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PUTATIVE ROLES OF *OCIMUM GRATISMUM* IN PARAQUAT-ALTERED MOTOR AND COGNITIVE BEHAVIORS OF MALE WISTAR RATS

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ABSTRACT: *Neurodegenerative diseases (NDs) are due to progressive loss of neurons, leading to a decline in motor and cognitive functions, memory, and learning. This study investigated the role of Ocimum gratissimum (Og) in paraquat-altered motor and cognitive abilities. 35 Wistar rats were assigned to five groups of 7 rats after 14 days of acclimatization. Group A was the control, Groups B, C, D, and E were exposed to 12 mg/kg of Paraquat (PQ) for 14 days; thereafter, Groups C, D, and E were treated with 200, 400, and 600 mg/kg, respectively. All administrations were oral, and the treatment with Og lasted 14 days. There was a reduced number of lines crossed in Group B and a significant increase in lines in Groups C and D ($p<0.05$). The time spent close to the wall significantly increased in Group B ($p<0.05$) but decreased in the treated Groups ($p<0.05$). In Group B, rearing time increased ($p<0.05$), while grooming and stretching time decreased ($p<0.05$). The discrimination index increased significantly in Group B, while it decreased in the treated Groups ($p<0.05$). High-density lipoprotein (HDL) decreased ($p<0.05$) in Group B, and increased significantly in the treated Groups. Superoxide dismutase (SOD) and catalase (CAT) were reduced in Group B and increased significantly in the treated Groups, while Malondialdehyde increased ($p<0.05$) in Group B, and significantly decreased in the treated groups. Alterations ranging from necrosis, hemorrhage, pyknosis, and layer separations were seen in the Group B section. Og is a good antioxidant that can ameliorate paraquat toxicity.*

KEYWORDS: Neurodegeneration, Paraquat, *Ocimum gratissimum*, Oxidative stress, Motor activity, Cognitive function, Antioxidant enzymes.

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BACKGROUND

Neurodegenerative diseases (NDs) are a broad range of conditions, mostly known for the gradual deterioration of nerve cells and associated structures within specific brain areas (Harms *et al*., 2018). These include Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), and Huntington's disease (HD). The latter two conditions involve impaired coordination of movements resulting from the degeneration of neurons in the basal ganglia (Prado-Prado & Garcia, 2012). AD, the most prevalent type of ND worldwide, is predicted to triple by 2050 (Njan *et al*., 2023). NDs are characterized by a progressive decline in cognitive functions, memory, and learning due to neuronal loss in the cortex and hippocampus (Enciu *et al*., 2011). The development of NDs is linked to various factors, including the deposition of metal ions, which can disrupt the biochemical equilibrium of the nervous system, disturbances in cholinesterase and monoamine oxidase (MAO), oxidative stress, the formation of amyloid and tau plaques, and the loss of dopaminergic neurons and reduced dopamine levels (Smeyne *et al*., 2016).

It has been shown that exposure to environmental pollutants, such as pesticides, heavy metals, and herbicides, can have fatal consequences for both human and animal health and proper brain function (Edobor *et al*., 2021). Agrochemicals pose a serious risk to human health in several parts of the world, particularly when employed as weed killers. According to Goldman (2014) and Zyoud (2018), paraquat (PQ) is one of the primary herbicides that can cause both purposeful and accidental poisoning. It also causes a significant number of illnesses, such as neurodegenerative disease states and abnormal biological function changes. It is an environmental neurotoxicant that is widely used as a weed killer worldwide. The proposition that exposure to PQ may contribute to the pathogenesis of neurodegenerative disorders like Parkinson's disease (PD) is bolstered by the evidence that PQ induces toxicity in key brain regions such as the cerebrum and substantia nigra, which are critical for motor coordination (Colle *et al*., 2018; Kumar *et al*., 2016). The primary mechanisms through which PQ induces neurological conditions include protein aggregation, mitochondrial dysfunction, disturbances in dopamine levels, and heightened oxidative stress (Edobor *et al*., 2021; Rappold *et al*., 2011; X. Zhang *et al*., 2016). Dietary sources of cholinesterase inhibitors, particularly from food plants with no or little toxicity, could be an alternate strategy for the prevention/treatment of these disorders, given the unfavorable effects of traditional medications for the management of NDs (Ademosun & Oboh, 2014). Many culinary and medicinal herbs such as *Crocus sativus, Nigella sativa, Coriandrum sativum, Thymus vulgaris, Ferula assafoetida, Zataria multiflora, Curcuma longa,* and *Gongronema latifolium* have been used for centuries to treat AD and other ND because of their anti-inflammatory and antioxidant properties (Harms *et al*., 2018). *Ocimum gratissimum*, a perennial herb in the Lamiaceae family, is also referred to as "Scent leaf" or "Chit-Chan-Than" (Yuan *et al*., 2016). The plant is indigenous to tropical areas, including West Africa and India. This plant can be found in the coastal regions and savannahs of Nigeria. It is a popular seasoning in traditional cuisines, valued for its fragrant flavor. In various regions of the world, salads, soups, pepper soups, pastas, vinegars, and jellies are made (Yuan *et al*., 2016).

In traditional medicine, the leaves of *O. gratissimum* are utilized to address various ailments, including menstrual irregularities, fever, diarrhea, abdominal pain, convulsions, ear infections, conjunctivitis, and epilepsy (Ojewumi *et al*., 2024; Taran *et al*., 2025). Additionally, dried leaves are often sniffed to alleviate fever and headaches (Ojewumi *et al*., 2024; Tuan Anh *et al*., 2019). The plant possesses several therapeutic properties, including antibacterial,

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antioxidant, hepatoprotective, neuroprotective, diuretic, and anticarcinogenic effects. These properties are attributed to phytochemical components such as alkaloids, tannins, flavonoids, phenolics, saponins, glycosides, cardiac glycosides, resins, steroids, phlorotannins, anthraquinones, and terpenoids (Alexander, 2016). While numerous extracts of *O. gratissimum* have demonstrated neuroprotective properties and inhibitory effects on cholinergic targets in various experimental models, there remains a dearth of documentation regarding the specific neurotherapeutic components underlying these actions (Harms *et al*., 2018). Therefore, the present study aimed to investigate the putative roles of Ocimum gratissimum on paraquat-altered motor and cognitive abilities in male Wistar rats.

METHODOLOGY

Ethical Clearance

Approval was obtained from the Animal Handling and Ethics Committee of the Faculty of Basic Medical Sciences of Alex Ekwueme Federal University, Ndufu-Alike, Ebonyi State. The experiment followed the operational guidelines of the Institutional Animal Ethics Committee of Experiments on Animals and conformed to the recognized International experimental animal rights.

Collection, Identification, and Preparation of Extract

Ocimum gratissimum leaves were procured from Ikwo, Ebonyi state, Nigeria, and authenticated at the Department of Biology, Alex Ekwueme Federal University, Ndufu Alike, Ikwo, Ebonyi state, Nigeria. The fresh scent leaves were washed and air-dried at ambient temperature (30 ±2 °C) for two weeks and then pulverized with a laboratory mechanical grinder to obtain fine powders. The powdered sample was soaked in distilled water at a 1:10 ratio for 72 hours and stirred at intervals. The mixture was then decanted and filtered with a sieve and then the Whatman filter paper.

Experimental Protocols

The 35 Wistar rats that were used for the study were randomly assigned into five groups of 7 rats per group after 14 days of acclimatization. The groups are as follows: Group A served as control and was exposed to normal saline using oral gavage. Group B was exposed to 12 mg/kg of Paraquat via oral gavage. Groups C, D, and E received 12 mg/kg of Paraquat via the oral route and, after that, were treated with 200mg/kg, 400mg/kg, and 600mg/kg serving as low, medium, and high doses, respectively. The oral administration of paraquat to groups B, C, D, and E lasted for fourteen days using oral gavage. Groups C, D, and E were then treated with OG for another fourteen days. The experiment lasted for 28 days outside the acclimatization period. All the animals were exposed to the same stress of oral gavage to determine its effect on the animals.

Assessment of recognition memory

The Novel Object Recognition (NOR) test has been used in the study of memory functions in rodents Ennaceur (2010), in which the recognition of novel objects requires more cognitive skills from the rodent, and measuring the exploration of novel objects (Silvers *et al*., 2013). The NOR is specifically used to evaluate recognition memory and object recognition memory.

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Assessment of Novel Object Recognition (NOR) Test

The task procedure consists of three phases: (i) habituation, (ii) familiarization, and (iii) test phase. During the habituation phase, each Wistar rat is allowed to explore the open-field arena freely in the absence of objects. Then, it is removed from the arena and placed in its holding cage. During the familiarization phase, a single rat is placed in an open-field arena containing two identical sample objects (usually of the same color, shape, texture, and size) for a few minutes (retention interval) to familiarize with the objects. The rats are placed at the center of the two objects to prevent coercion from exploring the objects. During the test phase, the rat is returned to the open-field arena with two sample objects, one of which it's familiar with and the other, a novel object (A + B) (Silvers *et al*., 2013). During the familiarization and the test phase, the objects are placed in opposite and symmetrical corners of the open-field arena, and the novel's location versus the familiar object is counterbalanced (Hammond, 2004). After the test phase, the following parameters will be collected: Mean time spent sniffing a familiar object, Mean time spent exploring a familiar object, Mean time spent exploring a novel object, Percentage of object discrimination (%), and Discrimination index.

Animal Sacrifice and Sample Collection

At the end of the experiment, the rats were sacrificed via cervical dislocation. The skull was opened and the brain was homogenized, and the homogenate was centrifuged at 4,000 rpm for 10 minutes and thereafter, decanted to separate the supernatant from the residue. The supernatant was then used to estimate the total cholesterol, triglycerides (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride (TG), Malondialdehyde (MDA), Glutathione (GSH), Glutathione reductase (GR), Superoxide dismutase (SOD), and Catalase (CAT) activity level in the brain. The other brain parts were fixed in Bouin's fluid for 48 hours and then further refixed in 10% formalin saline for histological studies.

Estimation of MDA Level

MDA level was determined based on the reaction of MDA with thiobarbituric acid to produce thiobarbituric acid reactive substance (TBARS), which was measured spectrophotometrically at 532 nm and was calculated using the molar extinction coefficient for MDA TBA-complex of 1.56 × 105M-1CM-1 and its concentration expressed as micromole of MDA/g of tissue.

Estimation of SOD and CAT activities

Spectrophotometric estimation of the Superoxide dismutase (SOD) activity will be adopted from a descriptive technique in a study by Weydert and Cullen (Weydert & Cullen, 2010). A single unit of SOD will be defined as the amount of the enzyme required to inhibit the reduction of nitro-blue tetrazolium (NBT) by 50% under specific conditions.

Estimation of GSH and GR activities

Glutathione activity will be determined by a widely accepted and sensitive enzyme recycling assay based on a procedure reported by Smith *et al*. (1993) and modified by Tipple and Rogers (2012) that requires no specialized equipment. GSH is oxidized by 5,5′-dithiobis-(2-nitrobenzoic acid) (DTNB), resulting in the formation of GSSG and 5-thio-2-nitrobenzoic acid (TNB). GSSG is then reduced to GSH by glutathione reductase (GR) using the reducing equivalent provided by NADPH. The rate of TNB formation is proportional to the sum of GSH

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and GSSG present in the sample and is determined by measuring the formation of TNB at 412 nm. Glutathione reductase activity was determined spectrophotometrically with a Shimadzu Spectrophotometer UV-1208 at 25°C. The assay system contained 435 mM K-phosphate buffer, pH 7.3, including 1 mM EDTA, 1 mM GSSG, and 0.1 mM NADPH. One enzyme unit is the oxidation of 1 µmol NADPH per minute under the assay conditions.

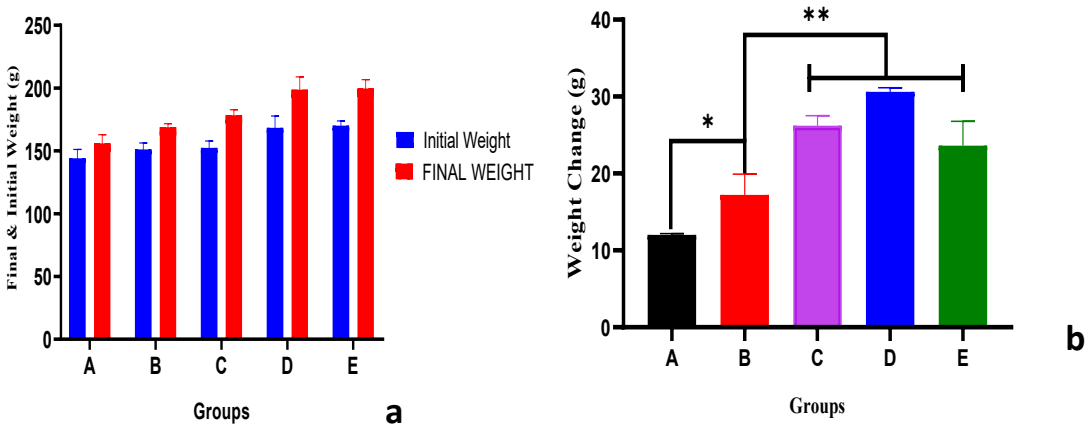
Data Analysis

The data generated will be analyzed and expressed as mean ± Standard Error of Mean (SEM). Statistical differences in the mean between groups will be analyzed using one-way ANOVA and compared using a paired Student's t-test. The statistical significance level will be established at a $p < 0.05$ with the aid of Statistical Package for Social Sciences (SPSS) software, version 23.

RESULTS

Figures 1a and b below represent the animal weight during the experimental duration. The final weight kept increasing, as seen in Figure 1a. In Figure 1 below, the Og caused a significant increase in the weight change ($p<0.05$) compared to Group B. Even though group B also showed an increase in weight, it was not as high as the treated groups (Figure 1b).

Fig. 1: The charts showing (a) the final and initial body weight of the rats and (b) the weight change of the rats. *Significant increase compared to Group A at p<0.05; **Significant increase compared to Group B at p<0.05.



Effects of Paraquat and Og Motor and Abnormal Behaviors

Figures 2a-c represent the parameters obtained from the open-field test apparatus. In Figure 2a, the animal's locomotive activities significantly dropped in Group B ($p<0.05$) compared to the control Group A ($p<0.05$). The number of lines crossed increased significantly in Groups C and D compared to Group B ($p<0.05$), as seen in Figure 2a. In Figure 2b, the time spent in the center and close to the wall represents the measure of contextual fear in rats. The contextual fear (time spent close to the wall significantly increased in Group B ($p<0.05$) compared to the control Group A, while the time spent close to the walls decreased significantly in the treated Groups ($p<0.05$) compared to Group B, as seen in Figure 2b. In contrast, the Groups C and D

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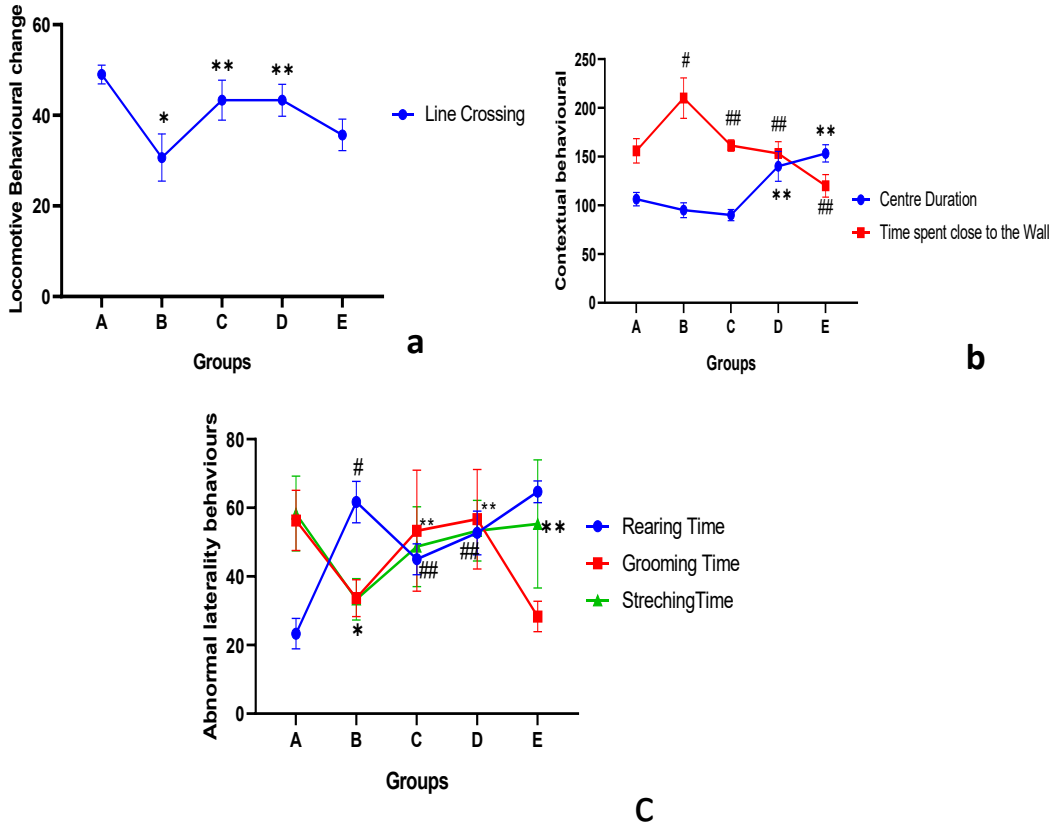
rats spent significantly more time at the center of the open-field apparatus compared to the Group B rats (Figure 2b). Rearing, grooming, and stretching are all measures of abnormal laterality behaviors leading to anxiety in animals, and they are represented in Figure 2c. In Group B, the duration of rearing increased significantly ($p<0.05$), while the time spent grooming and stretching decreased significantly ($p<0.05$) compared to Group A, see Figure 2c. In Groups C and D, the time spent rearing decreased significantly ($p<0.05$), while the stretching and grooming time increased significantly ($p<0.05$) compared to Group B. In contrast, the stretching time significantly increased ($p<0.05$) compared to Group B, as seen in Figure 2c.

Fig. 2: The graphs show (a) locomotive activity, (b) contextual fear behaviors, and (c) abnormal laterality behaviors. *Significant decrease compared to Group A at p<0.05; **Significant increase compared to Group B; #Significant increase compared to Group A; ##Significant decrease compared to Group B at p<0.05.



Effects of Paraquat and Og on spatial memory

The spatial memory was assessed using the T-Maze, and a measure of the time spent in each arm and the discrimination index represents the level of memory of the rats, as shown in Figures 3a-d. In Figures 3a and c, the time spent in arms A and C by Group B rats significantly reduced ($p<0.05$) compared to Group A, while the time spent in arm B significantly increased ($p<0.05$) compared to Group A (Figure 3b). The discrimination index of the rats increased significantly ($p<0.05$) in Group B compared to Group A, as seen in Figure 3d. There was a significant reduction in the time spent in arm B by Groups C, D, and E compared to Group B (Figure 3b), while the time spent in arms A and C by Groups C, D, and E significantly increased ($p<0.05$) compared to Group B (Figures 3a and c). The discrimination index increased significantly in

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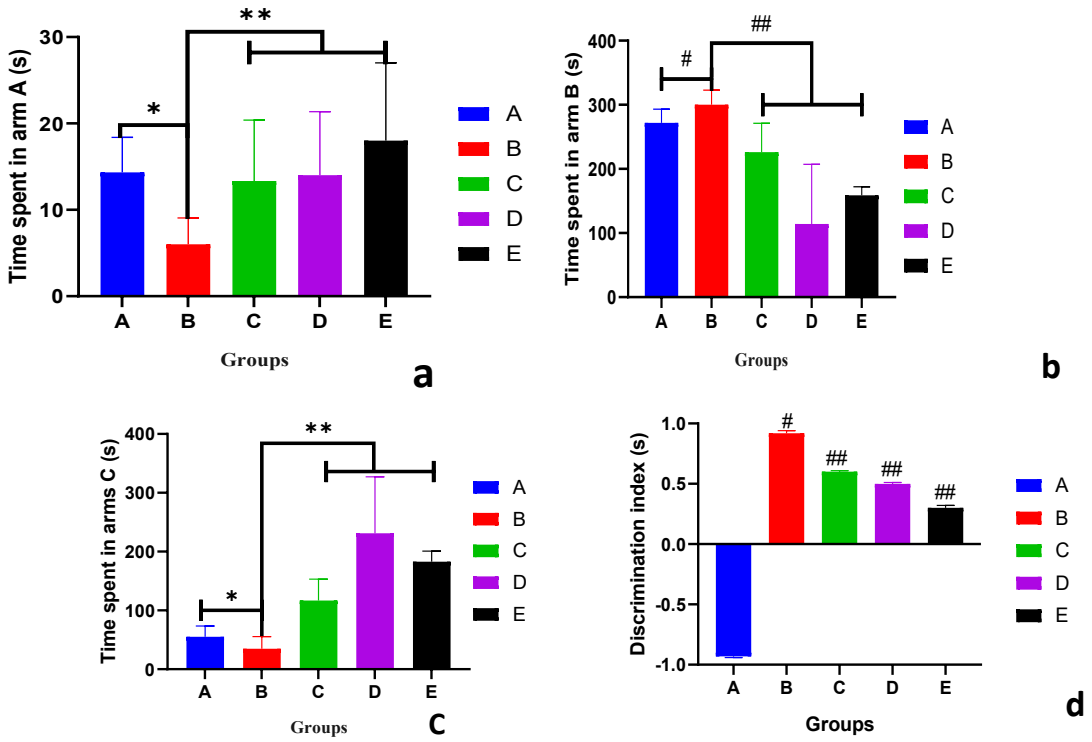
Group B compared to the control Group A, as seen in Figure 3d, and significantly decreased in the treated Groups ($p<0.05$) compared to Group B.

Fig. 3: The graphs showing (a) time spent in arm A, (b) time spent in arm B, (c) time spent in arm C, and (d) the discrimination index of the novel object test. *Significant decrease compared to group A at p<0.05; **Significant increase compared to group B at p<0.05; #Significant increase compared to group A at p<0.05; ##Significant decrease compared to group B at p<0.05.



Effects of Paraquat and Og on the Lipid Profile

Figure 4a-d shows the change in various forms of lipids found in the Wistar rats. The levels of lipids measured include total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TG). In Figure 4b, the level of HDL was significantly decreased ($p<0.05$) by the paraquat compared to the control Group A, while the Og significantly increased the level of HDL dose-dependently. In contrast to the above, the TG level was significantly increased ($p<0.05$) in paraquat-untreated Group B but was significantly decreased ($p<0.05$) in the Og-treated Group (Figure 4c).

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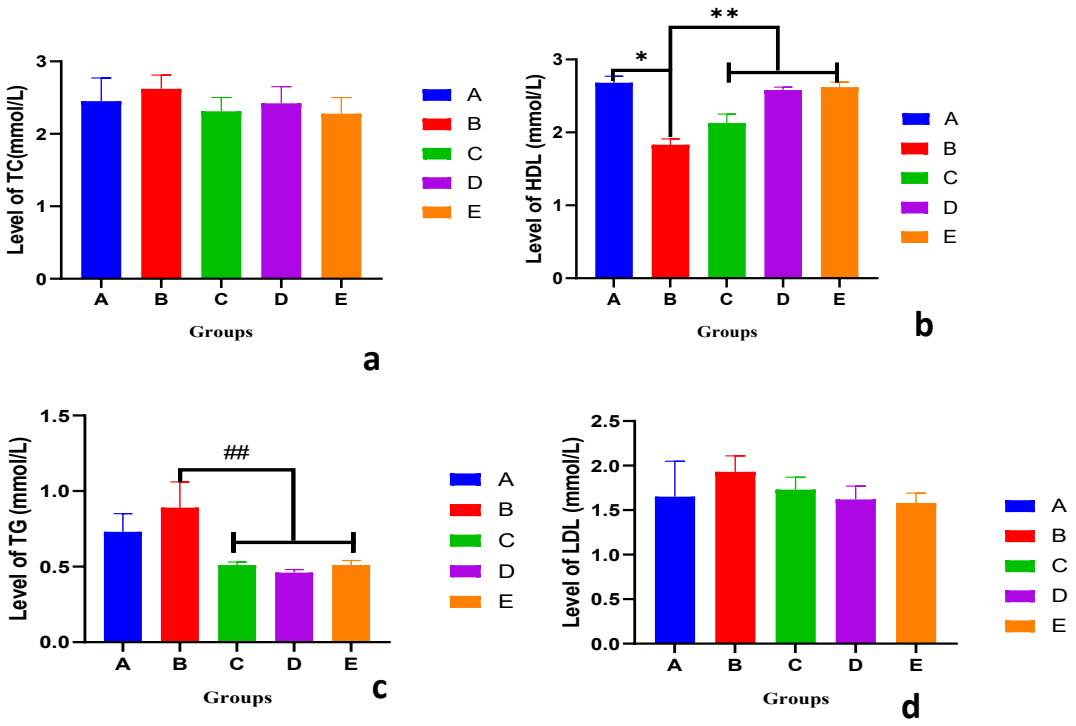
Fig. 4: The graphs showing (a) Total cholesterol, (b) High-density lipoprotein, (c) triglyceride, and (d) Low-density lipoprotein. *Significant decrease compared to group A at p<0.05; **Significant increase compared to group B at p<0.05; ##Significant decrease compared to group B at p<0.05.



Effects of Paraquat and Og on stress markers

Figures 5a-c represent the level of superoxide dismutase (SOD), catalase (CAT), and malondialdehyde (MDA), known as antioxidants and oxidative stress markers. The activity level of SOD and CAT was significantly decreased in the PQ-untreated Group B ($p<0.05$) compared to the control Group A, while the Og-treated Groups were significantly increased ($p<0.05$) compared to the PQ-untreated Group B, see Figure 5a and b. The MDA level was significantly increased by the Paraquat in the untreated Group B ($p<0.05$) compared to the control Group A, while the Og-treated Groups were significantly lowered ($p<0.05$) compared to the PQ-untreated Group, as seen in Figure 5c.

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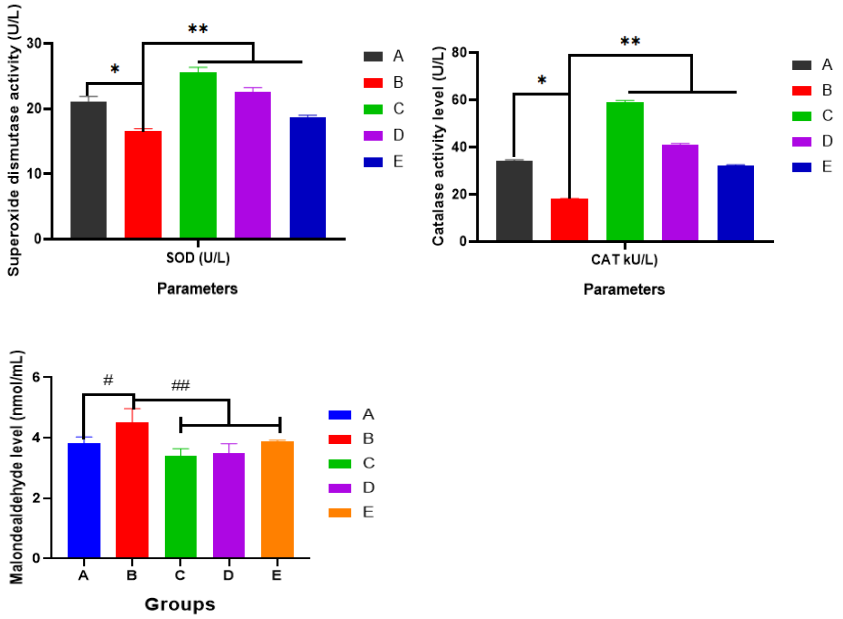
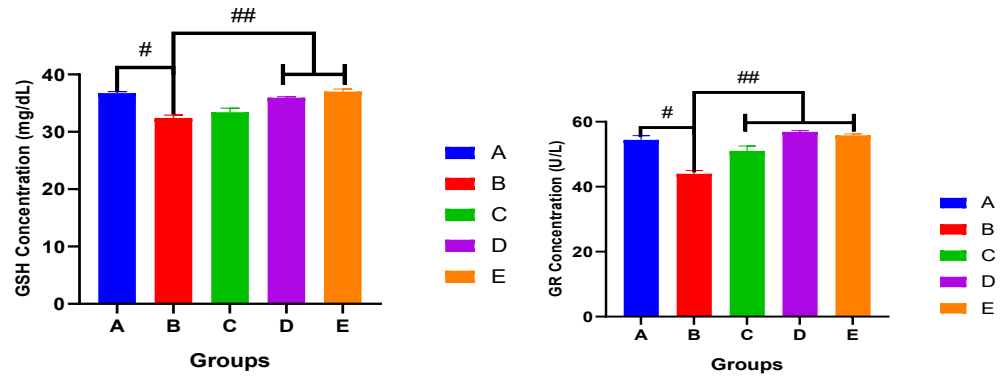
Fig. 5: The graphs showing (a) Superoxide dismutase, (b) Catalase, and (c) Malondialdehyde. *Significant decrease compared to group A at p<0.05; **Significant increase compared to group B at p<0.05; #Significant increase compared to group A at p<0.05; ##Significant decrease compared to group B at p<0.05.



Effects of Paraquat and Og on some -thiols

The –thiols measured in this research are glutathione (GSH) and glutathione reductase (GR) levels, which are markers of injury mechanism in the tissues, as represented in Figures 6a and b. The levels of GSH and GR were significantly lowered in the PQ-untreated Group B ($p<0.05$) compared to the control Group A, while in Groups D and E, the GSH and GR levels increased significantly compared to PQ-untreated Group B, see Figures 6a and b. The low-dose group C only significantly increased the level of GR ($p<0.05$) compared to the PQ-untreated Group B, as seen in Figure 6b.

Fig. 6: The graphs showing (a) Glutathione (GSH) and (b) Glutathione reductase. *Significant decrease compared to group A at p<0.05; **Significant increase compared to group B at p<0.05; #Significant decrease compared to group A at p<0.05; ##Significant increase compared to group B at p<0.05.



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Histology of Cerebellum

The sections of the cerebellum, as stained with hematoxylin and eosin (H & E), and crystal violet stains are represented in Plates 1A-E below. The control Group A presented healthy neurons and a generally healthy cerebellar tissue. The Untreated Group B shows various alterations ranging from distorted pia mater, necrosis, charred cells, and cell death to hemorrhage across the tissues, see Plate A. The treated groups showed signs of restoration, such as reduced hemorrhage, reduced necrosis, and healthy pyramidal cells, as seen in plates 1C, D, and E.

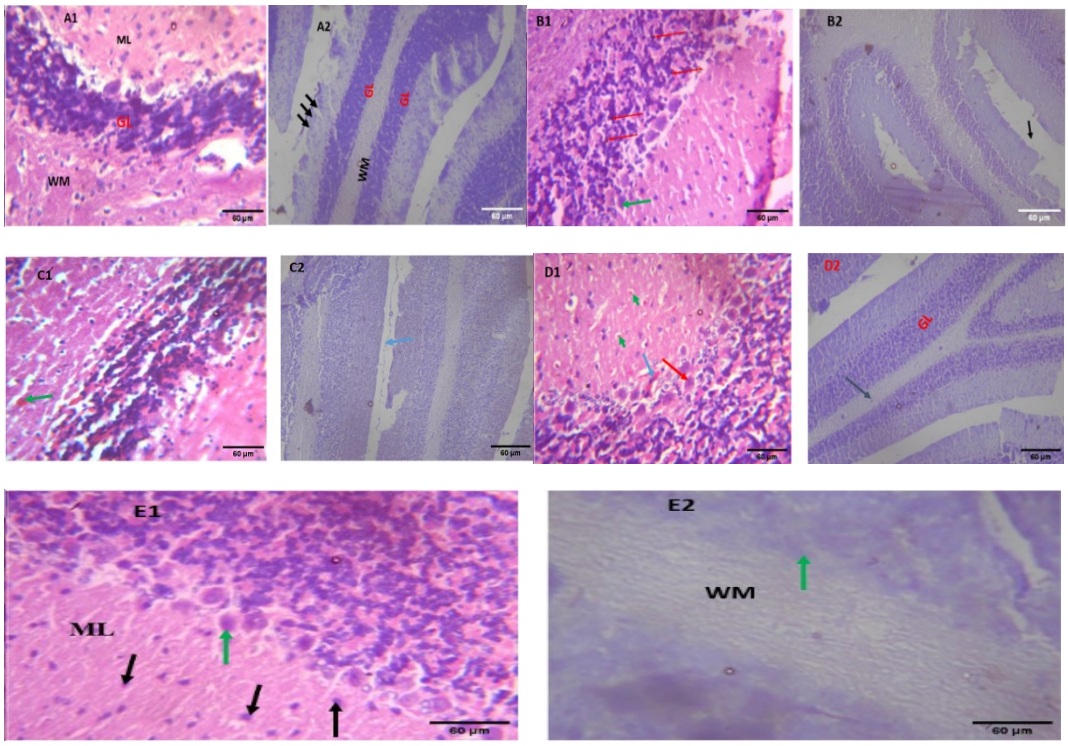

Plate 1: A Section of cerebellum showing normal cerebellar cortex with Pia mater (triple thick arrows), white matter (WM), molecular layer (ML), granular layer (GL), and healthy neuronal cells in A1 (H & E), and A2 (Crystal violet) stains. Distorted cerebellar cortex with altered Pia mater (thick arrow), necrotic granular cells (red arrows), charred pyramidal cell (green arrow), and general neuronal cell death in B1 (H & E) and B2 (Crystal violet) stains. Mild cerebellar cortex distortions with Pia mater (blue arrow), white matter, molecular layer, granular layer, a few hemorrhagic sites (green arrow), and healthy neuronal cells in C1 (H & E) and C2 (Crystal violet) stains. Normal pyramidal cell (red arrow), white matter (black arrow), hemorrhagic area (blue arrow), granular layer (GL), and hemorrhagic neurons (green arrows) in D1 (H & E), and D2 (Crystal violet) stains. Healthy neurons (black thick arrows), white matter (WM), molecular layer (ML), granular layer, and healthy pyramidal cells (green arrows). E1 (H & E) and E2 (Crystal violet) stains. X200 and scale of 60µm.

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Histology Hippocampus

Plate 2 represents the histological sections of the hippocampus showing various alterations as observed in the tissues. The control Group A showed healthy hippocampal sections (Plate 2A), whereas the Untreated Group B presented numerous alterations, including necrosis, hemorrhages, and layer separations, as seen in Plate 2B. The alterations were seen to be ameliorated by the extract, as seen in plates 2C, D, and E.

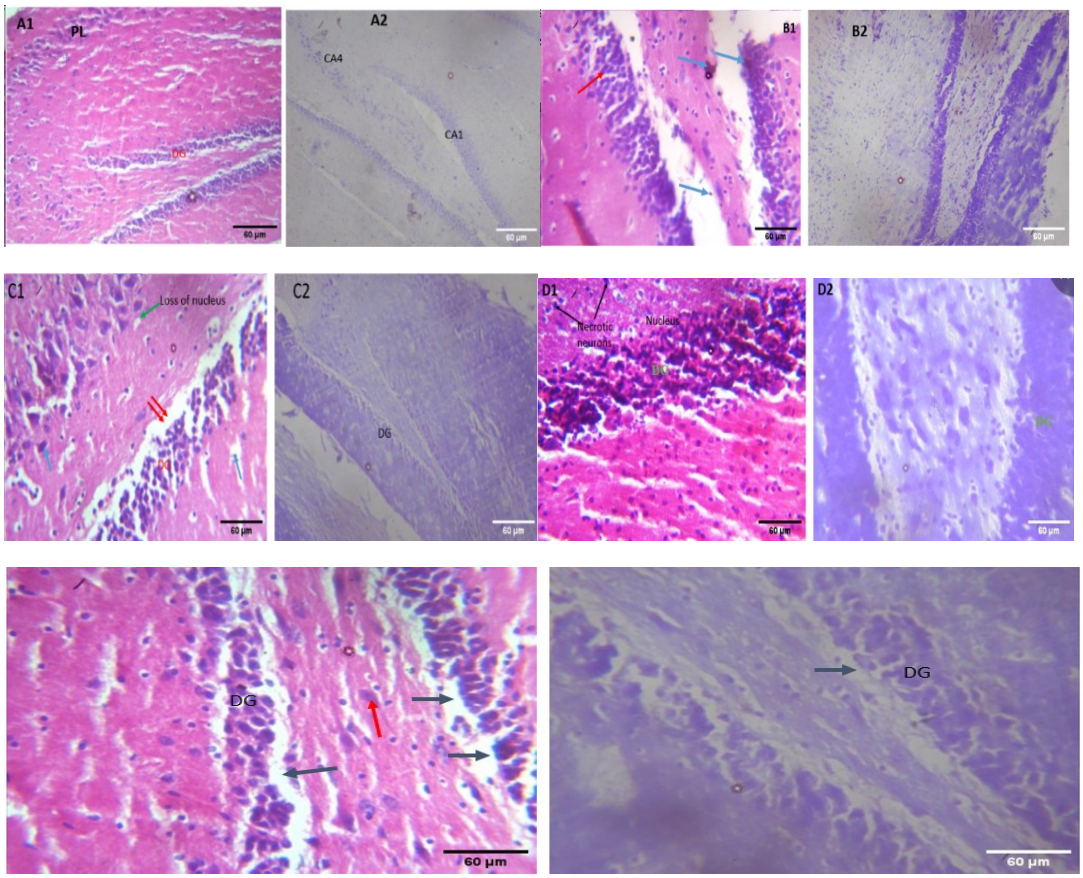

Plate 2: A section of group A hippocampus showing normal histology; DG-dentate gyrus, PL-pyramidal layer in A1 (H & E) and A2 (crystal violet) stain. Necrotic cells (blue arrows), pyramidal cells (red arrows), separation of the pyramidal layer in B1 (H & E) and B2 (crystal violet) stains. Mild necrosis (blue arrows), dentate gyrus layer separation (red arrows), loss of nucleus (green arrow) in C1 (H & E) and C2 (crystal violet) stain. DG-dentate gyrus has few necrotic nuclei in D1 (H & E) and D2 (crystal violet) stains. DG-dentate gyrus, layer separation (black arrows), and neuronal axon (red arrow) are present in E1 (H & E) and E2 (crystal violet) stains. X200 and scale of 60µm.

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DISCUSSION

The use of medicinal plants in the treatment of ailments in both developed and developing countries is increasing. Researchers have authenticated the therapeutic efficacy of most of these herbs (Balkrishna *et al*., 2024; Han *et al*., 2020; Pan *et al*., 2013). The increased weight caused by PQ agrees with a previous study conducted by Li *et al*. (2022). The result of the current research may be attributed to the duration of the study, which did not interfere with the animal's feeding. In addition, the findings showed an increased weight gain, which is consistent with a study carried out by Milagro *et al*. (2006). The slight increase in the mean body weight in treated groups may be attributed to the antioxidant property of *Ocimum gratissimum*, which could have mopped up the free radicals generated by paraquat administration in rats.

Studies have revealed that paraquat exposure produces neurological damage and behavioral disruptions in experimental animals, which may result in behavioral alternation, learning, and memory loss. The reduced line crossing and time spent at the center signify that the PQ-untreated rats lost some locomotive activities with increased anxiety due to the effects of the paraquat, a finding that shows that rats are terrified of open spaces, but once they become accustomed to them, they begin to explore the area in quest of food. The significant increase in the line crossing and time spent at the center with a reduction in the time spent close to the wall by the treated groups is a pointer that Og enhances exploratory, and lowers anxiety behaviors in rats dose-dependently, which agrees with Saadullah *et al*. (2022), who reported a decrease in the number of lines crossed and time spent at the center of the apparatus by the paraquat-untreated rats. The novel object recognition test showed a significant increase in the ability to discriminate between the novel and familiar objects following administration with paraquat. The increase in the discrimination index is a pointer to impaired cognitive abilities, while a significant reduction of discrimination abilities among animals observed in the treated groups suggests the ability of the extract to restore memory (Ding *et al*., 2020).

Glutathione (GSH) and glutathione reductase (GR) play vital roles in assessing the redox and metabolic status of biological systems, and their quantification gives a clue to the mechanisms of injury of certain substances or regulation of redox-sensitive pathways (Zhang & Forman, 2012). There was a decrease in GSH and GR levels in the PQ-untreated group, according to Forman *et al*. (2009). Excessive reduction in the levels of GSH and GR leads to chronic inflammation, and this is very dangerous to the body systems, including the brain, which agrees with the current research that showed a decreased level of GSH and GR causing cerebellar and hippocampal neuronal loss. The increased levels of GSH and GR recorded in the treated groups are in disagreement with the report of Cereser *et al*. (2001), in which they reported that Og significantly decreased the activities of GSH in brain tissue. CAT, SOD, and MDA were all significantly decreased and increased, respectively, in the PQ-untreated Group. The decline in MDA activity level is in agreement with the study of Colle *et al*. (2018). The results implied that PQ increases the oxidative level in the biological system, which may be due to increased reactive oxygen species (ROS) levels generated, leading to reduced antioxidants (SOD and CAT) and increased oxidative stress, such as MDA (Ademosun & Oboh, 2014; Ateş *et al*., 2019; Blanco-Ayala *et al*., 2014). The reduced level of MDA corroborated the decrease in the level of HDL in the paraquat Group as an indication of the increased level of lipid peroxidation caused by paraquat in a biological system. The activity level of SOD was significantly increased by the Og treatment, contrary to the report of Oyem *et al*. (2021), and increased the level of CAT and MDA in agreement with the report of Oyem *et al*. (2021). These findings are in line with (Ateş *et al*., 2019; Edobor *et al*., 2021; Mollace *et al*., 2003; Tinakoua *et al*., 2015),

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who reported significant elevation of MDA levels following paraquat administration in animal models.

Neuropathological changes are associated with neurodegeneration triggered by neurotoxins in different regions of the brain (He *et al*., 2020). Paraquat is a proven neurotoxin that has been implicated in neurodegeneration according to Goldman (2014) and Zyoud (2018). Microscopically, the cerebellum and hippocampus presented several alterations, ranging from altered Pia mater, necrosis, charred pyramidal cells, general neuronal loss, separation layer, and chronic hemorrhage to optical empty spaces. The changes are suggestive of paraquat neurotoxicity, which is in agreement with the reported toxic properties of paraquat on the brain by Edobor *et al*. (2021). It also agrees with Zhang and Forman (2012), who stated that the central nervous system (CNS) is vulnerable to paraquat toxicity, resulting in histoarchitectural distortions, neuronal damage, cell death, and glial cell reactivity in different regions of the brain. Neuronal damage has been associated with neurological disease conditions, including PD, with motor impairments as a major clinical hallmark (Jankovic, 2008; Kalyn *et al*., 2019). The alterations were observed to have been mitigated on the administration of Og, which is suggestive of its ameliorative properties against paraquat-triggered neurodegenerative changes. This finding is in agreement with reports related to the therapeutic properties of *O. gratissimum* in the treatment and management of oxidative stress-associated neurodegenerative disease conditions as a result of exposure to environmental toxins, as reported by Arrey Tarkang *et al*. (2013), Ribaudo *et al*. (2021), Rodríguez-Mesa *et al*. (2023), and Shah *et al*. (2025).

CONCLUSION

Aqueous extract of *O. gratissimum* is said to be potent against paraquat-altered pathological changes in the brain regions of Wistar rats. Neuroprotective properties could be attributed to the presence of bioactive compounds with potent antioxidant activities against ROS-associated Paraquat-triggered pathologies. The extract is dose-dependent in its action.

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