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ASSESSING THE EFFECTS OF MONOSODIUM GLUTAMATE ON RENAL OXIDATIVE STRESS AND FUNCTION IN A DIABETIC MALE ALBINO RATS MODEL

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***Abstract**: Food companies use Monosodium glutamate (MSG) as a flavor enhancer, yet its potential impact on renal oxidative stress and function in diabetic conditions remains underexplored. This study investigated the effects of MSG on renal health in a diabetic male albino rat model to assess its implications for diabetes-associated nephropathy. This study assigned 32 rats to four experimental groups, with 8 rat samples per group, including the research-induced Control, Diabetes Only, MSG Only, and Diabetes + MSG. Diabetes using alloxan monohydrate (150 mg/kg), and MSG was administered orally at 2 g/kg daily for 14 days. Renal function markers, including serum urea and creatinine, oxidative stress indicators such as malondialdehyde (MDA) and nitric oxide (NO), and antioxidant levels (reduced glutathione [GSH]) were measured. The study performed a histological analysis of renal tissues to complement biochemical findings. Results showed significant increases in urea, creatinine, MDA, and NO levels in diabetic and MSG-treated groups. This indicates impaired renal function and elevated oxidative stress. Notably, antioxidant defenses were compromised. However, the group with both diabetic and MSG exposures showed some reduction in oxidative stress compared to the diabetic group only group. These findings suggest that MSG may worsen kidney damage and oxidative stress in diabetic individuals. They highlight the need for cautious dietary habits and further research into strategies to mitigate MSG-related health risks in diabetic populations.*

***Keywords**: Monosodium glutamate, diabetes, oxidative stress, renal dysfunction, albino rats.*

Introduction

Diabetic nephropathy (DN), a primary microvascular complication of *Diabetes mellitus*, is a leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) globally (Abe *et al.*, 2017). Its prevalence continues to rise alongside the escalating global diabetes epidemic, creating a significant public health challenge (Greco and Hall, 2023). The characterization of DN by persistent albuminuria, declining glomerular filtration rate (GFR), and histopathological changes, including glomerulosclerosis and tubular atrophy, collectively contribute to renal dysfunction (Młynarska *et al.*, 2024)The progression of DN is determined by the hyperglycemia-induced oxidative stress, inflammation, and fibrosis underlying the vital role of oxidative injury in its pathogenesis.

Oxidative stress, an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defense mechanisms, is a crucial driver of cellular and tissue damage in DN. Elevated ROS levels promote lipid peroxidation, protein oxidation, and DNA damage, exacerbating renal injury and disease progression (Gwozdzinski *et al.*, 2021). Moreover, dietary and environmental factors, such as the consumption of flavor-enhancing agents like monosodium glutamate (MSG), may further exacerbate oxidative stress, particularly in individuals with diabetes.

MSG, the sodium salt of L-glutamic acid, is widely used in the food industry to enhance the "umami" flavor of various dishes. While recognized as safe by regulatory authorities, such as the United States Food and Drug Administration (FDA), emerging evidence suggests its potential health risks, mainly when consumed in high quantities. The association of chronic MSG exposure with metabolic disruptions, oxidative stress, and organ toxicity in animal models affects the kidneys, liver, and pancreas (Moldovan *et al.*, 2023). These effects are of particular concern in diabetic conditions, where the existing oxidative burden may amplify MSG-induced renal injury (Kayode *et al.*, 2023).

There is a limitation in the comprehension of the interaction among diabetes, oxidative stress, and dietary MSG ingestion, particularly concerning its impact on renal function. This study aims to investigate the nephrotoxic effects of MSG in diabetic male albino rats, focusing on its influence on renal oxidative stress markers and functional indices. By exploring criteria such as serum urea, creatinine levels, and oxidative stress biomarkers, this study aims to elucidate the function of MSG in modulating renal damage in diabetes. These findings could inform dietary recommendations and preventive strategies for mitigating DN progression (Ke *et al.*, 2020).

Materials and Methods

Sample Collection

The animals were obtained from a certified breeder in Oyo State, Nigeria, and acclimatized in the animal house of the Department of Physiology, Ladoke Akintola University of Technology (LAUTECH), Ogbomosho, Oyo State. The animal housing conditions included well-ventilated plastic cages, a standard 12-hour light/dark cycle, and a controlled temperature of approximately 25°C.

Study Design and Experimental Animals

A controlled laboratory experimental design was employed to evaluate the impact of monosodium glutamate (MSG) on renal oxidative stress and function in diabetic male albino rats. Thirty-two healthy male albino rats (200–250 g) were used, with 8 rat samples assigned to each group. All procedures adhered to institutional and international ethical guidelines for using and handling laboratory animals.

Experimental Design

The randomly divided four groups of treatment were (n = 8 per group):
Group 1: MSG only
Group 2: Diabetic + MSG
Group 3: Diabetic only
Group 4: Control (no treatment)

Induction of Diabetes and MSG Administration

Induced diabetes was administered with an intraperitoneal injection of alloxan monohydrate (150 mg/kg body weight), a known diabetogenic agent, dissolved in sterile normal saline. Fasting blood glucose levels were measured after 72 hours to confirm diabetes induction (blood glucose > 250 mg/dL). In addition, MSG (Ajinomoto Co., Inc., Japan) was administered orally using a feeding cannula at a dose of 2 g/kg body weight daily for 14 days
(Ke *et al.*, 2020).

Blood Sample Collection

At the end of the experimental period, the animals were anesthetized using intraperitoneal ketamine (1 mL per rat). Blood samples were collected through cardiac puncture into ethylenediaminetetraacetic acid (EDTA) tubes. The serum was centrifuged at 4000 revolutions per minute (rpm) for 15 minutes to separate it for biochemical analysis.

Tissue Collection and Preparation

The kidneys were excised, washed in an ice-cold 1.15% potassium chloride solution, and blotted dry. The study fixed one kidney in 10% formalin for histological analysis, while the other was homogenized in 0.25M phosphate buffer using a mortar and pestle on ice to prevent enzyme degradation. The study stored the homogenate at -20°C until further analysis.

Biochemical Analysis

The biochemical assays were conducted to measure renal function markers (serum urea and creatinine) and oxidative stress indices, including reduced glutathione (GSH), malondialdehyde (MDA), and nitric oxide (NO). Enzymatic and spectrophotometric techniques followed standard protocols (Hadwan, 2018).

Statistical Analysis

The data were expressed as mean ± standard error of the mean (SEM) and analyzed using one-way analysis of variance (ANOVA) with Tukey's post-hoc test for pairwise comparisons at statistical significance ($p < 0.05$). All analyses were performed using GraphPad Prism software (version 9.0, GraphPad Software Inc., USA).

Results

Results, expressed as mean ± SEM, demonstrated statistically significant differences at $p < 0.05$ across the groups.

Figures 1 to 5 present the effects of monosodium glutamate (MSG) on renal oxidative stress and function in diabetic male Albino rats. Urea concentrations in serum samples (Figure 1) showed significant variations. Urea levels were significantly increased in the Diabetes Only and MSG Only groups compared to the Control group. However, levels in the MSG + Diabetes group showed a significant decrease relative to the Diabetes Only group.

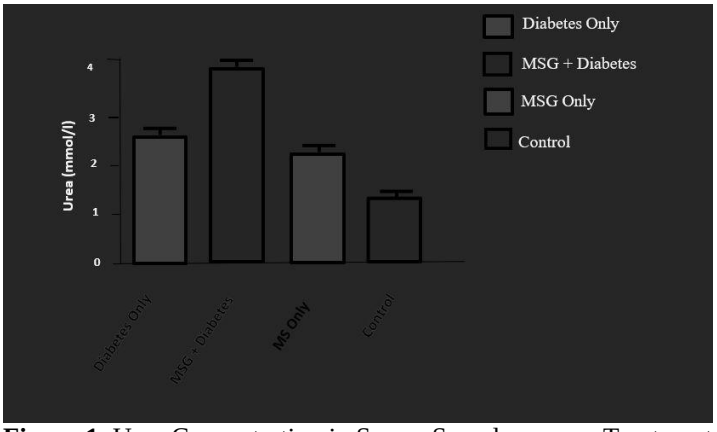

Figure 1: Urea Concentration in Serum Samples across Treatment Groups

Similarly, creatinine concentrations in serum samples (Figure 2) revealed a significant elevation in the Diabetes only and MSG only groups compared to the control group. At the same time, the levels of the MSG + Diabetes group were significantly reduced compared to the Diabetes Only group.

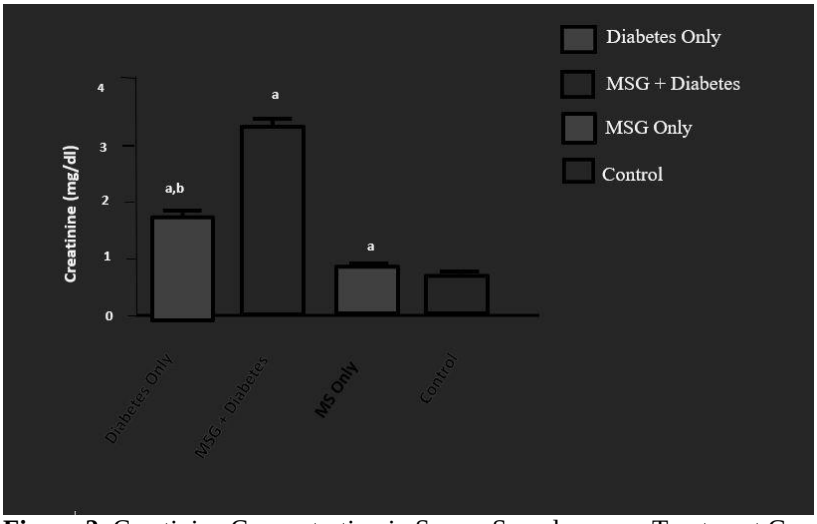

Figure 2: Creatinine Concentration in Serum Sample across Treatment Groups

The oxidative stress marker malondialdehyde (MDA) in kidney tissue (Fig. 3) was significantly elevated in the Diabetes-Only and MSG-only groups compared to the Control group. However, MDA levels in the MSG + Diabetes group were significantly reduced compared to the Diabetes-Only and MSG-only groups.

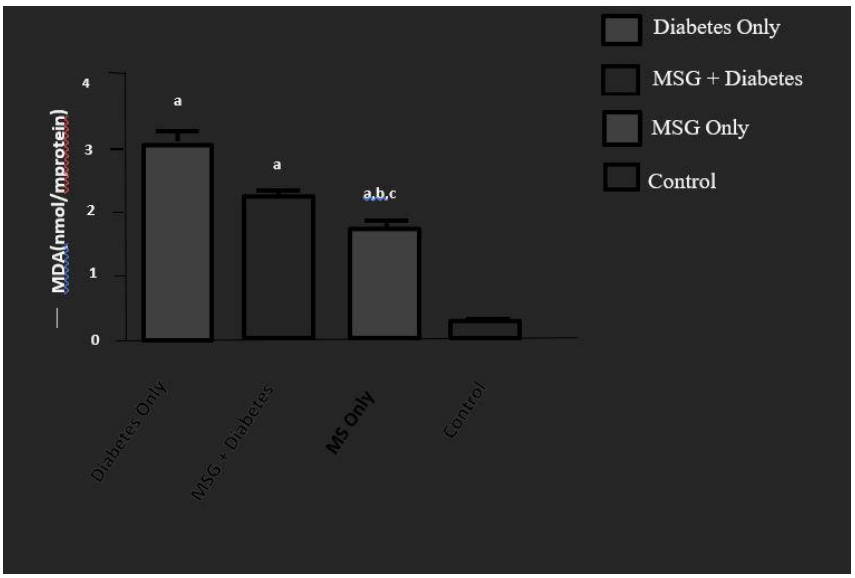

Figure 3: Malondialdehyde (MDA) Concentration in Kidney Tissue across Treatment Groups

Glutathione (GSH) concentrations in kidney tissue (Fig. 4) significantly decreased in the Diabetes Only and MSG Only groups compared to the Control group.

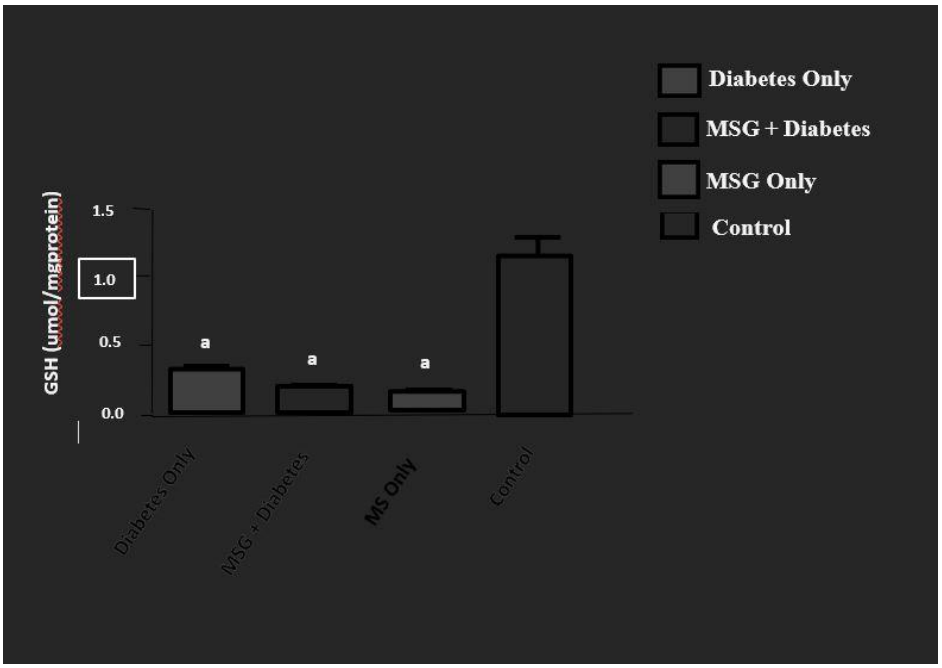

Figure 4: Reduced Glutathione (GSH) Concentration in Kidney Tissue across Treatment Groups

There was a significant increase in Nitric oxide (NO) levels in kidney tissue (Figure 5) in the Diabetes-Only and MSG-only groups compared to the Control group. In contrast, levels in the MSG + Diabetes group were significantly lower than in the Diabetes-Only group but higher than in the Control group.

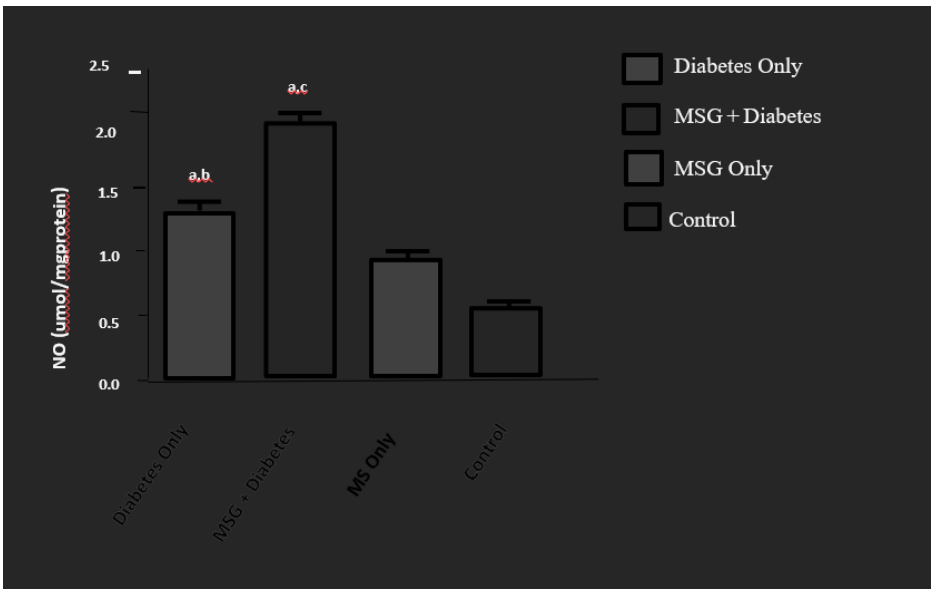

Figure 5: Nitric Oxide (NO) Concentration in Kidney Tissue across Treatment Groups

The findings observed that MSG intensified renal oxidative stress and weakened kidney function in diabetic rats, as shown through the alterations in biomarkers such as urea, creatinine, MDA, GSH, and NO. These findings highlight the potential risks of MSG ingestion in diabetic situations, justifying precaution and additional exploration.

Discussion

The findings revealed significant disruptions in renal markers, oxidative stress parameters, and antioxidant defense mechanisms, shedding light on the intricate interplay between MSG exposure and diabetes-related nephropathy. These findings expand the insightful academic literature on the impact of MSG on metabolic and renal disorders. The elevated urea and creatinine levels in the Diabetes and MSG Only groups strongly indicate renal impairment. Urea and creatinine, as biomarkers of renal function, are crucial for assessing kidney filtration efficiency. The significant increase in these markers aligns with prior research linking oxidative stress in diabetes to renal dysfunction (Sharma *et al.*, 2021; Wang and Zhang, 2024). However, the partial reduction of these markers in the MSG + Diabetes group compared to the Diabetes Only group indicates an intricate association between MSG and diabetes. This interaction contradicted the findings by Adeleke *et al.* (2022) and Zanfirescu *et al.* (2019), who observed exacerbation of renal dysfunction with MSG exposure. These discrepancies may stem from variations in experimental design, dosages, or species differences, emphasizing the need for further comparative studies.

The oxidative stress marker malondialdehyde (MDA) was significantly elevated in the Diabetes Only and MSG Only groups, indicating heightened lipid peroxidation. MDA, a byproduct of lipid peroxidation, is widely recognized as a marker of oxidative damage to cell membranes (Jadoon & Malik, 2017). This finding is consistent with studies by Thangachi et al. (2021), who reported MSG-induced lipid peroxidation in rodents. Interestingly, the relative reduction of MDA in the MSG + Diabetes group suggests potential interactions that alleviate lipid peroxidation under diabetic conditions. Similar findings in research exploring oxidative stress modulation through dietary components indicate that MSG's effects may be context-dependent (Egbuonu, 2023).

Depletion of glutathione (GSH), a critical antioxidant, in the Diabetes Only and MSG Only groups further underscores the oxidative burden induced by diabetes and MSG exposure. The observation of GSH depletion in oxidative stress conditions corroborates the findings of Adeoye *et al.*, 2018. However, the partial restoration of GSH levels in the MSG + Diabetes group aligns with Moldovan *et al.* (2023) and Zanfirescu *et al.* (2019), who highlighted the potential of some compounds to partially restore antioxidant defenses under specific pathological conditions. This alignment suggests a complex interaction between MSG metabolism and endogenous antioxidant systems.

Nitric oxide (NO) levels, significantly elevated in the Diabetes Only and MSG Only groups, reflect oxidative imbalance. While crucial in normal renal physiology, NO contributes to oxidative damage under pathological conditions by forming peroxynitrite amidst reactive oxygen species (ROS) (Gwozdzinski *et al.*, 2021). The partial reduction of NO levels in the MSG + Diabetes group suggests that MSG's effects on NO bioavailability can vary in

diabetic environments. This finding is in contrast with the discovery of Zanfirescu *et al.* (2019), who observed exacerbated NO-related damage with MSG, highlighting potential differences in experimental settings.

The comparability with other research work indicates both coherencies and discrepancies. While the role of MSG as a potential oxidative stress inducer is increasingly known, this study's findings suggest that its effects in diabetic states may not be strictly additive. Researchers noted similar observations in studies involving dietary antioxidants, where context-dependent interactions influenced the outcomes of oxidative stress markers (Vieceli Dalla Sega *et al.*, 2017). Meanwhile, the lack of protective effects in the MSG + Diabetes group highlighted the probability that MSG's oxidative burden may overwhelm the antioxidant defenses, even in the presence of potential modulatory factors.

The implications of these findings are extensive, primarily through the lens of rising worldwide diabetes prevalence and high MSG consumption in low-resource settings. Diabetic kidney disease (DKD) persists, causing a significant generation of morbidity and mortality, especially in developing countries (Hoogeveen, 2022). The potential contribution of MSG to DKD progression highlights the need for dietary caution and public health developments, specifically in regions with inadequate accessibility to health services. Dramatically, the function of dietary programs and antioxidant therapies in alleviating MSG-induced renal damage is a crucial intervention program. Research pointed out that dietary antioxidants, such as vitamins C and E, can lower oxidative stress and enhance renal outcomes in animal models (Hoogeveen, 2022). However, this study does not show significant protective effects, which highlights the possibility that MSG-induced oxidative stress and diabetes synergistically aggravate renal damage. These findings justify additional exploration into dose-dependent effects and possible therapeutic improvements.

This study's limitations merit consideration. The alloxan-induced diabetic model, while widely used, may not fully replicate the complexity of human diabetes (Moldovan et al., 2023). Additionally, the study did not explore varying MSG doses or associations with pharmacological treatments for diabetes. Longitudinal research integrating these variables, alongside advanced imaging and molecular techniques, could offer a more extensive comprehension of the MSG's effects on renal role in diabetic conditions (Moldovan et al., 2023).

The findings also raise broader questions about the safety of MSG ingestion in populations at risk of metabolic disorders. While MSG's flavor-facilitating criteria add to its extensive use, its possibility to aggravate oxidative stress and weaken renal function underlines regulatory oversight requirements. Public health agencies should examine these findings when improving dietary guidelines, especially for susceptible populace with increased diabetes prevalence.

This research underlines MSG's possibility to aggravate renal oxidative stress and dysfunction in diabetes, highlighting its public health implications. While MSG's effects seem complex and context-dependent, the findings stressed the requirement for dietary precaution and further study into alleviating strategies. Future research should explore the molecular trajectory underlying MSG's effects, examine dose-dependent responses, and analyze the efficacy of antioxidant supplementation in alleviating its impact on diabetic kidney disease. This understanding will be vital for enhancing dietary recommendations and improving the therapeutic framework to tackle MSG-related health hazards.

Conclusion

This research revealed that monosodium glutamate (MSG) ingestion induces oxidative stress, adding to renal damage marked by tubulointerstitial fibrosis. These findings underline the possible nephrotoxic effects of MSG, especially in diabetic situations, stressing the requirement for public health improvements. Attempts to increase awareness about the possible hazards of extreme MSG ingestion, particularly among the susceptible populace, are essential. Consequently, facilitating dietary alterations and enforcing protective strategies may alleviate the negative impact of MSG on renal health, in the long run, adding value to health services and lowering disease strains.

Recommendations

1. Diabetic patients should avoid meals flavored with monosodium glutamate (MSG) to minimize the risk of renal oxidative stress and associated damage.
2. Public health interventions should advocate for the awareness of MSG's possible nephrotoxic effects, especially among the populace with diabetes.
3. Additional study is required to examine secure dietary options and enhance our understanding of MSG's long-term impact on renal health in susceptible populace.
4.

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