GSAR Journal of Agriculture and Veterinary Sciences
ISSN: 3048-9075 (Online)
Abbreviated key title: Glob.J. Agri.Vet.Sci.
Frequency: Monthly
Published By GSAR Publishers
Journal Homepage Link- https://gsarpublishers.com/journal-gjavs-home/

EFFECTS OF CYPERMETHRIN AND MONOSODIUM GLUTAMATE ON SELECTED NEUROBEHAVIOURAL PATTERNS AND BIOMARKERS OF OXIDATIVE STRESS, LIVER AND KIDNEY FUNCTIONS IN WISTAR RATS

By

Ramon-Yusuf Suleiman Babatunde[1] and Ayo Joseph Olusegun[2]

[1]Department of Veterinary Pharmacology and Toxicology, Faculty of Veterinary Medicine, University of Abuja Federal capital Territory, 900001 Nigeria

[2]Department of Veterinary Physiology, Faculty of Veterinary Medicine, Ahmadu Bello University, Zaria 810107, Nigeria

Article History

Received: 01/09/2025
Accepted: 05/09/2025
Published: 08/09/2025

Vol – 2 Issue –9

PP: -59-70

Abstract

Cypermethrin (CYP), a widely used pyrethroid insecticide, and monosodium glutamate (MSG), a common dietary additive, have both been implicated in neurotoxicity, oxidative stress, and organ dysfunction. However, little is known about their potential interactive effects when concurrently present in biological systems. This study evaluated the effects of single and combined exposures to CYP (80 mg/kg/day) and MSG (5 g/kg/day) on neurobehavioral performance, oxidative stress biomarkers, and liver and kidney function indices in male Wistar rats. Twenty-eight rats were divided into four groups and treated orally for 14 days. Behavioral assessments (locomotion, excitability, depression, motor strength, and autonomic responses) were performed, followed by biochemical evaluations. CYP exposure significantly reduced locomotor activity, excitability, and grip strength, whereas MSG increased excitability and grip performance. Combined treatment produced intermediate behavioral outcomes, suggesting modulatory interactions. Biochemically, CYP induced lipid peroxidation (elevated MDA) and enhanced antioxidant enzyme activities (CAT, GPx), while MSG predominantly elevated liver enzymes (AST, ALT) and renal markers (urea, uric acid). Interestingly, combined exposure attenuated CYP-induced oxidative stress and restored liver enzyme activities toward control levels but produced mixed effects on renal function. These findings highlight both antagonistic and additive interactions between CYP and MSG, with implications for populations concurrently exposed through diet and environment. The study underscores the need for risk assessments that consider combined exposures to dietary additives and environmental toxicants.

Keywords: *Cypermethrin, Monosodium glutamate, Neurobehavioral alterations, Oxidative stress, Liver function, Kidney function, Toxicological interaction*

Introduction

Cypermethrin is a synthetic pyrethroid insecticide extensively used in agriculture and household pest control. Its widespread application has raised toxicological concerns due to its ability to induce neurotoxicity and systemic organ dysfunction. Cypermethrin exerts its toxic effects primarily by altering neuronal sodium channel kinetics, leading to prolonged depolarization and hyperexcitation manifested as neurobehavioral impairments, oxidative stress, and tissue damages (Elbetieha *et al*., 2001; Singh *et al*., 2025, Tavakkoli *et al*, 2025). Recent studies have shown that sub-chronic exposure to cypermethrin increases anxiety-like behaviors, impairs learning and memory, and elevates oxidative stress markers in brain tissues (Haddad *et al*., 2023; Abdou *et al*2025a). Mechanistically, these effects are associated with mitochondrial dysfunction, reduced brain-derived neurotrophic factor (BDNF) expression, and neuroinflammatory changes (Carloni *et al*., 2013; Tavakkoli et al, 2025). Higher doses have been linked to significant behavioral impairments and histopathological damage to the hippocampus and cortex ((Nazari et al., 2025)).

Monosodium glutamate (MSG), a widely used flavor enhancer, is generally recognized as safe in regulated quantities; however, increasing body of evidence indicates

*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**

that high doses can produce neurotoxic and adverse systemic effects including neurotoxic effects . MSG-induced neurotoxicity has been attributed to excitotoxicity through excessive glutamate receptor activation, oxidative stress, and inflammatory responses (Albrakati, 2022; Abdulghani et al., 2022). Experimental studies have demonstrated that prolonged high-dose MSG exposure increases malondialdehyde (MDA) levels, decreases antioxidant enzyme activities, and causes histological damage to the brain, liver, and kidneys Abdou *et al* 2025; (Albrakati, 2022; Banerjee *et al*., 2020)). Additionally, behavioral assessments indicate that MSG can impair spatial learning, memory, and motor coordination (Singh *et al*, 2023). The oxidative and neuroinflammatory responses elicited by MSG constitute potential risk factors for neurodegenerative diseases (Kumar et al., 2021; Singh *et al*, 2023).

Both cypermethrin and MSG have been independently reported to disrupt neurobehavioral responses, impair antioxidant defense systems, and impair liver and kidney functions. However, there is paucity of information on the combined effects of these agents, despite the possibility of their additive or synergistic toxicities , especially in populations with dietary MSG consumption and environmental exposure to pyrethroids. The elucidation of the interactive effects of the agents on neurobehavioral responses, oxidative stress biomarkers, and organ function indices is critical for toxicological risk assessment.

The study aimed to evaluate the effects of single and combined exposures to cypermethrin (80 mg/kg/day) and MSG (5 g/kg/day) on selected neurobehavioral parameters (locomotion, anxiety, excitability, depression, and motor strength) and biomarkers of oxidative stress, and functions of the liver (AST, ALT, ALP), and kidney (urea, uric acid, creatinine) in male Wistar rats. It was hypothesized that the findings may provide insight into potential interactions between dietary and environmental chemical exposures.

Materials and Methods

Animals

Twenty- eight male Wistar rats were sourced from the animal facility of the Department of Pharmacology and Toxicology, Ahmadu Bello University, Zaria. They were housed in plastic cages (7 rats per cage) with wood shavings, maintained on a 12-hour light/dark cycle, and fed chick mash with water *ad libitum*.

After two weeks of acclimatization, the rats were randomly divided into seven groups (n=7):

- Group 1 (Control): 2ml/kg soya oil only
- Group 2: Monosodium Glutamate only (5g/kg/day) dissolved in distilled water
- Group 3: Cypermethrin only (80mg/kg/day) dissolved in soya oil
- Group 4: Cypermethrin (80 mg/kg/day)) + Monosodium Glutamate (5 g/kg/day)

All treatments were administered orally by gavage daily for 14 days.

Behavioural parameters were assessed on Day 14 after the rats had been rested for an hour to acclimatise to the laboratory condition and following the administration of Cypermethrin and Monosodium Glutamate

Chemicals

Cypermethrin (Cypeforce®, 10% EC, Nagarjuna Agrochemicals Ltd, Hyderabad, Telangana, India), Monosodium Glutamate (MSG) manufactured by Ajinomoto Company , Tokyo Japan were procured from a reputable agrochemical store in Zaria. Cypermethrin was dissolved in soya oil, while MSG was dissolved in distilled water. Working solutions were prepared based on required concentrations.

Evaluation of Neurobehavioral Parameters

Open-field assessment

The assessment was conducted on all Wistar rats by utilising the open-field apparatus as delineated by Zhu *et al*. (2001). The open-field device was fabricated from a cardboard box of 50 × 50 × 46 cm, including a transparent plexiglass inner surface (base). The box's floor was partitioned into 25 equal squares. The parameters determined included otor activity and anxiety, assessed through horizontal locomotion (number of line crossings on the floor) and the frequency of rearing, grooming, defaecation and urination. The protocol for evaluating motor activity included positioning a rat within the enclosure. The rat was permitted to traverse freely for a duration of 3 minutes of pre-conditioning to the surroundings. Subsequently, the total number of squares traversed by all paws of the rat was recorded for the ensuing 2 minutes. The rearing behaviour was quantified by assessing the frequency at which each rat stood on its hind-limbs and elevated the forepaws or rested the fore-paws on the apparatus wall. Rearing was quantified over a 2-minute interval following an initial 3-minute pre-conditioning period. The frequencies of grooming (extended coat washing), defaecation (quantity of faecal pellets expelled), and urination (number of urine puddles produced) were recorded. The open-field evaluation was performed on day 14 of the treatment.

Assessment of excitability score

The excitability score of the rats was assessed using the procedure described by Ambali and Ayo (2012). Briefly, each rat was suspended by the tail in an inverted position for 30 seconds. The responses of each rat were evaluated using an ordinal scale, ranging from 0 to 5 as follows:

Grade 0: The rat exhibited no signs of wiggling at all.

Grade 1: The rat exhibited minimal wiggling and weak fore-paw movement.

Grade 2: The rat displayed a more vigorous wiggling motion with enhanced fore-paw activity.

Grade 3: The rat exhibited aggressive wriggling and demonstrated pronounced movement of both fore- and hind-limbs.

Grade 4: In addition to the observations stated in grade 3, the rat made an unsuccessful attempt to ascend using the tail.

*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**

Grade 5: In addition to the findings in grade 3, the rat successfully ascended to the tip of the tail.
The excitability score was evaluated on day 14 of the experiment.

Assessment of depression

The depression status of the rats was assessed via the forced swimming test as outlined by Porsolt *et al*. (1977). Briefly, each rat was placed inside a transparent glass (height 25 cm; diameter 24 cm), containing 10 cm of water at 25°C and left in the glass for 5 minutes. Each rat was compelled to swim and soon became immobilised, floating in an upright posture and exhibiting very minimal movements. The duration required for the rat to become immobile was recorded as an indicator of the depression status. The evaluation was carried out on day 14 of the study.

Assessment of motor strength

The fore-paw grip duration was utilised to assess the motor strength of the rats, as outlined by Abou-Donia *et al*. (2001). The process entailed suspending each rat from a wooden dowel with a diameter of 5 mm, held by both fore-paws. The duration of each rat's hold before release was recorded in seconds. The assessment was carried out on day 14 of the study.

Sample Collection

On day 15, rats were sacrificed under anesthesia with ether and blood samples were collected via jugular venesection into potassium ethylenediaminetetraacetic acid (K_2EDTA)-coated tubes for haematological examination. Whole blood was also collected and Serum was separated by centrifugation at 100xg for 20 minutes and stored at −20°C until used.

Evaluation of Biochemical, Haematological parameters and Oxidative Stress Biomarkers

Serum was analyzed for liver function biomarkers: Alanine transaminase (ALT), Aspartate aminotransferase (AST) , and Alkaline phosphatase (ALP) ,Kidney function parameters(Urea, Uric acid and creatinine) and biomarkers of oxidative stress- Malondialdehyde (MDA), Catalase (CAT) ,Glutathione peroxidase (GPx) , and Super oxide dismutase (SOD) using standard biochemical kits.

Data Analyses

Values obtained were expressed as mean± SEM. Data were analysed using one way ANOVA, followed by Tukey's post hoc test to determine the significance of the difference between the means. Values of $P<0.05$ were considered significant

Data were analyzed using GraphPad Prism version 9.7.1. (GraphPad Software, LLC California, USA)

Results

Behavioral Study

Table 1: Behavioral responses of rats to cypermethrin and glutamate exposure

Parameters	Soya Oil 2 mg/kg)	Monosodium Glutamate (5g/kg)	Cypermethrin (80 mg/kg)	Cypermethrin (80 mg/kg) + Monosodium Glutamate (5 g/kg)
Fore Paw grip Test	14.60±1.89	18.60±1.72	13.30±1.05	19.20±2.92
Excitability Score	4.29±0.29^{ab}	4.43±0.37^{a}	2.86±0.51^{b}	4.29±0.29^{ab}
Locomotion	7.60±2.40	4.00±1.95	3.00±1.18	2.86±1.50
Rearing	3.00±0.68	1.14±0.46	1.86±0.51	2.17±0.54
Grooming	13.20±1.32	9.17±3.49	9.40±2.36	11.20±1.74
Defecation	3.80±0.97^{a}	1.29±0.52^{ab}	1.57±0.69^{ab}	0.86±0.34^{b}
Urination	2.86±0.60	2.71±0.47	2.57±0.48	2.86±0.34

Means in the same rows with different superscript letters are significantly different ($p\leq0.05$)

The behavioral assessment of Wistar rats following exposure to soya oil, monosodium glutamate (MSG), cypermethrin (CYP), and their combination revealed distinct alterations in motor and neurobehavioral parameters. In the forepaw grip test, rats administered MSG exhibited a higher grip strength compared to the soya oil controls, while cypermethrin alone induced a lower grip strength. Interestingly, the combined administration of CYP and MSG markedly elevated grip performance (Table 1)

The locomotor activity of soya oil–treated rats was the highest, whereas CYP exposure induced a marked reduction in locomotion, an effect that was further sustained when combined with MSG. Similarly, rearing behavior was most pronounced in the control group but markedly reduced in MSG and CYP groups,

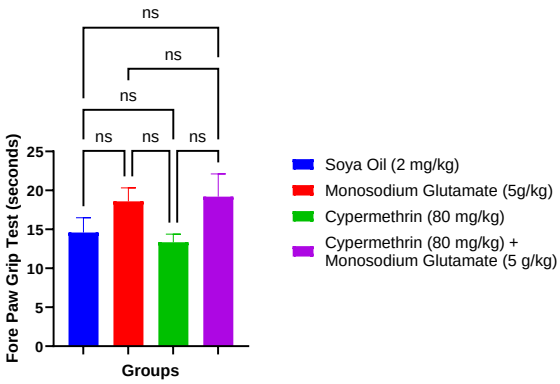
The excitability score showed significant variation across groups, with MSG-treated rats presenting the highest excitability response, which was significantly different from CYP-treated rats that demonstrated suppressed excitability. Rats that received the combined treatment of MSG and CYP

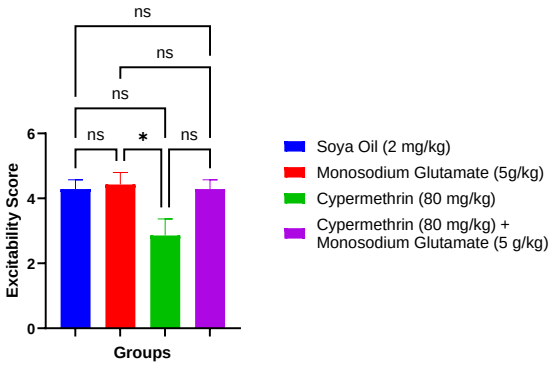
*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**

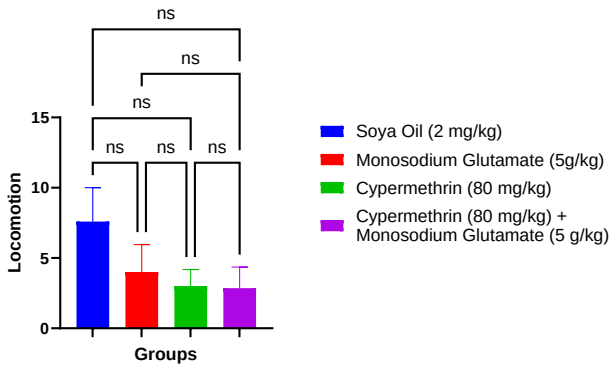
displayed intermediate responses, which were statistically similar to the control group (Table 1).

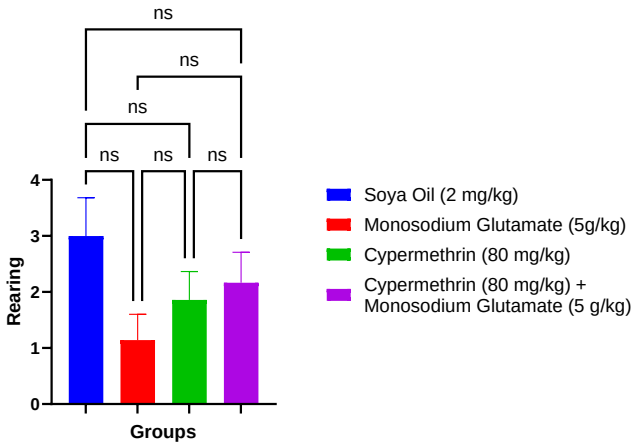
Grooming frequency, reduced significantly in the MSG and CYP groups compared to controls but was relatively preserved when the two compounds were co-administered

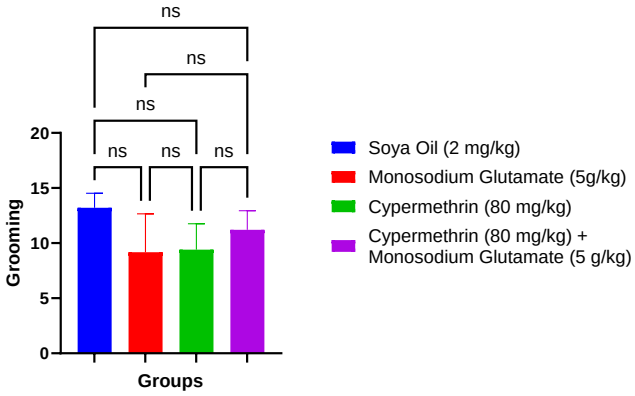
For autonomic parameters, defecation frequency was significantly higher in the soya oil controls but reduced markedly in the treatment groups. The lowest defecation score was recorded in the CYP + MSG group, showing a significant ($p < 0.05$) difference from the control. Urination scores, however, did not show any significant ($p < 0.05$) difference among the groups.

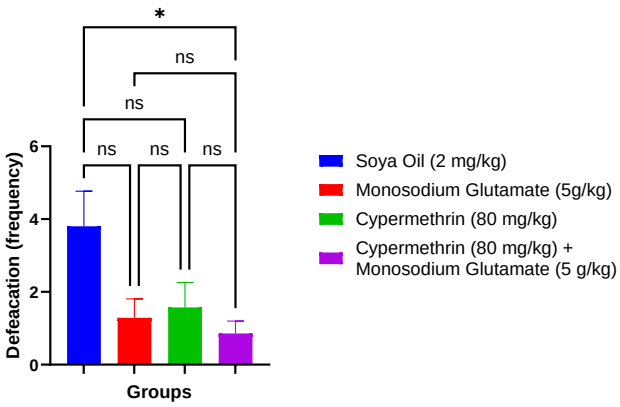


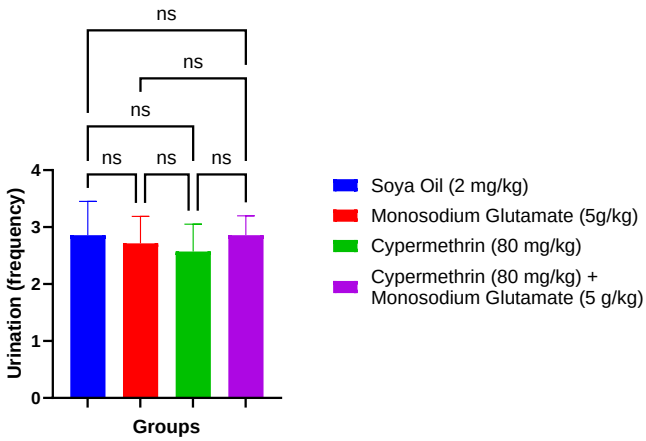












*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**

Hematology

Table 2: Hematologic responses to cypermethrin and glutamate exposure in Wistar rats

Parameters	Soya Oil 2 mg/kg)	Monosodium Glutamate (5g/kg)	Cypermethrin (80 mg/kg)	Cypermethrin (80 mg/kg) + Monosodium Glutamate (5 g/kg)
Packed Cell Volume	41.40±0.69	42.00±0.90	44.40±1.11	43.90±0.60
Hemoglobin	13.80±0.22	13.60±0.41	14.60±0.46	15.00±0.27
White Blood Cells	6.13±0.67 [ab]	4.67±0.74 [b]	8.53±0.99 [a]	6.67±0.42 [ab]
Red Blood Cells	4.16±0.11	4.53±0.22	4.77±0.20	4.90±0.22
Neutrophils	3.39±0.33 [b]	3.10±0.30 [b]	7.01±1.07 [a]	6.67±0.68 [a]
Lymphocytes	7.80±0.94	5.76±1.06	5.70±0.87	6.60±0.52
Monocytes	0.31±0.12	0.49±0.10	0.29±0.12	0.50±0.13
Eosinophils	0.00±0.00	0.00±0.00	0.01±0.01	0.00±0.00
Basophils	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
Band	0.24±0.09	0.27±0.12	0.15±0.06	0.10±0.06

Mean values within the same rows with different superscript letters are significantly (P<0.05) different.

The hematological parameters of Wistar rats exposed to soya oil, monosodium glutamate (MSG), cypermethrin, and their combination showed both adaptive and toxicological responses. The packed cell volume (PCV) and hemoglobin concentration were comparable across all groups, with CYP + MSG producing slightly higher values than the soya oil controls.

Similarly, red blood cell (RBC) counts were higher in the CYP-treated groups, particularly in the combination group, in contrast, white blood cell (WBC) counts showed significant increase in groups, with CYP-treated rats exhibiting a marked WBC count compared to the controls and MSG groups (Table 2).

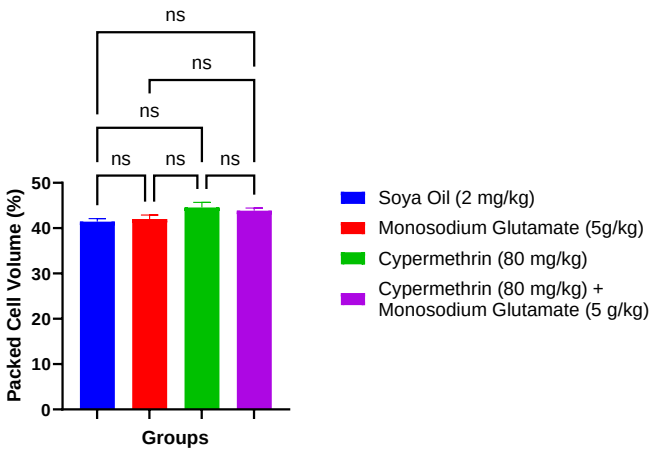
The combined CYP + MSG exposure produced intermediate WBC counts, which were not significantly different from those of the controls (Table 2).

Analysis of differential WBC counts revealed significant changes. Neutrophil counts were markedly elevated in CYP and CYP + MSG groups compared to soya oil and MSG alone,

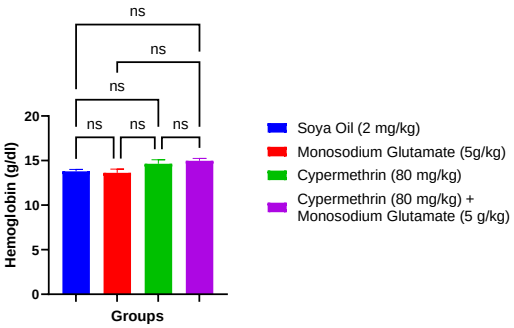
Conversely, lymphocyte counts were significantly (P<0.05) reduced in all exposed groups relative to the controls.

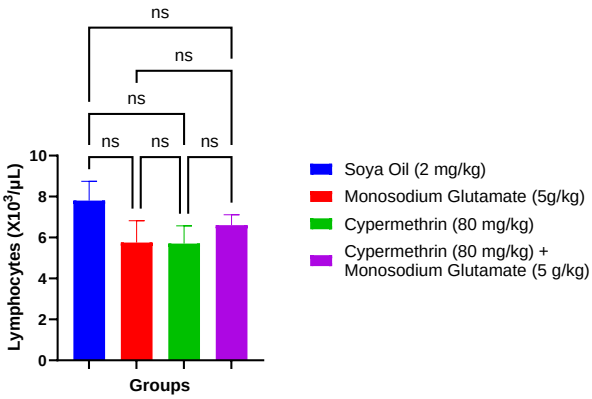
Monocyte counts fluctuated relatively but insignificantly across the groups. Eosinophil and basophil counts were not significantly different among all exposed groups. The band cells (immature neutrophils) showed a non-significant downward trend in CYP + MSG rats.

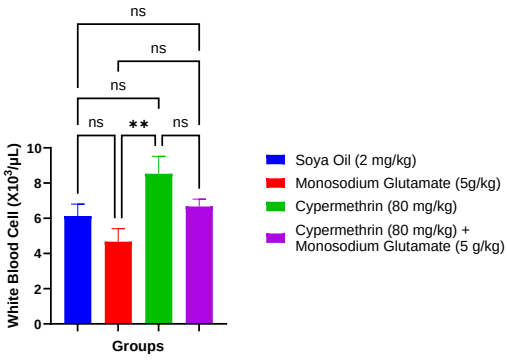
The activities of liver function enzymes varied significantly across treatment groups. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities were elevated in MSG-treated rats compared to the soya oil controls, Conversely, CYP-treated rats exhibited significantly reduced AST and ALT activities relative to MSG, In the combined CYP + MSG group, AST and ALT activities were restored towards control values, Alkaline phosphatase (ALP) activities did not differ significantly among the groups.

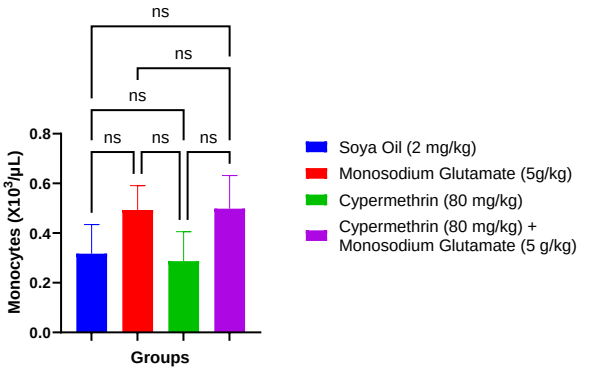


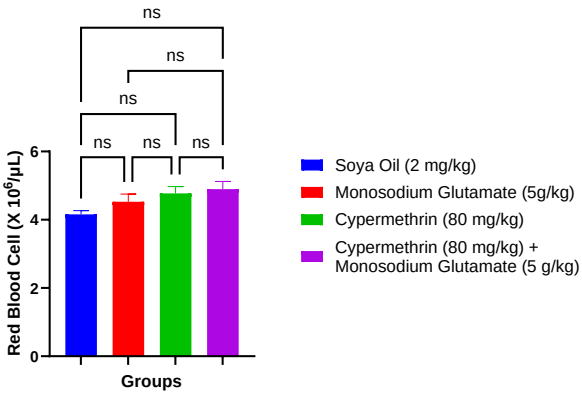
*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**

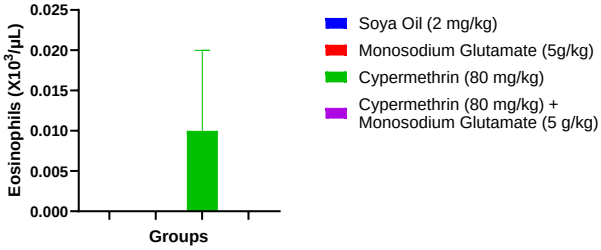


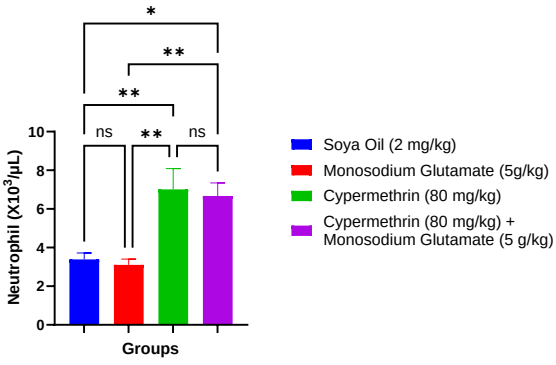


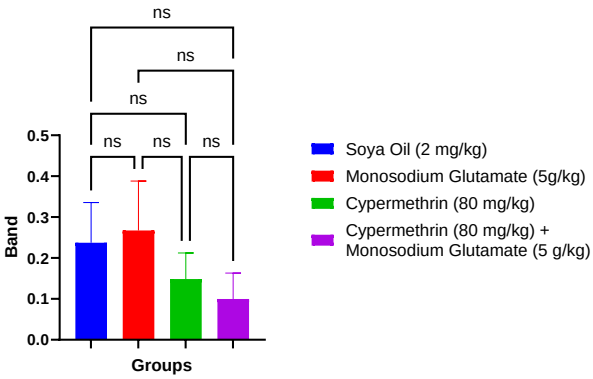












Serum Chemistry and Electrolytes

Table 3: Values of Serum chemistry and Electrolyte parameters in Wistar rats exposed to cypermethrin and glutamate

Parameters	Soya Oil 2 mg/kg)	Monosodium Glutamate (5g/kg)	Cypermethrin (80 mg/kg)	Cypermethrin (80 mg/kg) + Monosodium Glutamate (5 g/kg)

*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**

AST(**U/L**)	8.00±0.62 [ab]	9.86±0.60 [a]	6.83±0.98 [b]	8.00±0.55 [ab]
ALT(**U/L**)	12.40±1.70 [ab]	16.30±1.56 [a]	10.20±1.40 [b]	11.60±0.68 [ab]
ALP(**U/L**)	16.30±1.65	15.00±1.99	17.40±1.53	16.90±1.96
Urea (mg/dl)	120.0±22.20 [bc]	234.0±22.40 [a]	66.80±13.40 [c]	186.0±22.30 [ab]
Uric Acid (mg/dl)	7.06±1.67 [b]	15.40±2.55 [a]	6.63±0.80 [b]	12.30±0.80 [ab]
Creatinine (umol/L)	0.91±0.08	0.89±0.10	1.08±0.13	0.92±0.07
Sodium (mmol/L)	203.0±18.80 [b]	301.0±22.90 [a]	288.0±36.40 [ab]	284.0±17.50 [ab]
Potassium (mmol/L)	13.90±0.99	13.90±1.57	13.10±1.52	13.00±0.86
Chloride (mmol/L)	18.80±1.25	19.10±1.32	20.40±1.25	18.70±1.57
Bicarbonate(mmol/L)	94.60±6.00	96.90±7.65	93.10±5.56	95.60±5.03

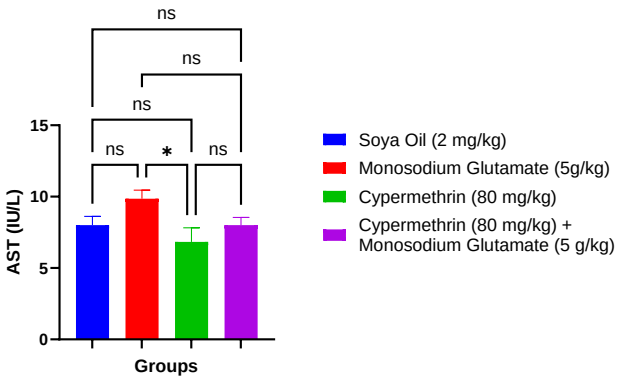
Rows with different superscript letters are significantly ($p<0.05$) different.

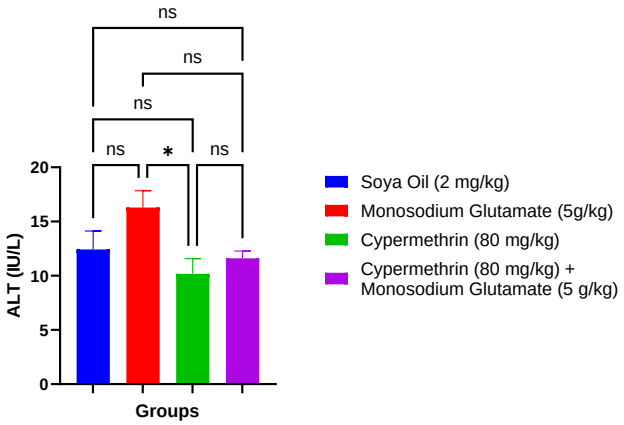
The activities of liver function enzymes varied significantly across treatment groups. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities were elevated in MSG-treated rats compared to the soya oil controls, Conversely, CYP-treated rats exhibited significantly reduced AST and ALT activities relative to MSG, In the combined CYP + MSG group, AST and ALT activities were restored towards control values, Alkaline phosphatase (ALP) activities did not differ significantly among the groups(Table 3).

Renal biomarkers showed notable alterations. Serum urea levels were significantly elevated in MSG-treated rats, while CYP alone markedly reduced urea concentration compared to control. The combination of MSG and CYP produced intermediate values, which were higher than in controls but lower than MSG alone (Table 3).

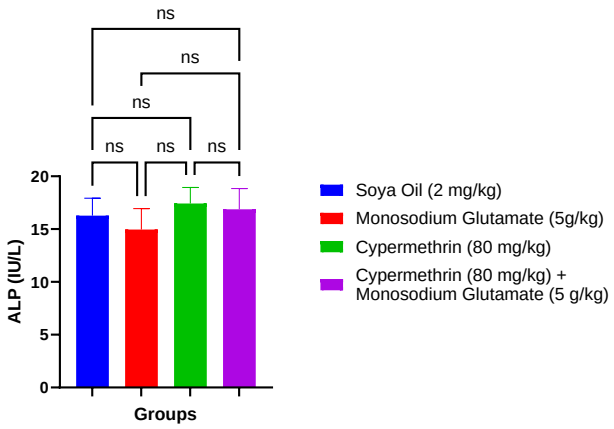
Similarly, uric acid was significantly($P<0.05$) elevated in MSG-treated rats but reduced in CYP-treated rats, with the combination again producing intermediate values. Serum creatinine levels remained relatively stable across groups,

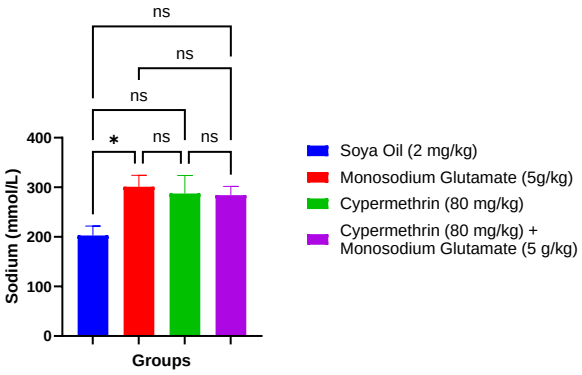
The electrolyte profile further revealed systemic effects. Serum sodium levels were significantly elevated in MSG-treated rats, Cypermethrin (CYP) also increased sodium ion concentration but to a lesser extent, and the combined exposure produced intermediate values. Potassium, chloride, and bicarbonate ion concentrations did not differ significantly among the groups(Table 3).

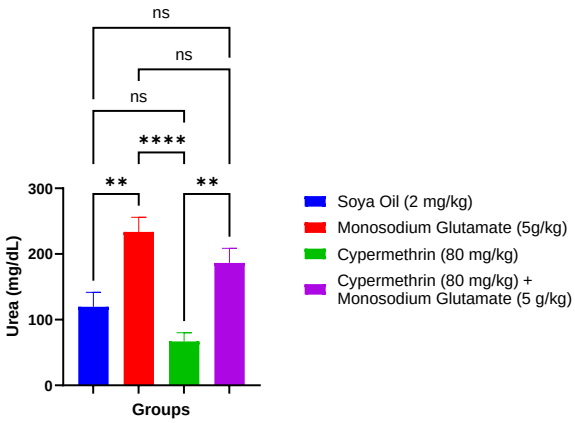


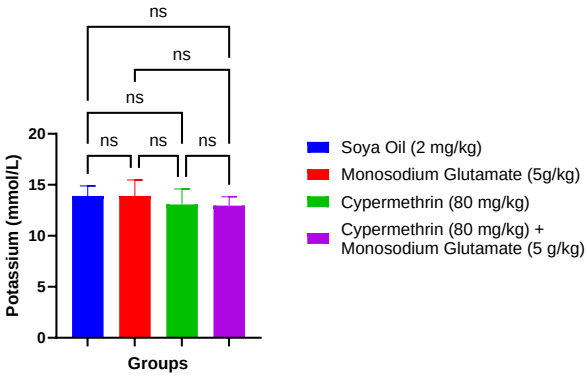


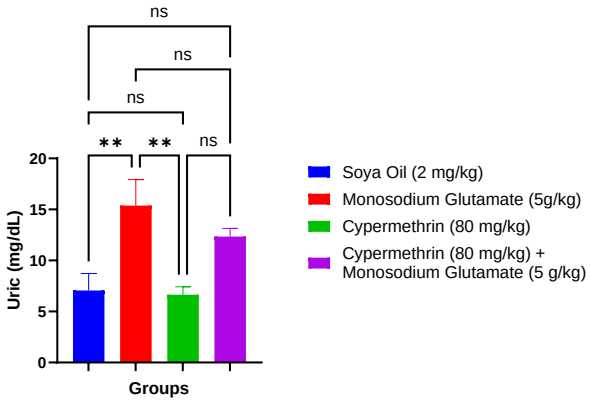
*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**

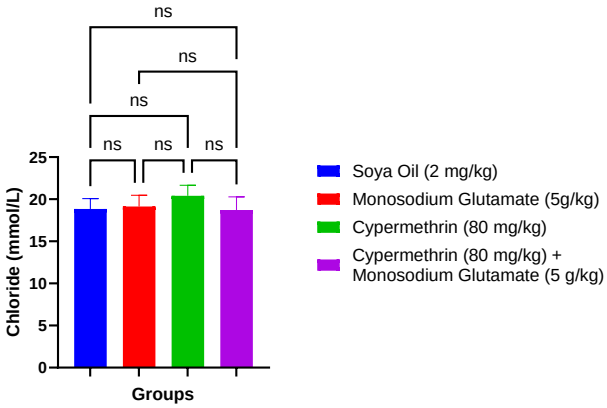


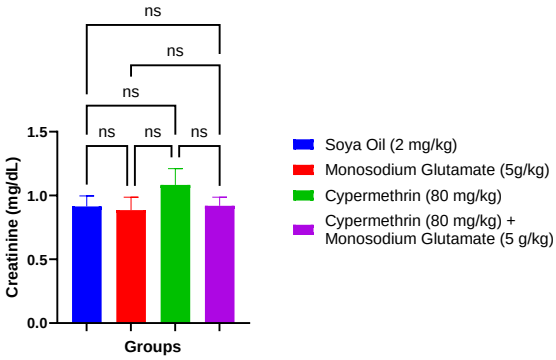


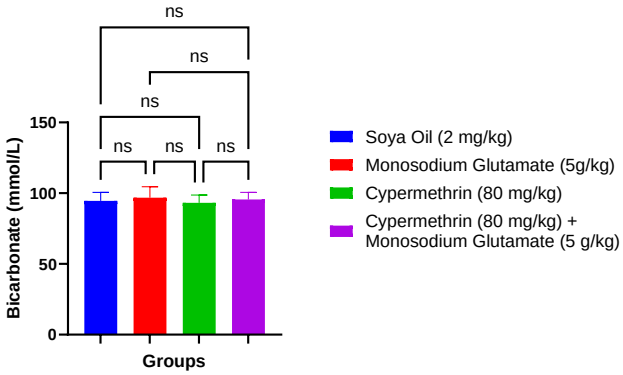












*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**

Oxidative stress

Table 4: Activities of biomarkers of Oxidative Stress in Wistar rats exposed to cypermethrin and glutamate

Parameters	Soya Oil 2 mg/kg)	Monosodium Glutamate (5g/kg)	Cypermethrin (80 mg/kg)	Cypermethrin (80 mg/kg) + Monosodium Glutamate (5 g/kg)
MDA(mmol/ml)	18.30±1.81 [b]	22.90±3.03 [b]	56.30±6.06 [a]	28.30±3.93 [b]
CAT(U/ml)	0.78±0.22 [ab]	0.70±0.29 [ab]	1.64±0.28 [a]	0.50±0.12 [b]
GPx (mU/L)	11.80±1.56 [b]	15.70±2.55 [ab]	22.50±2.73 [a]	22.10±2.26 [a]
SOD (mU/L)	6.53±0.14	6.34±0.25	6.29±0.16	6.31±0.13

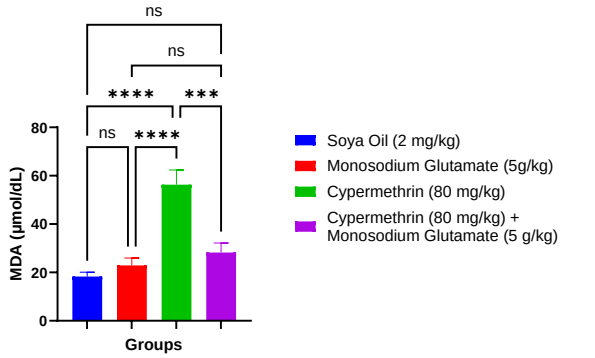
Means in rows with different superscript letters are significantly($P< 0.05$) different.

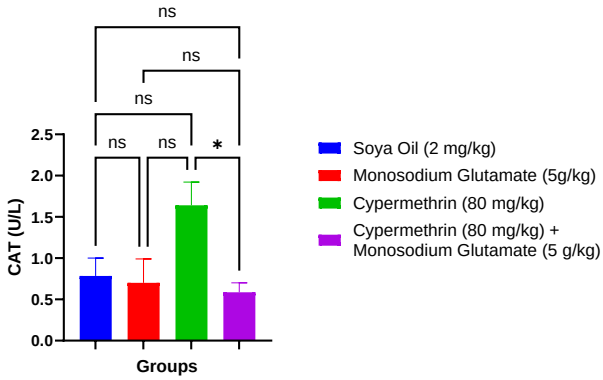
The assessment of oxidative stress markers demonstrated clear evidence of CYP-induced oxidative imbalance and differential modulatory effects of MSG.

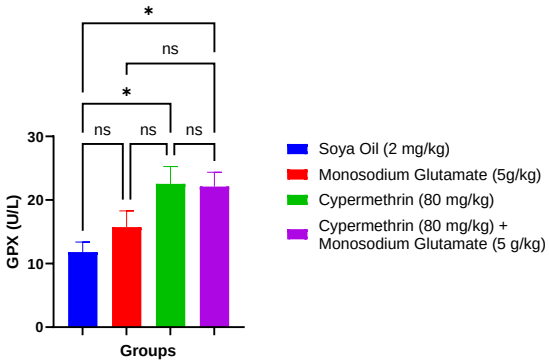
The malondialdehyde (MDA) concentration, an index of lipid peroxidation, was markedly elevated in CYP-treated rats compared to all other groups ($p < 0.05$). In contrast, MDA levels in the controls, MSG, and CYP + MSG groups were significantly ($P< 0.05$) lower, with the combination treatment showing a moderate reduction compared to CYP alone (Table 4).

The activities of antioxidant enzymes revealed that Catalase (CAT) activity was significantly ($p< 0.05$) elevated in CYP-treated rats compared to controls and MSG groups. However, in the CYP + MSG group, CAT activity declined significantly, even below the control values,

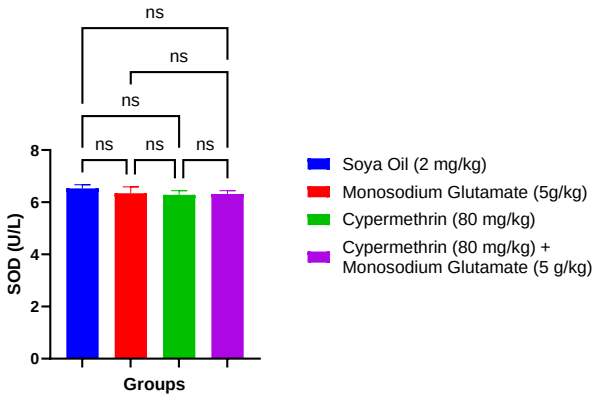
Similarly, glutathione peroxidase (GPx) activity was highest in CYP-treated rats, consistent with increased demand for detoxification of peroxides. Interestingly, the CYP + MSG group also maintained high GPx activities, statistically similar to CYP alone. In contrast, MSG alone modestly elevated GPx activity, relative to controls. For superoxide dismutase (SOD) activities, no significant differences were observed among the groups (Table 4).







*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**



Discussion

In the present study we evaluated the effects of single and combined exposures to CYP and MSG on selected neurobehavioral parameters (locomotion, anxiety, excitability, depression, and motor strength) and biomarkers of oxidative stress, and functions of the liver (AST, ALT, ALP), and kidney (urea, uric acid, creatinine) in male Wistar rats. Our findings indicated that the combined administration of CYP and MSG markedly elevated grip performance in the rats, suggesting a possible modulatory effect of MSG on cypermethrin-induced motor deficits. These findings are consistent with earlier reports of glutamate-induced neuronal hyperexcitability due to its role as a major excitatory neurotransmitter in the central nervous system (Farombi & Onyema, 2011).

Conversely, CYP exposure reduced locomotor activity and excitability, in agreement with the findings of Kalender et al. (2010), who demonstrated neurotoxic suppression of motor activity and cholinergic dysfunction following pyrethroid exposure

The fact that rats who received the combined treatment of MSG (5 g/kg/day) and CYP (80 mg/kg/day) displayed intermediate responses, similar to rats in the control group (which received 2ml/kg soya oil only) showed that MSG may abolish the inhibitory effects of CYP on rats' excitability. Similarly, the observation that rearing behavior was most pronounced in the control group but markedly reduced in MSG and CYP groups, is plausible evidence of impaired exploratory activity.

The observed reduction of grooming frequency in the MSG and CYP groups which was relatively preserved when the two compounds were co-administered points to the likelihood of an ameliorative and compensatory influence exerted by MSG. Similar reductions in exploratory and self-care behaviors have been described by Shaikh et al. (2019) following pesticide exposure, supporting the notion that chronic exposure to xenobiotics alters motivation and emotional reactivity

We also evaluated the effects of CYP and MSG individually and in combination on some hematological parameters. The concentrations of packed cell volume (PCV) and hemoglobin concentration were comparable across all groups, with CYP + MSG producing slightly higher values than the soya oil controls. This suggests that the exposure did not markedly compromise erythropoiesis but rather maintained or slightly enhanced red cell parameters Similarly, red blood cell (RBC) counts were higher in the CYP-treated groups, particularly in the combination group, indicating that MSG may exhibit compensatory erythropoietic response to alleviate the toxic stress occasioned by exposure to CYP .

In contrast, the significant decrease in WBC counts especially in the CYP-treated rats compared to controls and MSG groups is indicative of an elevated immune response to CYP exposure while the reduction in WBC counts in the rats exposed to MSG alone suggests possible immunosuppression. The intermediate WBC counts observed in rats that were exposed to the combination of CYP+MSG which were not significantly different from those of control rats implies that MSG may modulate CYP-induced increase in WBC count

Whereas the eosinophil and basophil counts were not significantly different among all exposed groups, the band cells (immature neutrophils) showed a non-significant downward trend in CYP + MSG rats, suggesting reduced release of immature granulocytes into circulation.

Although the activities of liver function enzymes varied significantly across treatment groups, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities were elevated in MSG-treated rats compared to the soya oil controls, indicating possible hepatocellular stress or mild hepatotoxicity. This finding was consistent with findings of Tawfik and Al-Badr (2012), who demonstrated hepatocellular leakage and oxidative damage in MSG-exposed rats.

Conversely, CYP-treated rats exhibited significantly reduced AST and ALT activities relative to MSG, suggesting either enzyme suppression or impaired release due to hepatocellular damage aligning with the hepatotoxic potential of pyrethroids described by Singh et al. (2018). Interestingly, co-administration of MSG and CYP restored enzyme activities toward control levels, suggesting that MSG may attenuate some CYP-induced hepatocellular disruptions.

Regarding renal biomarkers, the results showed notable alterations with Serum urea levels being significantly elevated in MSG-treated rats. This agrees with reports by Eweka and Om'Iniabohs (2011), who associated MSG exposure with nephrotoxicity and glomerular dysfunction. One the other hand, rats exposed to CYP alone exhibited markedly reduced urea concentration compared to control, consistent with altered renal excretion patterns reported by Bhardwaj *et al.* (2012). Rats that were exposed to a combination of MSG and CYP had intermediate values, which were higher than in controls but lower than rats which were exposed to MSG alone. The result suggests that MSG may potentiate nitrogen retention while CYP may impair protein metabolism or urea cycle activity. It is noteworthy that Serum creatinine levels remained relatively stable across groups, indicating preserved glomerular filtration despite fluctuations in urea and uric acid concentrations.

*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**

The electrolyte profile further revealed systemic effects with serum sodium levels being significantly elevated in MSG-treated rats, suggesting hypernatremia which may be linked to osmotic imbalance or altered renal handling of sodium. However, potassium, chloride, and bicarbonate ion concentrations did not differ significantly among the groups, indicating that overall electrolyte buffering capacity and acid–base regulation remained relatively stable.

The malondialdehyde (MDA) concentration, an index of lipid peroxidation, was markedly elevated in CYP-treated rats compared to all other groups. This reflects enhanced oxidative damage to membrane lipids and confirms CYP's role in increasing the generation of reactive oxygen species.This is consistent with the findings of Yousef et al. (2010) and Kalender et al. (2010) In contrast, MDA levels in the controls, MSG, and CYP + MSG groups were significantly lower, with the combination treatment showing a moderate reduction compared to CYP alone. This suggests that MSG attenuated, at least partially, the severity of CYP-induced lipid peroxidation and its administration may ameliorate negative effects of CYP.

The activities of antioxidant enzymes revealed compensatory responses. Catalase (CAT) activity was significantly elevated in CYP-treated rats compared to controls and MSG groups, reflecting an adaptive response to excessive hydrogen peroxide generation. However, in the CYP + MSG group, CAT activity declined significantly, even below the control values, indicating possible enzyme exhaustion or suppression under combined exposure to the agents.

Similarly, glutathione peroxidase (GPx) activity was highest in CYP-treated rats, consistent with increased demand for detoxification of peroxides. Interestingly, the CYP + MSG group also maintained high GPx activities, statistically similar to CYP alone, suggesting persistent oxidative pressure despite MSG co-administration. In contrast, MSG alone modestly elevated GPx activity, relative to controls, indicating that MSG may ameliorate oxidative stress. The compensatory upregulation of catalase (CAT) and glutathione peroxidase (GPx) in CYP groups in this study corroborates earlier findings by El-Demerdash (2011).

For superoxide dismutase (SOD) activities, no significant differences were observed among the groups, suggesting that superoxide radical detoxification remained relatively stable and unaffected by the treatments compared to downstream oxidative pathways.

Conclusion

The present study demonstrates that exposure to monosodium glutamate (MSG), cypermethrin (CYP), and their combined administration elicits distinct neurobehavioral, hematological, hepatic, renal, and oxidative stress responses in Wistar rats. MSG was associated with increased excitability, elevated liver enzyme activities, and altered renal biomarkers, while CYP induced neurobehavioral suppression, hematological perturbations, and marked oxidative stress, as evidenced by elevated malondialdehyde and antioxidant enzyme activities. Interestingly, combined MSG and CYP administration produced intermediate or partially ameliorated effects compared to single exposures, particularly in neurobehavioral outcomes and liver enzyme activities, suggesting a possible modulatory interaction.

The implications of these findings extend to human health, given the widespread consumption of MSG as a food additive and the pervasive use of cypermethrin as a household and agricultural pesticide. Chronic low-level exposure to these agents may pose cumulative risks, particularly to vulnerable populations such as children, agricultural workers, and individuals with pre-existing metabolic or hepatic disorders.

Overall, the findings underscore the need for stricter regulatory oversight of MSG consumption and cypermethrin usage, as well as heightened public awareness of their potential combined effects.

References

1. Abdou, H.M/, El-Gendy, A.H., Aly, R.G.Abouzied, M.M., Eltahir, H.M.,Althagfan, S.S. and ERweda, S.M. (2025**.** Evaluation of the effects of monosodium glutamate on metabolic, hepatic, renal and cardiac toxicity. *Metabolites, 15*(3), 64. https://doi.org/10.3390/metabo15030064
2. Abdulghani, M. A. M., Alshehade, S. A., Kamran, S., & Alshawsh, M. A. (2022). Effect of monosodium glutamate on serum sex hormones and uterine histology in female rats: Molecular docking and in-silico toxicity. *Heliyon, 8*(10), e10967. https://doi.org/10.1016/j.heliyon.2022.e10967
3. Albrakati, A. (2022). Monosodium glutamate induces cortical oxidative, apoptotic, and inflammatory challenges in rats: The potential neuroprotective role of apigenin. *Environmental Science and Pollution Research, 30*(2), 24143–24154. https://doi.org/10.1007/s11356-022-23719-3
4. Ambali, SF, Ayo JO(2012) Vitamin C attenuates chronic chlorpyrifos-induced alteration of neurobehavioural parameters in Wistar rats Toxicol. Int. 29(2): 144-152
5. Badr, G., Alwasel, S., Ebaid, H., Mohany, M., & Alhazza, I. (2012). Perinatal supplementation with thymoquinone improves diabetic complications and T cell immune responses in male offspring of diabetic mothers. *International Immunopharmacology, 12*(4), 611–620. https://doi.org/10.1016/j.intimp.2012.01.021
6. Bains, J. S., & Shaw, C. A. (2017). Neurodegenerative disorders in humans: The role of glutathione in oxidative stress-mediated neuronal death. *Brain Research Reviews, 55*(2), 145–168. https://doi.org/10.1016/j.brainresrev.2017.01.002
7. Bhardwaj, S., Srivastava, M. K., Kapoor, U., & Srivastava, L. P. (2012). A 90 days oral toxicity of imidacloprid in female rats: Morphological, biochemical and histopathological evaluations.

*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**

Food and Chemical Toxicology, *50*(2), 330–342. https://doi.org/10.1016/j.fct.2011.10.017

8. Carloni, M., Nasuti, C., Fedeli, D., Montani, M., Amici, A., Vadhana, M. S. D., & Gabbianelli, R. (2013). Early-life permethrin exposure induces long-term brain changes in Nurr1, NF-κB, and Nrf-2. *Brain Research*, *1515*, 19–28. https://doi.org/10.1016/j.brainres.2013.03.030
9. Elbetieha, A., Da'as, S. I., Khamas, W., & Darmani, H. (2001). Evaluation of the toxic potentials of cypermethrin pesticide on some reproductive and fertility parameters in the male rats. *Archives of Environmental Contamination and Toxicology*, *41*(4), 522–528. https://doi.org/10.1007/s002440010274
10. El-Demerdash, F. M. (2011). Lipid peroxidation, oxidative stress and acetylcholinesterase in rat brain exposed to organophosphate and pyrethroid insecticides. *Food and Chemical Toxicology*, *49*(6), 1346–1352. https://doi.org/10.1016/j.fct.2011.03.018
11. Eweka, A. O., & Om'Iniabohs, F. A. (2011). Histological studies of the effects of monosodium glutamate on the kidney of adult Wistar rats. *North American Journal of Medical Sciences*, *3*(5), 235–239. https://doi.org/10.4297/najms.2011.3235
12. Farombi, E. O., & Onyema, O. O. (2011). Monosodium glutamate-induced oxidative damage and genotoxicity in the rat: Mitigating effect of quercetin. *Human & Experimental Toxicology*, *30*(11), 1869–1880. https://doi.org/10.1177/0960327110391384
13. Haddad, S., Chouit, Z., Djellal, D., Gasmi, S., Hachemi, M., Hanfer, M., Zama, D., Kebieche, M., & Soulimani, R. (2023). Evaluation of mitochondrial and neurobehavioral disorders in offspring after gestating and lactating female rats exposure to low-dose imidacloprid and cypermethrin. *Journal of Microbiology, Biotechnology and Food Sciences*, *12*(5), e9541. https://doi.org/10.55251/jmbfs.9541
14. Kalender, S., Kalender, Y., Durak, D., Uzunhisarcikli, M., Ogutcu, A., & Cevrimli, B. S. (2010). Methyl parathion induced nephrotoxicity in male rats and protective role of vitamins C and E. *Pesticide Biochemistry and Physiology*, *97*(2), 105–112. https://doi.org/10.1016/j.pestbp.2009.12.003
15. Nazari, M, Sabahi, M., Salehipour, A., Ahmadi, S,A.,, Kazem, A.Razipour, S.Faraji, N. And Komaki, A (2025) Effects of cypermethrin exposure on learning and memory functions and anxiety-like behavior in rats. *Antioxidants*, *14*(5), 1047. https://doi.org/10.3390/antiox14051047
16. Olorunsogo, O. O., Olaleye, T. M., & Akinmoladun, F. O. (2014). Haematological and biochemical alterations in Wistar rats exposed to graded doses of dichlorvos. *Journal of Applied Biomedicine*, *12*(3), 211–219. https://doi.org/10.1016/j.jab.2014.01.004
17. Singh, R., Kaur, N., Kishore, L., & Singh, R. (2018). Neurotoxic and hepatotoxic effects of pyrethroid insecticides: An update. *Toxicology International*, *25*(2), 111–122. https://doi.org/10.4103/tj.ti_25_18
18. Shaikh, H., Ali, M., & Kaleem, A. (2019). Effect of pesticide exposure on behavioral and biochemical parameters in rodents: A review. *Environmental Science and Pollution Research*, *26*(9), 9045–9055. https://doi.org/10.1007/s11356-019-04316-3
19. Singh, R., et al. (2025). Cypermethrin neurotoxicity and oxidative stress: Emerging insights. *Environmental Toxicology and Pharmacology*, *96*, 104108. https://doi.org/10.1016/j.etap.2025.104108
20. Tavakkoli, M.Dadkhah, M., Saadati, H., Afshari, S and Mostafalou, s. (2025) *Neurobehavioral toxicity of cypermethrin in association with oxidative, inflammatory and neurotrophic changes in the hippocampus of rats*. *International Journal of Environmental Health Research* DOI: 10.1080/09603123.2025.2503472
21. Tawfik, M. S., & Al-Badr, N. (2012). Adverse effects of monosodium glutamate on liver and kidney functions in adult rats and potential protective effect of vitamins C and E. *Food and Nutrition Sciences*, *3*(5), 651–659. https://doi.org/10.4236/fns.2012.35089
22. Yousef, M. I., Awad, T. I., & Mohamed, E. H. (2010). Deltamethrin-induced oxidative damage and biochemical alterations in rat and its attenuation by Vitamin E. *Toxicology*, *227*(3), 240–247. https://doi.org/10.1016/j.tox.2006.08.006

*Corresponding Author: **Ramon-Yusuf Suleiman Babatunde**