory, hippocampal histomorphology, and synaptophysin immunoreactivity in rats.

Materials and Methods

2.1. *Chemicals and drugs*

Magnesium glycinate (250 mg, New York, USA), normal saline, Cyclophosphamide injection (xGen Pharmaceutical DJB). ELIZA assay kits for dopamine, acetylcholine, Serotonin, brain-derived neurotropic factor, interleukin 1β, interleukin-10, and tumour necrosis factor (TNF-α) were procured from R&D Systems (Bio-Techne, USA).

2.2. *Animals and experimental design*

The experimental procedure was accomplished in accordance with the methods approved by the animal research ethical committee of the Faculty of Basic Medical Sciences, University of Ilesa, Ilesa, Osun State, Nigeria, with approval code (UNILESA/FBMS/2025/04). These procedures adhered to the European Council Directive 2010/63/EU guidelines governing the protection of animals used for scientific purposes

Forty-eight (48) Wistar rats (eight weeks old), each weighing 150–170 g, were procured from animal breeders in Iwo, Osun state, Nigeria. The animals were conveyed in the cool of the day to the research animal house of the University of Ilesa, Ilesa, Osun State, Nigeria, where the experiment was done. Plastic cages (45 × 24 × 20 cm) were maximized for the animal housing in a temperature-controlled environment (22°C) under a 12-hour light-dark cycle throughout the experimental period (21 days). Before the commencement of the experiment, acclimatization of the animals was done for two weeks, after which the animals were allocated into four experimental cohorts (n = 8), while animals across all

groups were fed with normal feed (Top Feeds®, Nigeria), and clean water *ad libitum*. Additionally, Animals in groups B and C orally received magnesium glycinate at 22.8 mg/kg and 32.8mg/kg, respectively, according to Aniebo (2023) [11]. Groups D, E, and F received cyclophosphamide injection 3 times at 150mg/kg intraperitoneally every other day (days 1, 3, and 5), while groups D and E additionally received oral magnesium glycinate at 22.8 mg/kg and 32.8mg/kg, respectively. The animal's body weight was measured weekly using an electronic scale throughout the experimental period.

On the 22nd day, animals were introduced to the Y-maze neurobehavioral test for memory evaluation. Following the spatial working memory evaluation test in the Y-maze model, the animals were sacrificed by cervical dislocation on the 23rd day.

Following this was the dissection of the cranium for the removal of the brain tissues, after which the right hemisphere of each of the animals was homogenized using iced cold phosphate-buffered saline (PBS) as a medium at a ratio of 1:9 (weight of brain tissue/ volume of iced cold PBS). Tissue homogenate supernatant was used for the assessment of neurotransmitters (Serotonin, dopamine, and acetylcholine) levels, the activities of neuromodulator (Brain-Derived Neurotropic factor), and levels of inflammatory markers (interleukin 1beta, interleukin 10, and Tumour Necrosis Factor alpha).

Furthermore, the left hemisphere was dissected and fixed in 10% buffered formalin, processed in paraffin embedding, cut at 5μ m for histological evaluation (H&E and Cresyl fast violet stain) and synaptophysin immuno-reactivity.

2.3. Assessment of change in body weight (weekly)

As previously documented by Ojo *et al*. (2025) [12], individual animal's Body weight were evaluated weekly using an electronic weighing balance. Following this, the weekly change in body weight was determined using the formula $\text{Final (last week)} - Initial\ (first\ week)$. The results were statistically analyzed to determine the mean values.

2.4. Neurobehavioral test for Memory (Y-maze)

As previously reported by Onaolapo (2023) [13] and Ojo et al. (2025) [13], the Y-maze model was used in measuring the spatial working memory. Spatial working memory was scored by monitoring unpremeditated alternation behaviour. Unpremeditated alternation behaviour is the predisposition of rats to alternate customarily non-reinforced choices of the Y-maze on sequential chance. Each rat was positioned in one of the arms of the Y maze and was left to explore the arms for 5 minutes without restriction until its tail completely moved into the other arm.

2.5. Enzyme Linked Immunosorbent Assay (ELISA) analysis

Enzyme-linked immunosorbent assay protocols with the commercially available kits (Enzo Life Sciences Inc., NY, USA), made to determine the total levels of individual cytokines as previously reported by Onaolapo et al. (2023) [14] was used to determine the levels of interleukin-1Beta (IL-1β), interleukin-10

(IL-10), and Tumor Necrosis factor-α levels. Similarly, the levels of dopamine, serotonin, acetylcholine, and brain-derived neurotropic factor were measured from the supernatant of the homogenized brain tissue, through the usage of commercially available Enzyme-linked immunosorbent assay kits, following the manufacturer's method (ABCAM, Cambridge, UK).

2.6. Synaptophysin Immunohistochemical Evaluation

The left hemisphere of the brain tissue was fixed in 10% neutral buffered formalin, embedded in paraffin, and cut into 5μm sections, which were placed on positively charged slides. Sections of the hippocampus were embedded at 53–65°C for 30 minutes. Following this, slides were dewaxed in xylene (2 changes, 5 min each), rehydrated through graded ethanol (100%, 95%, 70%, for 5 minutes each, and rinsed in distilled water.

As reported by Krenacs (2010), Heat-induced epitope retrieval (HIER) was done using citrate buffer (pH 6.0) for 25 minutes in an automated stainer. Following this, slides were cooled to room temperature and rinsed in PBS/TBST. Endogenous peroxidase was blocked with 3% H_2O_2 for 15 minutes and incubated in 10% normal goat serum in PBS for 30 minutes to reduce non-specific binding. Anti-synaptophysin monoclonal antibody (clone IHC669) was applied overnight at 4°C and at room temperature. After which it was rinsed thrice in phosphate-buffered saline for 5 minutes each. Slides were incubated with biotinylated secondary antibody for 20 minutes, then HRP-streptavidin complex for 20 minutes. For brown precipitate, slides were developed with DAB chromogen for 10 minutes. Counterstained with hematoxylin for 1–5 minutes, dehydrated, cleared in xylene, and mounted [15].

2.7 Photomicrography

Sellon-Olympus trinocular microscope (XSZ-107E, China) was used to microscopically examine the histologically processed section of the hippocampus. The hippocampal photomicrographs were captured with a digital camera (Canon Powershot 2500). A pathologist who was naïve to the experimental cohorts evaluated the histopathological changes.

2.8 Statistical analysis

Data were presented as mean ± standard error of the mean. Normally distributed data was analyzed using One-way analysis of variance (ANOVA). Statistical analyses of data were carried out using GraphPad Prism ver. (9.0 for Windows, GraphPad Software, San Diego, CA, USA). Statistically significant difference was considered as $p < 0.05$.

Results

3.1. Effects of Magnesium-glycinate on body weight in rats.

Effects of Magnesium glycinate on the weekly change in body weight in rats treated with CYP (Fig. 1). No significant difference was observed in the Mg-glycinate control groups [22.8mg/kg (B) and 32.8mg/kg (C)] compared to the control group. Significant ($p < 0.05$) decrease in weight gain (weekly) was noted in the CYP-treated group compared to the normal control and Mg-glycinate control groups. Moreover, a significant increase was noted with CYP/Mg-glycinate (22.8mg) and CYP/Mg-glycinate (32.8mg) compared to the CYP control group (D).

3.2 Effect of Mg-glycinate on working memory (spatial) in the Y-Maze model in rats.

Effects of Magnesium glycinate on the percentage correct alternation in rats treated with CYP (Fig. 2). A significant ($P < 0.05$) increase was observed in the Mg-glycinate control groups [22.8mg/kg (B) and 32.8mg/kg (C)] compared to the control group. Significant ($p < 0.05$) decrease in percentage correct alternation was observed in the CYP-treated group compared to the normal control and Mg-glycinate control groups. Also, a significant increase was noted with CYP/Mg-glycinate (22.8mg) and CYP/Mg-glycinate (32.8mg) compared to the CYP control group (D).

3.3. Effects of Mg-glycinate on levels of serotonin, acetylcholine, dopamine, and Brain-Derived Neurotropic Factor.

Table 1. Shows the effects of Magnesium glycinate on levels of brain neurotransmitters and neuromodulators (Serotonin, Acetylcholine, Dopamine, and BDNF) in rats treated with Cyclophosphamide. In comparison with the normal control group (A), the sole administration of CYP. (group D) shows a significantly increased level of serotonin activities, while dopamine, acetylcholine, and BDNF activities significantly ($p < 0.05$) decrease. However, in comparison with the sole administration of CYP, administration of CYP/Mg-glycinate (22.8mg) and CYP/Mg-glycinate (22.8mg) showed a significant ($p < 0.05$) decrease in the activities of serotonin, while the levels of acetylcholine, dopamine, and BDNF significantly increased.

Table 1
Effects of Mg-glycinate on levels of serotonin, acetylcholine, dopamine, and Brain-Derived Neurotropic Factor.

Groups	Serotonin (pmol/mg tissue)	Acetylcholine (pmol/mg tissue)	Dopamine (pmol/mg tissue)	BDNF (pmol/mg tissue)
Control	10.78 ± 1.10	5.50 ± 0.11	33.11 ± 0.09	26.21 ± 0.41
Mg-glycinate (22.8mg)	13.67 ± 0.20^{a}	5.59 ± 0.19	39.23 ± 0.08^{a}	30.10 ± 0.32^{a}
Mg-glycinate (32.8mg)	14.32 ± 0.41^{a}	6.97 ± 0.09	41.20 ± 0.07^{a}	34.42 ± 0.29^{a}
CYP	21.21 ± 1.21^{ab}	2.02 ± 0.07^{a}	18.10 ± 1.01^{a}	14.22 ± 0.26^{a}
CYP/Mg-glycinate (22.8mg)	13.00 ± 0.18^{ab}	3.21 ± 0.03^{ab}	24.12 ± 0.16^{ab}	17.41 ± 0.11^{ab}
CYP/Mg-glycinate (32.8mg)	12.11 ± 0.09^{ab}	5.18 ± 0.08^{ab}	28.10 ± 0.10^{ab}	20.11 ± 0.23^{ab}

Data was presented as Mean ± S.E.M, *$p < 0.05$ against control, $^{\#}p < 0.05$ significant difference from CYP. The number of rats in each group equals eight (8). Mg: Magnesium, CYP: Cyclophosphamide

3.4. Effects of Mg-glycinate on interleukin-1beta levels in rats.

Effects of Magnesium glycinate on levels of interleukin 1beta (IL-1β) in rats treated with CYP (Fig. 3). No significant difference was observed in the Mg-glycinate control groups [22.8mg/kg (B) and 32.8mg/kg (C)] compared to the control group. Significant ($p < 0.05$) increase in (IL-1β) levels was observed in the CYP-treated group compared to the normal control and Mg-glycinate control groups. However, a significant decrease was noted with CYP/Mg-glycinate (22.8mg) and CYP/Mg-glycinate (32.8mg) compared to the CYP control group (D).

3.5. Effects of Mg-glycinate on levels of interleukin 10 (IL-10) in rats.

Effects of Magnesium glycinate on levels of interleukin 10 (IL-10) in rats treated with CYP (Fig. 4). A significant ($p < 0.05$) increase was observed in the Mg-glycinate control groups [22.8mg/kg (B) and 32.8mg/kg (C)] compared to the normal control group. Significant ($p < 0.05$) decrease in (IL-10) levels was observed in the CYP-treated group compared to the normal control and Mg-glycinate control groups. However, a significant ($p < 0.05$) increase was noted with CYP/Mg-glycinate (22.8mg) and CYP/Mg-glycinate (32.8mg) compared to the CYP control group (D).

3.6 Effects of Mg-glycinate on levels of Tumour Necrosis Factor Alpha (TNF-α) in rats.

Effects of Magnesium glycinate on levels of interleukin 10 (TNF-α) in rats treated with CYP (Fig. 5). No significant difference was observed in the Mg-glycinate control groups [22.8mg/kg (B) and 32.8mg/kg (C)] compared to the normal control group. Significant ($p < 0.05$) increase in TNF-α levels was observed in the CYP-treated group compared to the normal control and Mg-glycinate control groups. However, a significant ($p < 0.05$) decrease was noted with CYP/Mg-glycinate (22.8mg) and CYP/Mg-glycinate (32.8mg) compared to the CYP control group (D).

3.7 Hippocampal histomorphology

3.7.1. Histomorphological examination of H & E-stained section of dentate gyrus

The granular cell layer (GL) of the dentate gyrus and the subgranular layer (SGL) were distinctly revealed in Fig. 6A, more stained granule cells (red arrow head) were revealed in Fig. 6B and 6C, while numerous vacuolated granular cells (black arrow head) were observed in Fig. 6D. Figure 6E showed fairly restored vacuolated granular cells (black arrow head), while Fig. 6F revealed the unremarkable granular cells (black head arrow).

Cresyl fast Violet stain

3.7.2. Histomorphological examination of Cresyl violet-stained section of dentate gyrus

The photomicrographs revealed Nissl granular components of the cells. Nissl granular components of the cytoplasm of cells in fig. 6D (CYP) were decreased compared to controls (fig. 1A). Fig 6E and Fig. 6F shows a slifghtly more expressed nissl substances (x 400).

3.7.3 Synaptophysin Immunohistochemical Staining of the Hippocampus

Figure 8(a-f). shows synaptic plasticity via evaluation of synaptophysin immunoreactivity in the hippocampus of rats. Normal control (Fig. 8A) shows strong synaptophysin reactivity. 8B, 8C, and 8D: Sections show a decreased synaptophysin expression, as presented as a blurry brown stain (area circled red). 8E and 8F show a moderate synaptophysin expression. Figure 8A: normal control rats, Fig. 8B: Mg-glycinate (22.8mg/kg) treated rats, Fig. 8C: rats administered Mg-glycinate (32.8mg/kg), 8D: animals treated with CYP alone, 8E: animals that received CYP/Mg-glycinate (22.8mg/kg), and Fig. 8F: CYP/Mg-glycinate (32.8mg/kg) treated rats.

Discussion

The present study evaluated the ameliorative effects of magnesium glycinate against impaired memory, altered markers of inflammation, brain neurotransmitters, neuromodulators, degenerated hippocampal

histomorphology, and synaptophysin immunoreactivity following cyclophosphamide administration. Magnesium glycinate combines magnesium with glycine (an amino acid that enhances the uptake, absorption, and bioavailability of elemental magnesium).

In agreement with several studies [14, 16, 17] that have reported the adverse effect of CYP on body weight, CYP administration in this study results in a significant weight loss compared to the normal control. However, the Magnesium Glycinate administration alleviates these effects, as noted with a significant increase in body weight in the groups administered CYP/Mg. Glycinate 22.8 and CYP/Mg. Glycinate 32.8 compare the sole administration of CYP. Administration of Cylophosphamide, an alkylating agent, induces weight loss primarily through cytotoxic impact by depleting adipogenic precursors and reducing fat storage capacity [18]. Conversely, Studies [19, 20, 21] have shown that magnesium improves insulin sensitivity and glucose uptake, preventing muscle wasting while regulating inflammation-driven appetite loss via CCK release. In tandem with the reports by studies that have reported the memory-impairing effects of cyclophosphamide, the percentage correct alternation in the CYP control group was statistically decreased compared to the control group. While it increased in the groups solely administered magnesium at 22.8mg/kg and 32.8mg/kg. However, the decreased percentage correct alternation in the CYP sole administered group was reversed with magnesium treatment. Magnesium has been shown to have a memory enhancing effects in both animal studies and clinical trials (Clinical trial number: not applicable) by enhancing long-term potentiation [22].

A study done by Ibrahim (2024) [5] showed that neurotransmitters and neuromodulators are major victims of cyclophosphamide administration in animal studies. Disruption of inhibitory and excitatory neurotransmitter activities is often attributed to CYP toxicity [23]. In corroboration of the reported debilitating impact of CYP, levels of dopamine, acetylcholine, and brain-derived neurotropic factor (BDNF) activities were significantly decreased with CYP usage compared to the control, while their levels increased in groups administered Mg. glycinate at 22.8mg/kg and 32.8mg/kg. Acetylcholine and dopamine primarily act as excitatory neurotransmitters; they could act indirectly as inhibitory neurotransmitters depending on certain receptors and brain regions [24]. While BDNF serves as an important neurotrophic protein that enhances neuronal well-being, growth, and neuroplasticity, vital for learning and memory conservation [25]. Primarily, Acetylcholine promotes Long-term potentiation, while dopamine modulates through D1/D5 receptors [26]. On the other hand, serotonin is neither inhibitory nor excitatory, as its effect is often determined by its receptor; postsynaptic neurons are depolarized via IP3/$Ca^{2+,}$ with 5-HT2A/2C receptors enhancing excitability. It exerts inhibitory effects primarily through 5-HT1A receptors and induces postsynaptic hyperpolarization through potassium (K^+) channel activation. In this study, a significant disruption in serotonin levels was observed in the group administered CYP alone compared to the normal control.

Interestingly, magnesium administration regulates the levels of neurotransmitters and neuromodulators as previously reported by Patel *et al*. (2024) [8]. The ameliorative impact of Magnesium is attributed to its ability to affect ion channel activities, synaptic vesicle release, and signaling pathways.

Concerning the activities of inflammatory cytokines, CYP administration is often associated with significantly increased levels of pro-inflammatory cytokines, while it decreases the levels of anti-inflammatory cytokines [27]. Consistent with these reports is the result of inflammatory and anti-inflammatory cytokines in this study. Levels of Interleukin 1beta and Tumour Necrosis Factor alpha significantly increase compared to the normal control. On the other hand, the levels of the pro-inflammatory cytokine significantly decreased in the groups administered CYP/Mg-glycinate (22.3mg/kg) and CYP/Mg-glycinate (32.8mg/kg). The anti-inflammatory effects of Mg-glycinate are attributed to its intracellular modulatory effects on NF-κB signaling and calcium homeostasis [28]. As previously reported by Onaolapo et al. (2023), levels of IL-10 significantly decrease with CYP administration. Interestingly, treatment with Mg-glycinate reversed these effects, particularly at 32.8mg/kg [14].

The general histolomorphological evaluation of the hippocampal dentate gyrus reveals well-stained granular cells and a sub-granular layer of the dentate gyrus in the control group (Fig. 6A). The group treated with magnesium shows the neuronal-enhancing effects of magnesium (Fig. 6B and 6C) in tandem with reports by Varga *et al*. (2025) [29]. The photomicrograph in the CYP administered group revealed a significant loss of granular cells in corroboration with studies that have reported similar effects [30]. Interestingly, treatment with Mg-glycinate (Fig. 6E and 6F) against CYP toxicity revealed an ameliorating impact of Mg-glycinate, particularly at 32mg/kgb.w (Fig. 6F). This could be attributed to its ability to reverse neuro-inflammation and modulates neurotransmitters levels as previously reported in this study and in agreement with other studies that have reported that Mg-glycinate possesses anti-inflammatory and neuro-modulatory properties [8]. Furthermore, the cresyl fast violet-stained section of the dentate gyrus corroborates the effects seen with the H and E-stained sections in this study. The Nissl substances were slightly more pronounced in the Mg-glycinate sole-administered group, while the CYP-administered group (Fig. 7D) showed less stained Nissl substances. More interesting is the slight ameliorative effects of Mg-glycinate shown in Figs. 7E and 7F. Synaptic integrity was evaluated in this study with Synaptophycin immuno-reactivity, an endogenous presynaptic vesicle glycoprotein and a viable marker for synaptic health. Strong punctate staining, indicating positive synaptophycin immuno-reactivity is well expressed in the normal control and the group sole administered Mg. Glycinate at 22.8mg/kg b.w and Mg. Glycinate at 32.8mg/kg (Figs. 8A, 8B, and 8C). However, synaptic injury was observed with CYP administration, as expressed with a pale and decreased immunoreactivity (Fig. 7D). Studies [31, 32] have continued to report oxidative stress and neuro-inflammation as mechanisms through which CYP impairs brain health. In agreement with these reports are the elevated levels of pro-inflammatory cytokines (TNF-α and IL-1β) evaluated in this study. Decreased synaptic integrity is obviously the factor for the decreased levels of spatial working memory that were observed with CYP in this study.

Conclusion

To summarize, the results presented in this study emphasize a potential therapeutic application of Mg. Glycinate as a supplement in the management of cancer, particularly in alleviating the adverse effects

(weight loss, inflammation, decreased spatial working memory, and neurodegeneration) of chemotherapeutic agents such as Cyclophosphamide. While we hope to harness Mg. glycinate in this regard. There is, however, a need for further findings on its possible molecular interaction with conventional anti-cancer agents, particularly Cyclophosphamide.

Declarations

Ethics Approval and consent to participate

The experimental procedure was accomplished in accordance with the methods approved by the animal research ethical committee of the Faculty of Basic Medical Sciences, University of Ilesa, Ilesa, Osun State, Nigeria, with approval code (UNILESA/FBMS/2025/04).

Consent to Publication

Not applicable

Competing Interest

The authors declared no competing interest

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Author Contribution

Conceptualization: FOO, KPF, LAH. Data curation: FOO, BEO, AAO, AO. Formal analysis: LMB, AO, OAA, BEO, and ATE. Funding acquisition: TETFUND. Methodology: FOO, LAH, and MTO. Resources: BEO, ATE. Writing original draft: FOO. Writing review & editing: KPF, BEO, AO, LMB, MTO, OAA, LAH. Approval of final manuscript: all authors.

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Data Availability

The datasets generated during the study are available from the corresponding author on reasonable request.

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Figures

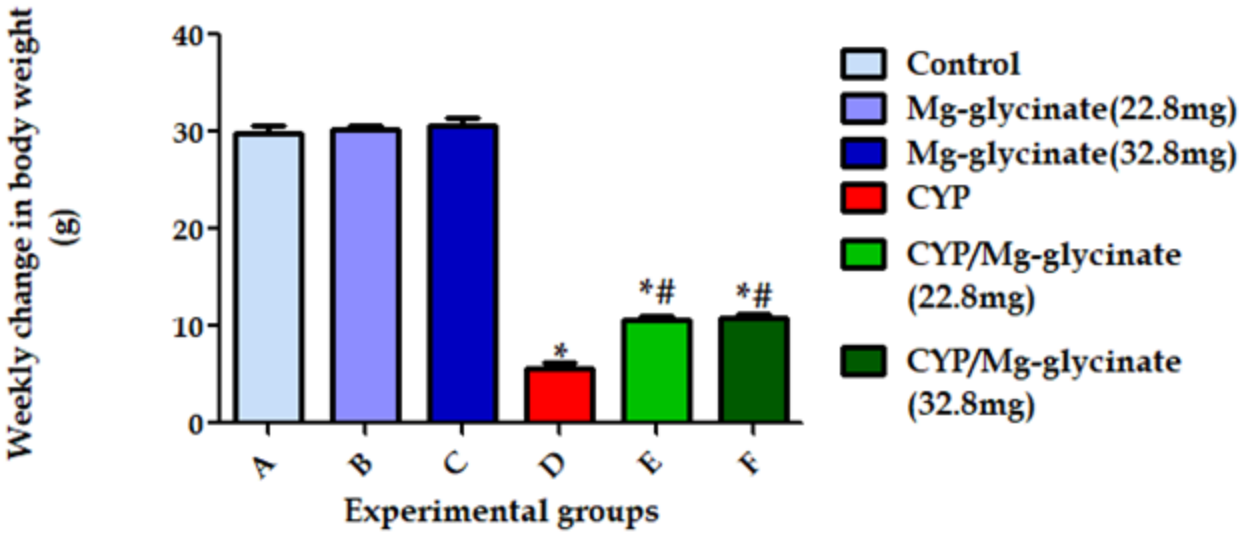


Figure 1

Effects of Magnesium glycinate on the change in body weight (weekly) in Cyclophosphamide-treated rats. Each bar is presented as Mean ± S.E.M, *p < 0.05 against control, #p < 0.05 significant difference from CYP. The number of rats in each group equals eight (8). Mg: Magnesium, CYP: Cyclophosphamide.

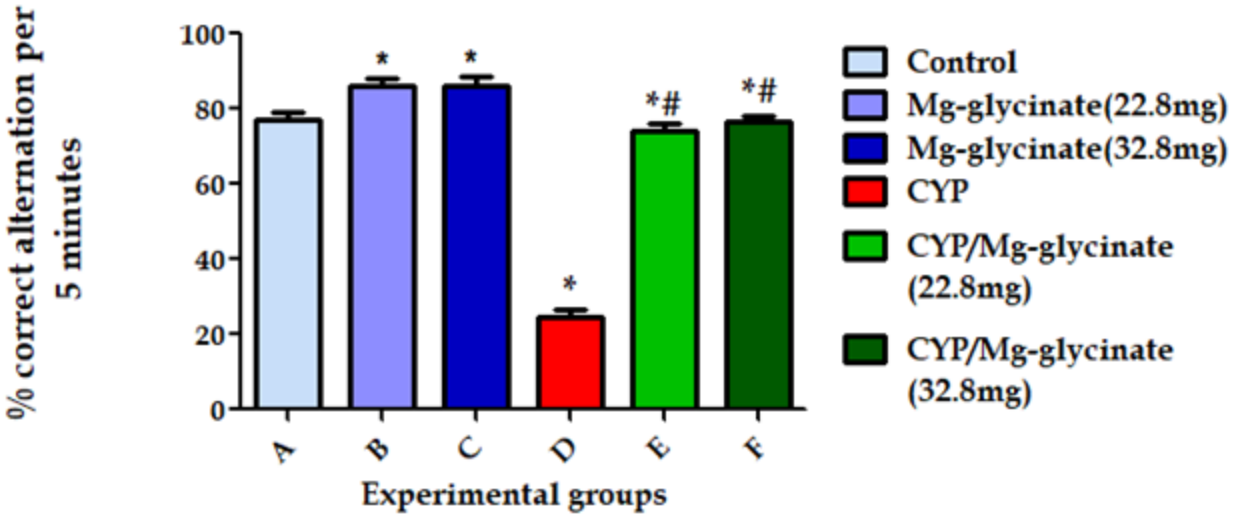


Figure 2

Effects of Magnesium glycinate on percentage correct alternation (weekly) in Cyclophosphamide-treated rats. Each bar is presented as Mean ± S.E.M, *p < 0.05 against control, #p < 0.05 significant difference from CYP. The number of rats in each group equals eight (8). Mg: Magnesium, CYP: Cyclophosphamide.

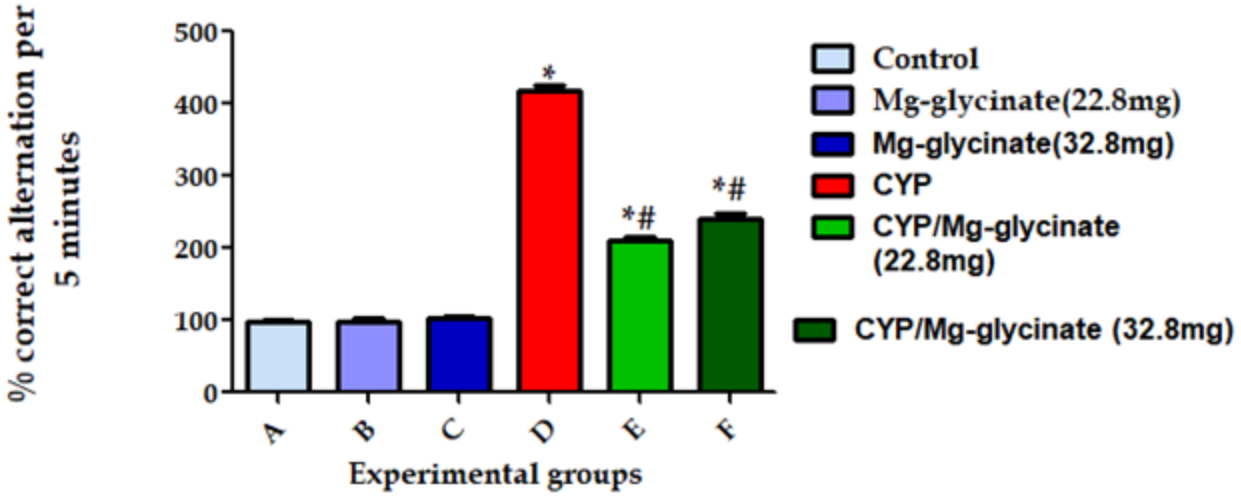


Figure 3

Effects of Magnesium glycinate on IL-1β levels in Cyclophosphamide-treated rats. Each bar is presented as Mean ± S.E.M, *p < 0.05 against control, #p < 0.05 significant difference from CYP. The number of rats in each group equals eight (8). Mg: Magnesium, CYP: Cyclophosphamide.

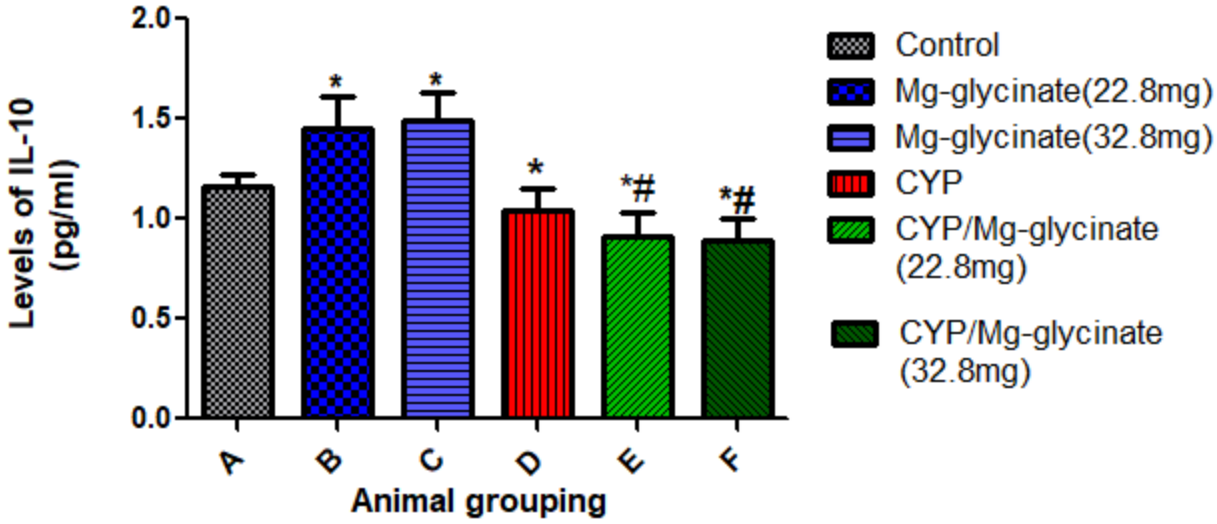


Figure 4

Effects of Magnesium glycinate on IL-10 levels in Cyclophosphamide-treated rats. Each bar is presented as Mean ± S.E.M, *p < 0.05 against control, $^{\#}$p < 0.05 significant difference from CYP. The number of rats in each group equals eight (8). Mg: Magnesium, CYP: Cyclophosphamide.

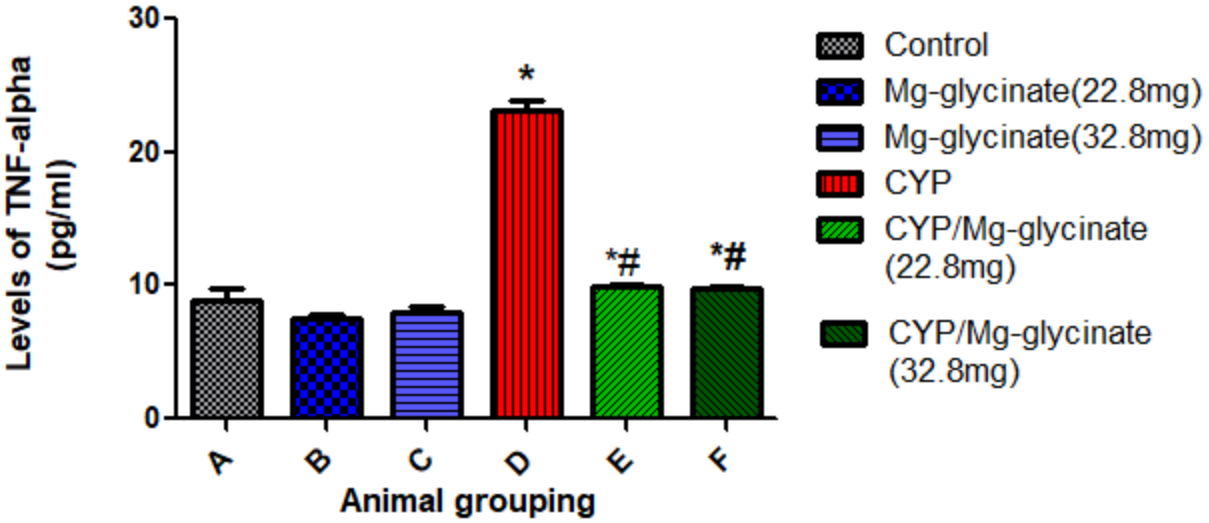


Figure 5

Effects of Magnesium glycinate on TNF-α level in Cyclophosphamide-treated rats. Each bar is presented as Mean ± S.E.M, *p < 0.05 against control, $^{\#}$p < 0.05 significant difference from CYP. The number of rats in each group equals eight (8). Mg: Magnesium, CYP: Cyclophosphamide.

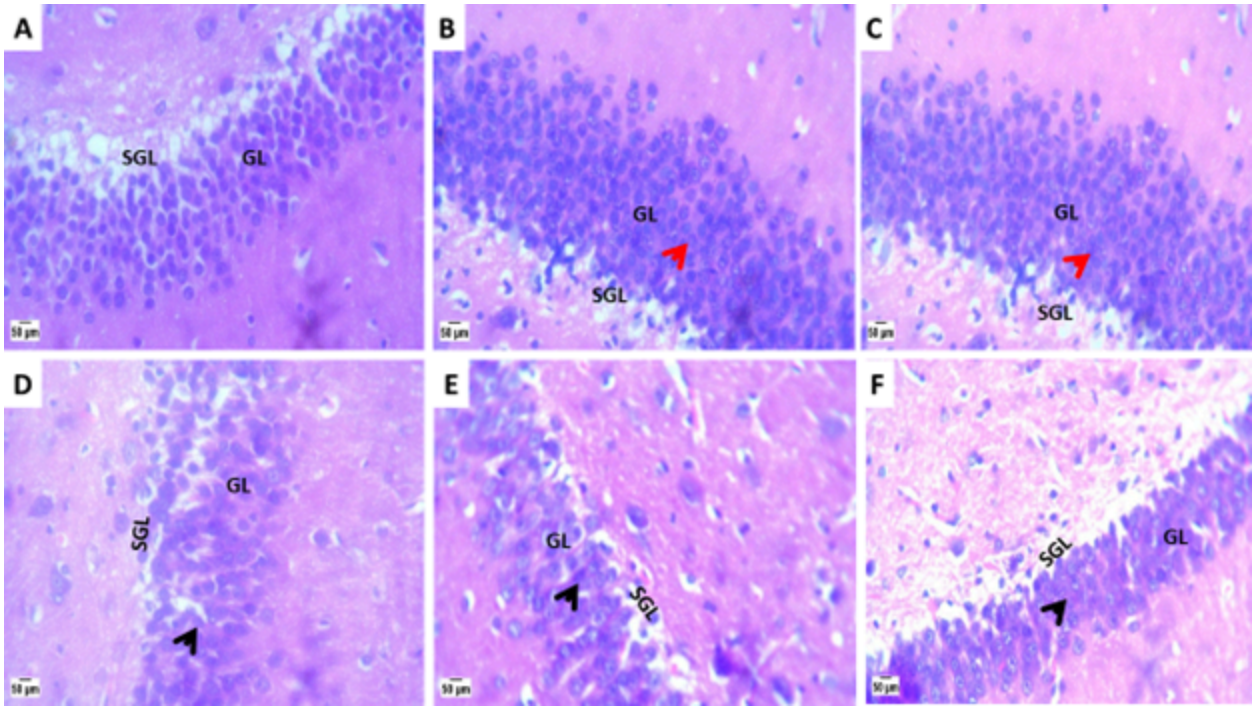


Figure 6

(A-F): Histomorphological examination of H & E-stained section of dentate gyrus (×400), group A (control), B (Mg-glycinate at 22.8mg/kg b.w.), C (Mg-glycinate at 22.8mg/kg b.w), D (CYP), E (CYP/Mg-glycinate at 22.8mg/kg b.w), F (CYP/Mg-glycinate at 22.8mg/kg b.w+32.8 mg/kg b.w).

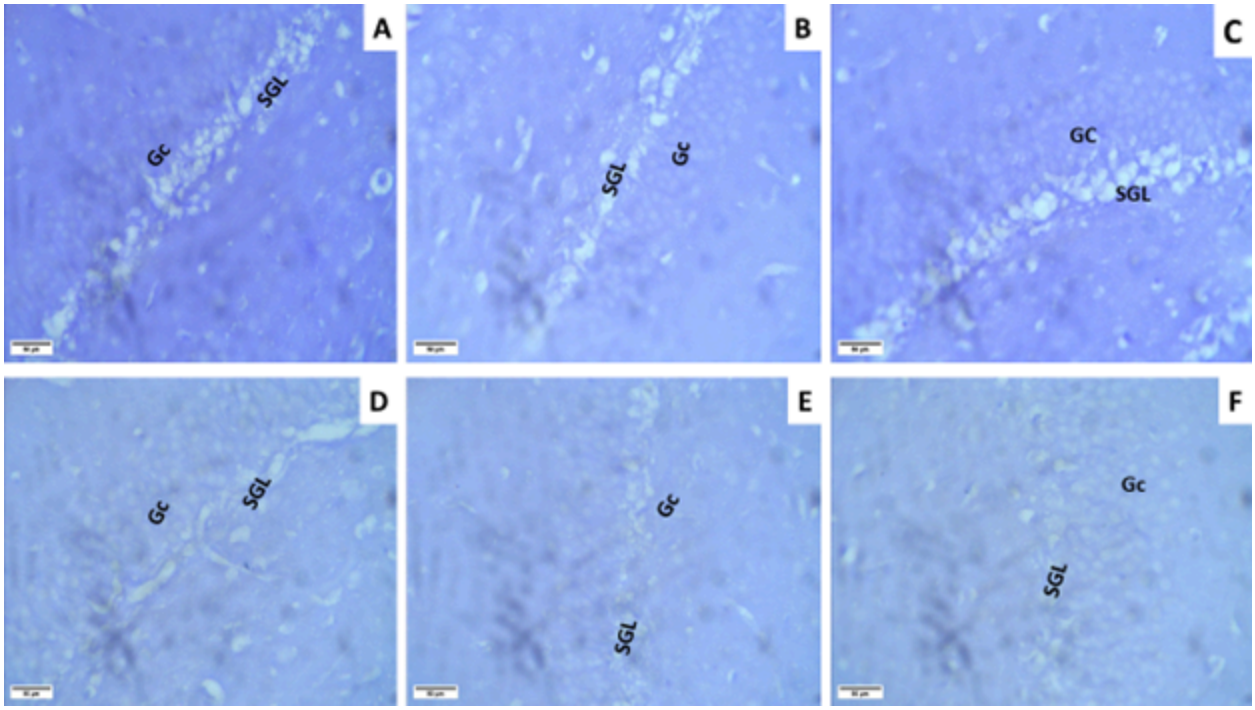


Figure 7

(A-F): Histomorphological examination of Cresyl violet-stained section of dentate gyrus (×400), group A (control), B (Mg-glycinate at 22.8mg/kg b.w.), C (Mg-glycinate at 22.8mg/kg b.w), D (CYP), E (CYP/Mg-glycinate at 22.8mg/kg b.w), F (CYP/Mg-glycinate at 22.8mg/kg b.w+32.8 mg/kg b.w).

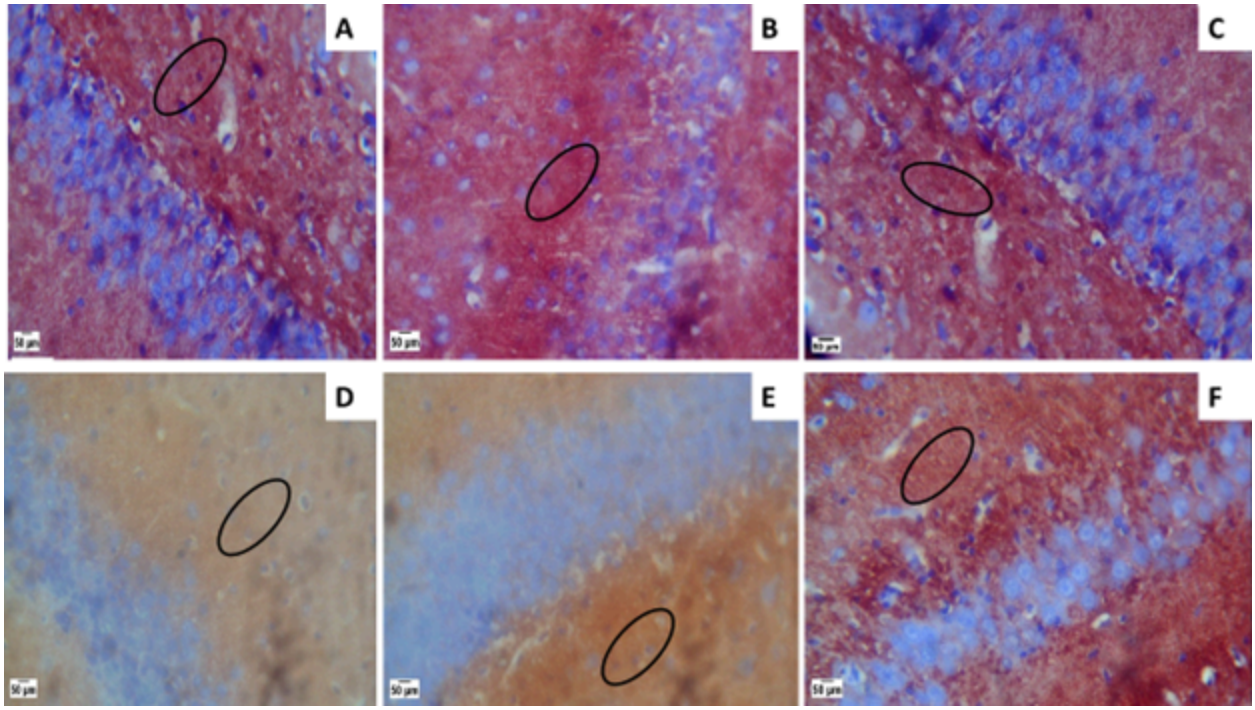


Figure 8

(A-F): Effects of Mg-glycinate on synaptophysin immunoreactivity in the section of hippocampal dentate gyrus in rats treated with cyclophosphamide. Fig. 8A shows strong synaptophysin reactivity. Fig. 8D shows a decreased synaptophysin expression, as presented as a blurry brown stain (area circled red). 10E and F show a moderate synaptophysin expression. Fig. 8A: normal control rats, fig. 8B: Mg-glycinate (22.8mg/kg) treated rats, fig. 8C: rats administered Mg-glycinate (32.8mg/kg), 8D: animals treated with CYP alone, 8E: animals that received CYP/Mg-glycinate (22.8mg/kg), and fig. 8F: CYP/Mg-glycinate (32.8mg/kg) treated rats.

Supplementary Files

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