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Ameliorative Effects of *Elaeis guineensis* fruit oil (EGFO) on Monosodium Glutamate (MSG)-Induced oxidative and cholinergic Alterations in Male Wistar Rats

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Abstract: Monosodium glutamate (MSG), a widely used flavor enhancer, has been implicated in neurotoxicity, primarily through mechanisms of excitotoxicity and oxidative stress. *Elaeis guineensis* (red palm oil) is recognized for its high concentration of natural antioxidants, such as tocotrienols and carotenoids, which have known neuroprotective potential. This study aimed to evaluate the ability of *Elaeis guineensis* fruit oil to protect against the adverse neurobiochemical changes induced by chronic oral administration of MSG in male Wistar rats. Twenty-four male Wistar rats were divided into four groups (n=6): control, MSG only (3 g/kg), *Elaeis guineensis* oil (5 ml/kg) + MSG, and *Elaeis guineensis* oil only. After 21 days of oral administration, brain homogenates were prepared and assayed for levels of glutathione (GSH), malondialdehyde (MDA), catalase (CAT), superoxide dismutase (SOD), acetylcholinesterase (AChE), and nitric oxide (NO). Compared to the control group, rats treated with MSG alone showed a significant ($p<0.05$) depletion of brain GSH, CAT, and SOD. Concurrently, there was a significant increase in the levels of MDA, AChE activity, and NO concentration, indicating severe oxidative stress and neurochemical imbalance. Co-administration of *E. guineensis* fruit oil with MSG significantly counteracted these changes, restoring all measured parameters towards the levels observed in the control group. *Elaeis guineensis* fruit oil exhibits significant neuroprotective activity against MSG-induced neurotoxicity. Its ability to normalize markers of oxidative stress and cholinergic function suggests its high antioxidant content is effective in mitigating excitotoxic damage, highlighting its potential as a functional food supplement against neurotoxic insults.

Keywords: Monosodium glutamate (MSG), *Elaeis guineensis,* Neurotoxicity, Oxidative stress

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Introduction

Monosodium glutamate (MSG), the sodium salt of the non-essential amino acid glutamic acid, is one of the most widely used food additives globally, prized for its ability to impart a savoury "umami" flavor. Despite its classification as 'generally recognized as safe' (GRAS) by regulatory bodies, extensive consumption of MSG has been linked to a variety of adverse health effects, with a growing body of evidence pointing towards its potential for neurotoxicity (Bellisle, 2018). Several investigations have reported that the mechanism of MSG neurotoxicity to involves excitotoxicity, uncontrolled activation of glutamate receptors leading to accumulation of calcium ions in the neuronal cells, oxidative stress triggered by calcium overload, and mitochondrial dysfunction. These processes overwhelm the brain's antioxidant status, leading to redox imbalance (Onaolapo *et al.*, 2011). Examples of the antioxidant defence system include glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT). They act by scavenging reactive oxygen species (ROS) and reactive nitrogen species (RNS), thereby preventing them from damaging neuronal cellular components (Hajimorad *et al.*, 2018). Thus, in conditions where these antioxidants are depleted, the ROS and RNS can react with cellular components, causing damage. Lipid peroxidation is one of the major processes involved in oxidative stress, and it is evaluated by measuring the concentration of malondialdehyde (MDA) generated (Brady *et al.*, 2015; Halliwell & Gutteridge, 2015; Srinivan *et al.*, 2015). The redox imbalance in the neuronal cells has been implicated in the dysregulation of neurotransmitter systems involving acetylcholine and dopamine (Zhou & Danbolt, 2014). Acetylcholinesterase (AChE) is a neurotransmitter enzyme that degrades acetylcholine after it has been released from the synaptic cell. Under oxidative stress, the activity of AChE is altered, causing neuroinflammation and neuronal cell death (El-Bakli *et al.*, 2018; Sayed *et al.*, 2017). Red palm oil (RPO) is obtained from *Elaeis guineensis* fruit. Red palm oil is

abundant in Nigeria and other parts of West Africa. It is a major ingredient in a traditional food delicacy that adds flavour to soup (Adekunle *et al.*, 2020). RPO is a rich source of tocopherols and tocotrienols, antioxidant compounds that have been reported to improve brain health and function (Sen *et al.*, 2007; Srivastava & Gupta, 2011). Another class of antioxidant compounds isolated from RPO is carotenoids such as lycopene, beta-carotene, lutein, alpha-carotene, and zeaxanthin. All these compounds have been reported to possess antioxidant and anti-inflammatory properties and their potential as an effective agent for protecting brain damage or slowing brain ageing processes (Hassim *et al.*, 2020; Ricci *et al.*, 2015). Given the central role of oxidative stress in MSG-induced neurotoxicity, the powerful antioxidant profile of *Elaeis guineensis* oil suggests it may serve as an effective neuroprotective agent against such damage.
This study, therefore, investigates the potential of *Elaeis guineensis* fruit oil to ameliorate the adverse neurobiochemical changes induced by oral administration of monosodium glutamate in male Wistar rats.

Materials and Methods

Chemicals and Reagents

Monosodium glutamate (MSG) of food-grade quality was purchased from a commercial supplier. Crude, unrefined Elaeis guineensis fruit oil was sourced locally in Nigeria. All other chemicals used for the biochemical analyses were of analytical grade

Experimental Animals: Twenty-four (24) male Wistar rats, weighing between 150-180g, were obtained and used for the study. The animals were housed under standard laboratory conditions (25 ± 2°C, 12-hour light/dark cycle) and were allowed free access to standard chow and clean drinking water ad libitum.They underwent a two-week acclimatization period before the experiment began. The study was conducted in strict adherence to ethical guidelines for the use and care of laboratory animals

Experimental Design: The rats were randomly allocated into four experimental groups, with six animals in each group. The administration of substances was carried out orally for 21 days (modified method of Ajuwon *et al.*, 2022).
Group 1 (Control): Received daily oral administration of distilled water.
Group 2 (MSG only): Received a daily oral dose of monosodium glutamate (3g/kg body weight) according to the method of Razali et al., 2021.
Group 3 (*E. guineensis* + MSG): Received a daily oral dose of *Elaeis guineensis* fruit oil (5 ml/kg body weight) one hour before the daily administration of monosodium glutamate (3g/kg body weight).
Group 4 (*E. guineensis* only): Received only a daily oral dose of *Elaeis guineensis* fruit oil (5 ml/kg body weight)

Sample Collection and Preparation: Following the 21-day treatment period, animals were fasted overnight and then humanely sacrificed. The brains were immediately harvested, rinsed in ice-cold saline to wash off blood, and blotted dry. Each brain was weighed and homogenized in a cold phosphate buffer (pH 7.4). The homogenate was then centrifuged (e.g., at 10,000 g for 15 minutes at 4°C) to obtain a clear supernatant, which was carefully collected and stored frozen (-20°C) for subsequent biochemical assays.

Biochemical Assays: The brain supernatant was used to determine the concentration or activity of the following biochemical markers using established standard laboratory protocols:

The brain malondialdehyde (MDA) :
concentrations (index of lipid peroxidation) was spectrophotometrically evaluated according to the method of Draper and Hadley (1990). Catalase **(**CAT) activity was assayed by the decomposition of hydrogen peroxide according to the method of Claiborne (1984). Superoxide dismutase (SOD) activity was determined by the method of Misra and Fridovich (1972). Acetylcholinesterase (AChE) activity in the brain homogenates was measured by the method of Lombardi *et al.* (1999). Nitrite assay was done using Griess reagent with some modifications of the method of Green *et al.* (1982). The total protein levels were measured by an enzymatic colourimetric kit (Wako Chemicals USA, Inc.).

Statistical Analysis: All data were expressed as the mean ± standard deviation (SD). The results were analyzed using a one-way analysis of variance (ANOVA), and differences between group means were evaluated using a suitable post-hoc test (e.g., Tukey's HSD). A probability value of $p<0.05$ was considered to be statistically significant.

Results

GSH is a major non-enzymatic antioxidant that plays a central role in protecting cells from ROS. It directly neutralizes free radicals and helps recycle other antioxidants. Depletion of GSH is a classic hallmark of cellular toxicity. The MSG group showed depleted GSH levels (8.56±0.64 mg/L) compared to the control group (9.87±0.24), confirming that the body's GSH reserves were being used up to fight the toxic insult. EGFO treatment dose-dependently restored GSH levels,

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with the 4 ml/kg dose bringing the level (9.55) very close to that of the control group. EGFO helps preserve the body's critical glutathione pool, which is essential for maintaining overall cellular health and detoxification. This effect is likely due to the oil's own antioxidants handling the stress, thus reducing the demand on GSH.

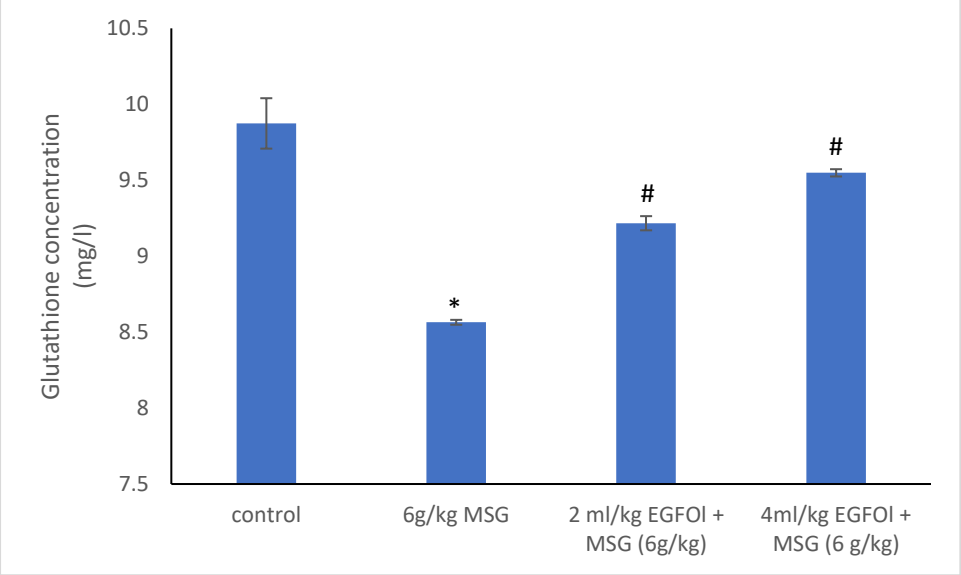

Figure 1: Effect of *E. guineensis* fruit oil on glutathione concentration in the brain of male wistar rats orally administered monosodium glutamate (MSG). Results are expressed as mean±standard deviation (SD) for 5 animals. *P<0.05 significantly different (Control vs MSG); # P<0.05 significantly different (MSG vs treatment). MSG= Monosodium glutamate; EGFO= *E. guineensis* fruit oil

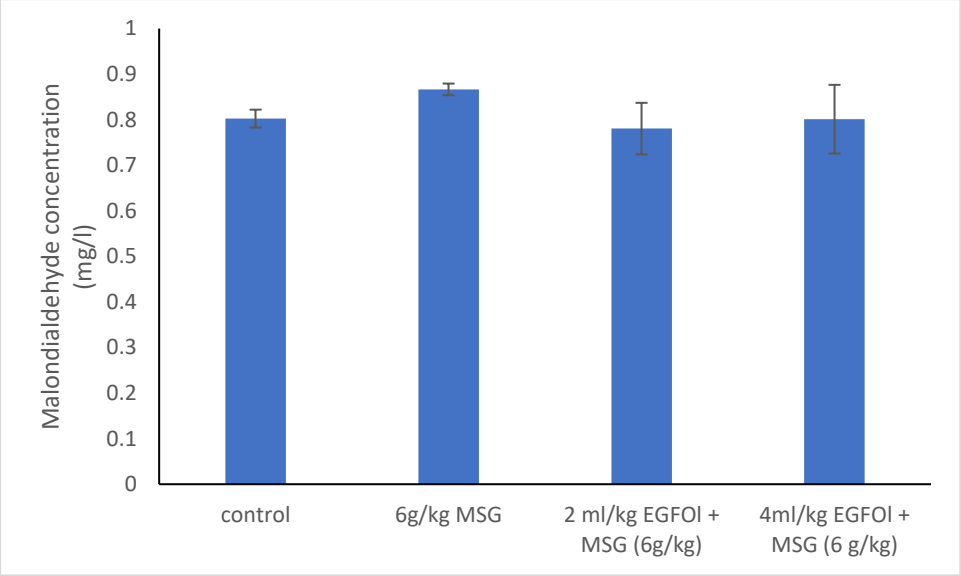

Figure 2: Effect of *E. guineensis* fruit oil on malondialdehyde concentration in the brain of male Wistar rats orally administered monosodium glutamate (MSG). Results are expressed as mean±standard deviation (SD) for 5 animals. MSG= Monosodium glutamate; EGFO= *E. guineensis* fruit oil

MDA is the most commonly used biomarker for lipid peroxidation. It is a compound formed when reactive oxygen species (ROS) attack and damage the fatty acids in cell membranes. Therefore, a higher level of MDA indicates greater oxidative stress and cellular membrane damage. The MSG group (0.87±0.01 mg/L) showed a slight but notable increase in MDA compared to the control group (0.80±0.02 mg/L). This confirms that MSG administration induced oxidative stress leading to damage of neuronal membranes. Pretreatment with both 2 ml/kg and 4 ml/kg of EGFO reduced MDA levels (0.78 and 0.80, respectively), effectively bringing them back to or even below

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the normal control level. EGFO demonstrates a potent ability to protect cell membranes from the lipid damage caused by MSG, likely due to the direct free-radical scavenging action of its antioxidant components (tocotrienols and carotenoids).

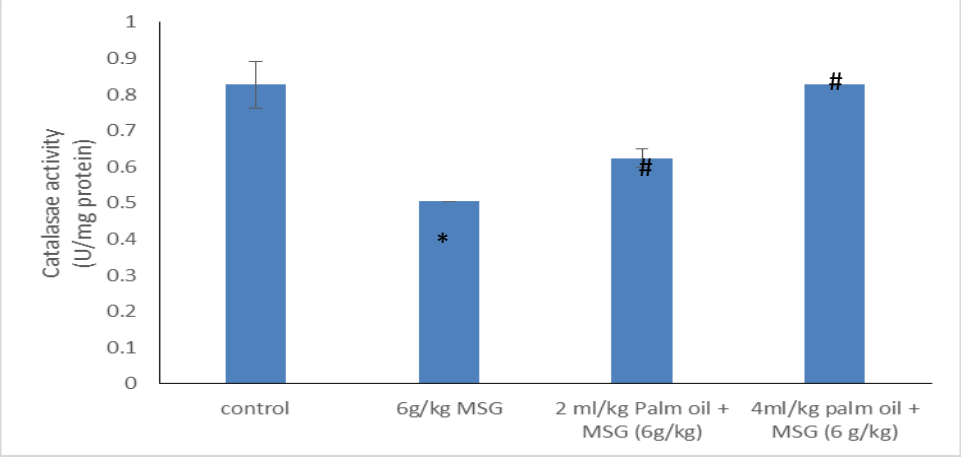

Figure 3: Effect of *E. guineensis* fruit oil on catalase activity in the brain of male Wistar rats orally administered monosodium glutamate (MSG). Results are expressed as mean±standard deviation (SD) for 5 animals. *P<0.05 significantly different (Control vs MSG); # P<0.05 significantly different (MSG vs treatment). MSG= Monosodium glutamate; EGFO= *E. guineensis* fruit oil

Catalase is a critical antioxidant enzyme located in cells. Its primary role is to break down harmful hydrogen peroxide (H_2O_2) into harmless water and oxygen. A decrease in CAT activity signifies that the enzyme is being consumed to combat high levels of oxidative stress. The MSG group showed a drastic reduction in CAT activity (0.50±0.00 U/mg protein) compared to the control (0.83±0.06). This sharp decline is a strong indicator of severe oxidative stress overwhelming the cell's defences. Pretreatment with EGFO led to a dose-dependent recovery. The 2 ml/kg dose provided partial restoration (0.62), while the 4 ml/kg dose completely restored CAT activity to the control level (0.83). The results show that EGFO "spares" the body's natural catalase enzyme by reducing the overall oxidative load, allowing its levels to return to normal. The complete restoration at the higher dose is a powerful indicator of EGFO's efficacy.

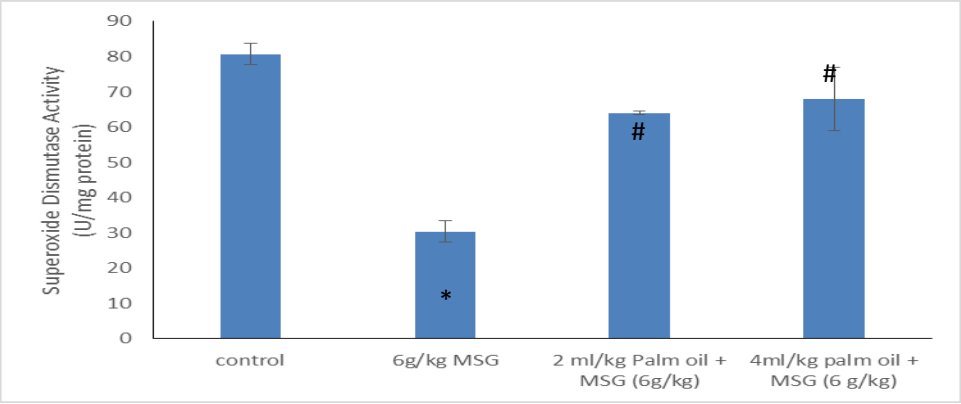

Figure 4: Effect of *E. guineensis* fruit oil on superoxide dismutase activity in the brain of male Wistar rats orally administered monosodium glutamate (MSG). Results are expressed as mean±standard deviation (SD) for 5 animals. *P<0.05 significantly different (Control vs MSG); # P<0.05 significantly different (MSG vs treatment). MSG= Monosodium glutamate; EGFO= *E. guineensis* fruit oil

Similar to catalase, SOD is considered the first line of enzymatic antioxidant defense. It neutralizes the highly reactive superoxide radical ($O2^-$), converting it into hydrogen peroxide, which is then handled by catalase. A decrease in SOD activity is a primary sign of significant oxidative insult. MSG caused a massive drop in SOD activity, from 80.72±2.98 U/mg in the control

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group to just 30.31±3.05 in the MSG group. This indicates that the primary antioxidant defense was severely compromised. Both doses of EGFO led to a substantial recovery in SOD activity (63.96 and 67.97). While not a full return to control levels, this represents a significant preservation of this crucial enzyme's function. EGFO provides robust protection to the primary antioxidant defense system, mitigating the damage from the flood of superoxide radicals generated by MSG toxicity.

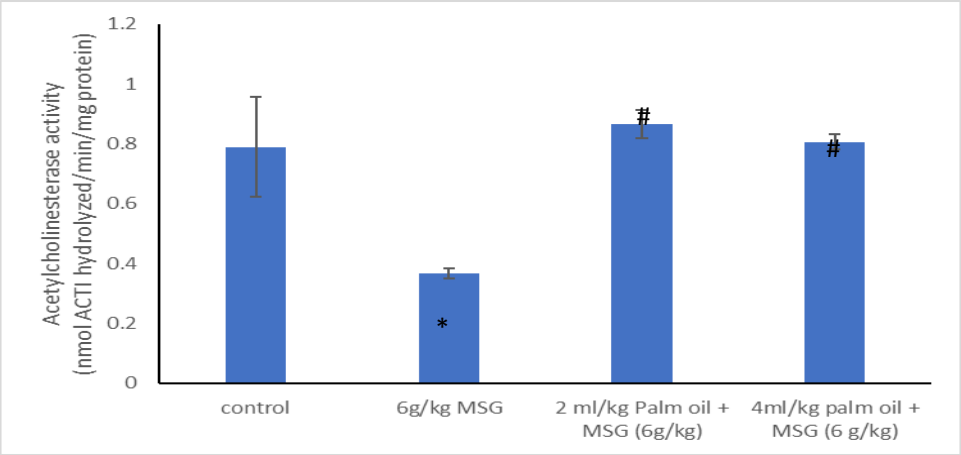

Figure 5: Effect of *E. guineensis* fruit oil on acetylcholinesterase activity in the brain of male Wistar rats orally administered monosodium glutamate (MSG). Results are expressed as mean±standard deviation (SD) for 5 animals. *P<0.05 significantly different (Control vs MSG); # P<0.05 significantly different (MSG vs treatment). MSG= Monosodium glutamate; EGFO= *E. guineensis* fruit oil

AChE is a vital enzyme in the nervous system responsible for breaking down the neurotransmitter acetylcholine. Proper AChE function is essential for regulating nerve impulses and is crucial for learning and memory. Inhibition or alteration of AChE activity is a direct marker of neurotoxicity. MSG administration caused a severe reduction in AChE activity (from 0.79±0.17 nmol/mL to 0.37±0.02), indicating significant disruption of cholinergic nerve function. This damage is likely a downstream effect of the oxidative stress on neurons. Remarkably, both doses of EGFO completely restored AChE activity (0.87 and 0.81), bringing it back to normal, healthy levels. This is a key finding. EGFO not only acts as a general antioxidant but also demonstrates a potent neuroprotective effect, preserving the functional integrity of the cholinergic system against MSG-induced damage.

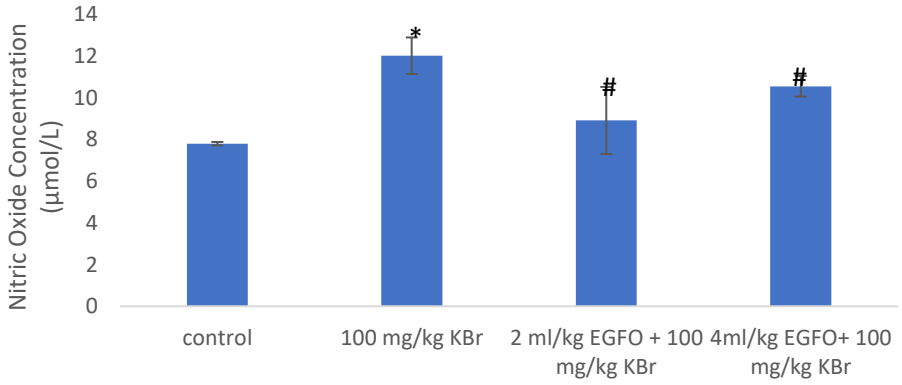

Figure 6: Effect of *E. guineensis* fruit oil on Nitric oxide concentration in the brain of male Wistar rats orally administered monosodium glutamate (MSG). Results are expressed as mean±standard deviation (SD) for 5 animals. *P<0.05 significantly different (Control vs MSG); # P<0.05 significantly different (MSG vs treatment). MSG= Monosodium glutamate; EGFO= *E. guineensis* fruit oil.

NO is a versatile signalling molecule, but in excess, it contributes to nitrosative stress and inflammation. It can react with superoxide radicals to form peroxynitrite, an extremely

potent and destructive oxidant that damages DNA, proteins, and lipids. MSG caused a dramatic increase in NO, more than doubling it from 12.02±3.88 µmol/L to 25.44±2.46. This indicates a severe inflammatory and nitrosative stress response in the brain tissue. EGFO was extremely effective at quenching this response. The 4 ml/kg dose was particularly potent, reducing NO levels to 9.89±1.16, a level even lower than the control group. EGFO exhibits strong anti-inflammatory and anti-nitrosative properties. Its ability to almost completely abolish the pathological increase in NO demonstrates its effectiveness in controlling the inflammatory cascade triggered by MSG.

Discussion

The results of this study are highly consistent with the established body of scientific literature on monosodium glutamate (MSG) neurotoxicity and the protective effects of antioxidant-rich natural products. The data shows that MSG administration decreased levels of SOD, CAT, and GSH while increasing MDA and NO aligns perfectly with numerous studies. MSG is known to act as an excitotoxin. Its primary component, glutamate, is a major excitatory neurotransmitter. In excessive amounts, it overstimulates glutamate receptors (like the NMDA receptor), leading to a massive influx of calcium ions (Ca^{2+}) into neurons. This process, known as excitotoxicity, triggers a cascade of damaging events, including the overproduction of reactive oxygen species (ROS) and reactive nitrogen species (RNS) (Goncalves-Ribeiro *et al*., 2019; Haroon *et al*., 2017; Zhou & Danbolt, 2014). The body's primary defense against this surge in ROS/RNS is the antioxidant enzymes superoxide dismutase (SOD) and catalase (CAT), along with the non-enzymatic antioxidant glutathione (GSH) (Halliwell & Gutteridge, 2015). As observed in this finding and confirmed by other investigations (Onyema *et al*., 2006; Singh & Ahluwalia, 2003), the system becomes overwhelmed, and the levels of these protective agents are significantly depleted as they are consumed in an attempt to neutralize the free radicals. The increase in Malondialdehyde (MDA) is a good indicator of lipid peroxidation, where ROS attack the lipids in cell membranes, causing cellular damage (Onufrovych *et al*., 2024). The significant increase in Nitric Oxide (NO) also corroborates findings that excitotoxicity activates neuronal nitric oxide synthase (nNOS), producing excess NO which can react with superoxide radicals to form the highly destructive peroxynitrite anion ($ONOO^-$) (Iova *et al*., 2023). The drastic reduction in acetylcholinesterase (AChE) activity is a key finding that links oxidative stress to functional neurotoxicity (Aroniadou-Anderjaska *et al*., 2023). Other studies have shown that oxidative damage to neuronal membranes and the AChE enzyme itself can impair its function (Ilesanmi & Ikpesu, 2020; Ilesanmi *et al*., 2020). This disruption of the cholinergic system is implicated in cognitive deficits, further supporting the neurotoxic effect of MSG. The most significant finding in this experiment is the ability of EGFO to reverse these toxic effects. This is strongly supported by our understanding of the oil's biochemical composition. Red palm oil (*E. guineensis*) is one of the richest natural sources of tocotrienols (a potent form of Vitamin E) and carotenoids (including beta-carotene) (Sen *et al*., 2007; Srivastava and Gupta, 2011). Tocotrienols are known to be more potent antioxidants than the more common tocopherols. They are exceptionally effective at integrating into cell membranes and neutralizing the lipid peroxidation chain reaction, which explains the normalization of MDA levels in the EGFO-treated groups (Figure 2). Carotenoids are also powerful free-radical scavengers (Hassim *et al*., 2020; Ricci *et al*., 2015). The treatment with EGFO can directly quench the ROS and RNS generated by MSG. This reduces the burden on the body's antioxidant systems. As a result, the levels of SOD, CAT, and GSH are "spared" from depletion and can be restored to normal, which is precisely what the data revealed. This protective mechanism is not unique to EGFO but is a common theme in studies using other antioxidant-rich substances. Research on ascorbic acid, curcumin, and resveratrol has shown similar protective effects against MSG-induced neurotoxicity by bolstering antioxidant defenses and reducing markers of oxidative damage (Danisman *et al*., 2023; Khalil *et al*., 2016; Onyeso *et al*., 2025). The results for EGFO place it firmly within this category of potent, natural neuroprotective agents. The observation that a higher dose of EGFO was more effective than lower dose is important. This dose-dependent relationship strengthens the conclusion that the components within EGFO are directly responsible for the protective effect.

In conclusion, this investigation confirms the oxidative and neurotoxic effects of monosodium glutamate and the potential of *E. guineensis* fruit oil (palm oil) to prevent and reverse these toxic *effects. Futher research can be conducted to investigate the long-term effects of E. guineensis fruit oil and its potential interactions with other neurotoxicants. Also, a detailed investigation into the*

specific molecular mechanisms by which the active compounds in E. guineensis fruit oil exert neuroprotective effects may help clarify their role in mitigating oxidative damage

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Institutional Review Board: To ensure animal welfare, the study adhered to the guidelines outlined in the Helsinki Declaration of 1975. All animals used were healthy. The experimental design received approval (code ART2023008) from the Federal University Otuoke's ethical committee on animal research and treatment (ART). The experiments were conducted in the Department of Biochemistry's animal house between May and July 2022.

Conflicts of Interest: None.

Data Availability: It will be made available on request

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