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RESEARCH ARTICLE

PROTECTIVE EFFECTS OF *ANNONA MURICATA* ETHANOL LEAF EXTRACT ON RENAL FUNCTION AND SERUM ANTIOXIDANT PARAMETERS IN MONOSODIUM GLUTAMATE INTOXICATED RATS

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Abstract

Background and Objective: Monosodium glutamate (MSG)-induced oxidative stress has been implicated in renal dysfunction through excessive generation of reactive oxygen species. *Annona muricata* is a medicinal plant reputed for its antioxidant and nephroprotective properties. This study evaluated the protective effects of ethanol leaf extract of *A. muricata* on renal function and serum antioxidant parameters in MSG-intoxicated albino rats.
Methods: Thirty male albino rats were randomly assigned into six groups (n = 5). Group I served as the normal control, Group II received MSG (800 mg/kg body weight), Group III received MSG plus silymarin (50 mg/kg), while Groups IV–VI received MSG plus ethanol leaf extract of *A. muricata* at doses of 200, 400, and 800 mg/kg body weight, respectively, for 14 days.
Results: Administration of MSG significantly ($p<0.05$) increased serum urea, creatinine, sodium, chloride, and MDA concentrations, with concomitant reductions in GSH, GPx, SOD, and CAT activities compared with the normal control. Treatment with *A. muricata* extract significantly ($p<0.05$) ameliorated these alterations in a dose dependent manner. The highest dose (800 mg/kg) produced the greatest nephroprotective effect, reducing serum urea (25.03±2.01 mg/dL) and creatinine (0.70±0.03 mg/dL), while significantly increasing GSH (13.70±0.41 µmol/mg protein), GPx (31.37±0.91 µmol/mg protein), SOD (37.76± 0.66 µmol/mg protein), and CAT (16.80±0.81 µmol/mg protein) compared with the MSG-treated group.
Conclusion: Ethanol leaf extract of *A. muricata* demonstrated significant dose-dependent antioxidant and nephroprotective effects against MSG-induced renal toxicity, suggesting its potential as a natural therapeutic agent for the management of oxidative stress-related kidney injury.
Keywords: *Annona muricata*, antioxidants, monosodium glutamate, nephroprotection, oxidative stress.

INTRODUCTION

Medicinal plants remain essential sources of therapeutic compounds due to the presence of bioactive phytochemicals such as flavonoids, alkaloids, tannins, terpenoids, and phenolic compounds. These phyto-chemicals possess antioxidant, anti-inflammatory, and protective biological activities[1].

Annona muricata (soursop) is a medicinal plant widely used in traditional medicine and recognized for its antioxidant and anti-inflammatory properties. Its leaves contain important phytochemicals such as flavonoids, tannins, alkaloids, and acetogenins that are capable of scavenging free radicals, reducing oxidative stress, and preserving tissue integrity. Previous studies have shown that *A. muricata* leaf extract possesses significant protective effects against oxidative damage in experimental animals. Alaebo *et al.*[2], reported that administration of *A. muricata* seed extract signi-ficantly improved antioxidant enzyme activity and reduced lipid peroxidation in rats exposed to toxic insults, confirming its therapeutic potential in oxidative stress related disorders. Monosodium glutamate is a commonly consumed flavour enhancer; however, excessive intake has been associated with oxidative stress, lipid peroxidation, and tissue damage, including nephrotoxicity[3]. The kidneys are vital organs involved in excretion, electrolyte regulation, and acid–base

balance; therefore, toxic damage to renal tissues may impair physiological homeostasis and compromise normal body function.

Oxidative stress plays a central role in monosodium glutamate (MSG)-induced toxicity by promoting excessive generation of reactive oxygen species (ROS), which overwhelms the endogenous antioxidant defense system[4]. This imbalance results in depletion of critical antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), leading to lipid peroxidation of cellular membranes, protein damage, and ultimately renal dysfunction[5]. The kidneys are particularly vulnerable to oxidative injury due to their high metabolic activity and role in detoxification, making them a primary target organ in MSG-induced toxicity[5]. Previous studies have shown that while synthetic antioxidants may mitigate oxidative damage, their long-term use is associated with adverse effects, thereby necessitating the search for safer plant-based alternatives.

Despite increasing evidence on the toxicological impact of monosodium glutamate (MSG) and the antioxidant potential of medicinal plants, significant gaps still exist in the integrated evaluation of plant-based interventions on both renal and systemic oxidative stress parameters. Egbuonu *et al*.[7,8], demonstrated that MSG exposure induces marked oxidative stress, lipid peroxidation, and biochemical alterations in renal and hepatic tissues of experimental animals, largely through disruption of antioxidant defense systems. These findings further confirmed that MSG toxicity is not organ-specific but involves a systemic imbalance in redox homeostasis.

However, most existing studies have focused either on antioxidant status alone or on renal function parameters independently, with limited comprehensive biochemical assessment of both systems in a single experimental model. This creates a clear knowledge gap in understanding the full protective potential of medicinal plants such as *A. muricata* under combined oxidative and nephrotoxic stress conditions.

Therefore, this study aimed to evaluate the protective effects of ethanol leaf extract of *A. muricata* on kidney function indices (urea, creatinine, and electrolytes) and serum antioxidant biomarkers (GSH, GPX, SOD, CAT, and MDA) in monosodium glutamate-intoxicated albino rats. The study further seeks to establish the dose-dependent nephroprotective and antioxidant potential of the extract in comparison with a standard drug (silymarin), thereby contributing to the validation of *A. muricata* as a potential natural therapeutic agent against oxidative stress–mediated renal injury.

MATERIALS AND METHODS

Chemicals and reagents

All chemicals and reagents used in this study were of analytical grade and obtained from certified commercial suppliers. Ethanol (95%) was used as the solvent for plant extraction. Monosodium glutamate (MSG) was used to induce oxidative stress and nephrotoxicity in experimental animals. Silymarin was used as the standard reference drug for comparison of antioxidant and nephroprotective effects. Biochemical assay reagents used for the determination of renal function parameters included urea reagent kit, creatinine reagent kit (Jaffe's method), sodium, potassium, chloride, and bicarbonate assay kits, all obtained from Randox Laboratories (UK) and/or Agappe Diagnostics (India). Reagents for antioxidant assays included reduced glutathione (GSH) reagent, glutathione peroxidase (GPX) kit, superoxide dismutase (SOD) assay kit, catalase (CAT) reagent.

Experimental animals

Thirty male albino rats weighing 120–160 g were obtained from a standard animal breeding facility in Veterinary animal house of Michael Okpara University of agriculture Umudike and were acclimatized for a period of two weeks under controlled laboratory conditions, including a temperature of 25±2℃ and a 12-hour light/dark cycle. The rats were fed standard pelletized feed and allowed free access to clean drinking water *ad libitum*.

Plant collection and identification

Fresh leaves of *A. muricata* were collected from Umuafor, Obingwa LGA, Abia State, Nigeria. The plant materials were authenticated at the Department of Plant Science and Biotechnology, Michael Okpara University of Agriculture, Umudike, and a voucher specimen was deposited in the departmental herbarium with voucher number MOUAU/PSB/2025/CL-ZO/018 for future reference. After collection, the rhizomes were thoroughly washed with tap water to remove soil and other contaminants, and then air-dried at room temperature under shade conditions to prevent degradation of active phytochemicals. The dried samples were subsequently milled into fine powder using an automated milling machine. The powdered samples were weighed using an analytical weighing balance, yielding a total weight of 200 g[9].

Preparation of extract

Leaves were washed, air-dried, pulverized, and soaked in ethanol for 72 hours. The filtrate was concentrated with rotary evaporator and oven-dried at 40℃. Ethanol extraction was carried out using 90% ethanol as the solvent in a maceration process. The mixture was allowed to stand with intermittent shaking for 72 hours at room temperature to ensure adequate extraction of bioactive constituents. After extraction, the mixture was filtered using Whatman No. 1 filter paper, and the filtrate was concentrated using a rotary evaporator (Model: RE-52A, Shanghai Yarong Biochemistry Instrument Company, China) under reduced pressure at controlled temperature. The concentrated extracts were further dried and stored in airtight containers at 4℃ in a refrigerator (Haier Thermocool, China) until use[10].

Experimental design

Group 1: Normal control
Group 2: MSG only (800 mg/kg)
Group 3: MSG + silymarin (50 mg/kg)
Group 4: MSG + extract (200 mg/kg)
Group 5: MSG + extract (400 mg/kg)
Group 6: MSG + extract (800 mg/kg)
Treatment lasted 14 days.

Biochemical analysis

Biochemical analysis was carried out using standard laboratory methods to determine kidney function markers, including urea, creatinine, sodium, chloride, potassium, and bicarbonate, as well as antioxidant parameters such as reduced glutathione (GSH), glutathione peroxidase (GPX), superoxide dismutase (SOD), catalase (CAT), and malondialdehyde (MDA), following established protocols for the evaluation of renal integrity and oxidative stress status in experimental animals[11-14].

Statistical analysis

Data were expressed as mean±standard deviation (SD). Statistical comparisons among groups were performed using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test for multiple comparisons[15]. Differences were considered statistically significant at $p<0.05$.

RESULTS AND DISCUSSION

Table 1 shows that MSG intoxication (Group 2) caused marked elevation in urea, creatinine, and electrolyte imbalance compared to the control (Group 1), indicating impaired kidney function. However, treatment with *A. muricata* extract (Groups 3–6) progressively reduced urea and creatinine levels and improved electrolyte balance, suggesting a dose-dependent nephroprotective effect and restoration of renal function.

Table 1: Kidney function of MSG intoxicated rats treated with *A. muricata* extract.

Group	UREA (mg/dL)	CREA (mg/dL)	Na (mmol/L)	Cl (mmol/L)	K (mmol/L)	HCO_3 (mmol/L)
Group 1	17.30±0.87	0.61±0.04	128.23±2.37	76.27±2.17	4.31±0.08	18.83±1.50
Group 2	38.03±0.85	1.03±0.10	142.93±2.41	87.23±3.12	4.64±0.10	20.37±0.06
Group 3	26.77±2.06	0.78±0.03	136.00±1.51	85.33±2.27	4.35±0.03	20.00±0.17
Group 4	27.37±2.48	0.77±0.03	138.90±1.61	83.13±2.79	4.40±0.09	20.07±0.15
Group 5	26.67±3.16	0.71±0.03	135.07±3.65	82.27±1.50	4.38±0.12	19.07±1.37
Group 6	25.03±2.01	0.70±0.03	135.57±2.37	83.07±0.81	4.39±0.12	19.87±0.21

Table 2: Antioxidant activity of MSG intoxicated rats treated with *A. muricata* extract.

Group	GSH (µmol/mg protein)	GPX (µ/mg protein)	SOD (µ/mg protein)	CAT (µ/mg protein)	MDA (nmol/ mg protein)
Group 1 (positive control)	14.28±0.12	31.45±1.17	40.78±0.58	16.36±0.34	0.22± 0.06
Group 2 (negative control)	11.57±0.96	25.74±2.66	30.78±2.75	13.77±0.64	0.52±0.37
Group 3 (50 mg/kg of silymarin)	12.98±0.27	28.65±0.99	34.10±0.94	15.22±0.78	0.39±0.04
Group 4 (200 mg/kg ethanol extract)	12.83±0.38	27.52±1.75	33.65±0.80	15.05±0.57	0.53±0.02
Group 5 (400 mg/kg ethanol extract)	13.67±0.08	30.22±0.25	34.82±1.45	15.24±0.54	0.38±0.05
Group 6 (800 mg/kg ethanol extract)	13.70±0.41	31.37±0.91	37.76±0.66	16.80±0.81	0.41±0.06

Table 2 shows that MSG intoxication (Group 2) significantly reduced antioxidant enzymes (GSH, GPX, SOD, CAT) and increased MDA compared to the control group (Group 1), indicating enhanced oxidative stress. However, treatment with *A. muricata* extract (Groups 3–6) improved antioxidant status by increasing enzymatic antioxidants and reducing lipid peroxidation (MDA) in a dose-dependent manner, with the highest dose (Group 6) showing the most pronounced protective effect.

The present study demonstrated that monosodium glutamate (MSG) administration induced significant nephrotoxicity and oxidative stress in experimental rats, as evidenced by elevated serum urea, creatinine, sodium, chloride, and malondialdehyde (MDA), alongside reduced antioxidant enzyme activities (GSH, GPX, SOD, and CAT). The elevation in urea and creatinine in Group 2 reflects impaired glomerular filtration rate (GFR) and reduced renal clearance capacity, indicating functional kidney damage. Biochemically, this suggests disruption of nephron integrity, glomerular filtration barrier damage, and impaired tubular reabsorption processes. These findings agree with Oda *et al.*[5], who reported that increased urea and creatinine are classical biomarkers of renal dysfunction. Similarly, Egbuonu *et al.*[7], demonstrated that MSG exposure induces oxidative stress–mediated renal and hepatic injury in Wistar rats through disruption of antioxidant defense systems. Comparable nephrotoxic mechanisms have also been reported by Onyema *et al.*[16], Diniz *et al.*[17], and Eweka & Om'Iniabohs[18], who showed that MSG promotes oxidative damage in vital organs via excessive ROS generation. The electrolyte imbalance observed (increased Na^+ and Cl^-) further suggests impaired tubular ion transport and defective renal osmotic regulation. This is consistent with findings by Tordoff *et al.*[19], and Sharma *et al.*[20], who linked renal electrolyte disturbances to tubular dysfunction under toxic stress conditions. Elevated MDA levels indicate enhanced lipid peroxidation of renal membranes due to ROS overproduction, consistent with Halliwell & Gutteridge[21], Valko *et al.*[22], and Bezerra *et al.*[3], who described oxidative stress–mediated membrane degeneration and mitochondrial injury in toxicological models.

Administration of *A. muricata* ethanol leaf extract significantly ameliorated MSG-induced renal dysfunction and oxidative stress in a dose-dependent manner. The reduction in urea and creatinine levels indicates improved glomerular filtration and restoration of renal excretory function, suggesting nephron recovery and stabilization of epithelial integrity. The normalization of sodium, chloride, potassium, and bicarbonate levels indicates improved tubular reabsorption and electrolyte homeostasis, reflecting restoration of renal physiological regulation. This supports the role of renal ion transport systems such as Na^+/K^+-ATPase and membrane channel integrity in recovery processes. These findings agree with reports by Omodanisi *et al.*[22], who demonstrated nephroprotective and antioxidant effects of *A. muricata* in toxin-induced oxidative stress. Other studies by Adewole and Ojewole[24], Arthur *et al.*[24], and Moghadam *et al.*[26], also confirmed that plant-derived polyphenols improve renal antioxidant defense and reduce lipid peroxidation. The improvement may be attributed to phytochemicals such as flavonoids, tannins, and acetogenins, which act as ROS scavengers, metal chelators, and membrane stabilizers, thereby reducing oxidative injury and enhancing endogenous antioxidant systems. Similar mechanisms have been reported by Li *et al.*[1], Kumar *et al.*[27], and Newman and Cragg[28], who emphasized the pharmacological relevance of plant secondary metabolites in disease modulation.

The findings of this study strongly align with previous literature demonstrating that MSG induces oxidative stress and renal dysfunction through depletion of antioxidant defenses and increased lipid peroxidation. Onyema *et al.*[16], and Farombi and Onyema[29] reported that MSG exposure leads to systemic oxidative imbalance and organ toxicity. Furthermore, Teede *et al.*[30], Legro *et al.*[31], and Azziz *et al.*[31], highlight the broader relevance of oxidative stress in metabolic disorders involving reproductive and endocrine dysfunctions, reinforcing the systemic impact of ROS-mediated injury.

The present study provides an added contribution by integrating renal biochemical indices with oxidative stress biomarkers in a single experimental model, offering a more holistic evaluation of *A. muricata* as a nephroprotective and antioxidant agent against MSG-induced toxicity.

Limitation of the study

This study was limited by its short experimental duration (14 days) and the use of an animal model, which may not fully represent human physiological responses. In addition, only biochemical and antioxidant parameters were evaluated without detailed molecular or histopathological analyses. Therefore, further long-term and clinical studies are needed to validate the nephroprotective potential of *A. muricata* in humans.

CONCLUSIONS

This study demonstrates that monosodium glutamate induces significant renal dysfunction and oxidative stress through disruption of antioxidant defense systems and impairment of kidney biochemical indices. Ethanol leaf extract of *A. muricata* effectively ameliorated these toxic effects by improving renal function parameters, restoring electrolyte balance, enhancing antioxidant enzyme activities, and reducing lipid peroxidation in a dose-dependent manner. The findings suggest that *A. muricata* possesses strong nephroprotective and antioxidant properties, likely due to its phytochemical constituents. Therefore, it may serve as a potential natural therapeutic agent in the management of oxidative stress–induced renal injury.

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AUTHOR'S CONTRIBUTION

Njoku CJ: conceived and designed the study, performed the experiments, collected and analyzed the data, and drafted the manuscript. **Anyiam PN:** supervision, study design, critically revision. **Alaebo PO:** experimental work, data interpretation, revision. **Chris-Eze CE:** laboratory analysis, data collection, literature review. **Ebeleagu JC:** data analysis, results interpretation, manuscript editing. **Francis BC:** study design, critical review. All authors read and approved the final manuscript.

DATA AVAILABILITY

The data generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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