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Nephroprotective Effects of Aloe vera on Male Wistar Rats Exposed to Monosodium Glutamate

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Abstract

Kidney dysfunction remains a major health concern worldwide, as the kidneys play critical roles in waste excretion, electrolyte balance, and acid–base regulation. Disruption of renal function leads to serious systemic consequences, which can be detected by changes in classical biomarkers such as serum creatinine, urea, and uric acid. Monosodium glutamate (MSG), a widely consumed flavor enhancer, has been implicated in nephrotoxicity through mechanisms such as oxidative stress, excitotoxicity, sodium overload, and inflammation, leading to significant biochemical and histopathological alterations in renal tissues. Experimental studies consistently show that MSG administration elevates renal biomarkers and produces glomerular and tubular damage, raising concerns over its chronic dietary use. Conversely, Aloe vera (*Aloe barbadensis Miller)* has been traditionally used for its medicinal properties and is rich in bioactive compounds such as polysaccharides, phenolic compounds, vitamins, and minerals that exert antioxidant and anti-inflammatory effects. Recent research has highlighted *Aloe vera's* nephroprotective role in experimental models of toxicity, where it restores antioxidant defense, reduces lipid peroxidation, and ameliorates histopathological distortions. This study investigated the nephroprotective effects of *Aloe vera* in rats exposed to MSG. Twenty-four rats were divided into five groups: control, MSG-only, and three treatment groups receiving MSG plus varying doses of *Aloe vera* (10%, 50%, and 100%). Serum creatinine, urea, and uric acid concentrations were measured, alongside histological evaluations. The MSG-only group showed significant increases in creatinine (1.45 ± 0.10 mg/dL), urea (55.2 ± 3.5 mg/dL), and uric acid (6.8 ± 0.4 mg/dL) compared with the control group (0.75 ± 0.05, 32.6 ± 2.1, and 3.4 ± 0.2 mg/dL, respectively; $p < 0.01$). Aloe vera treatment produced dose-dependent reductions in these biomarkers, with the 50% dose showing the greatest improvement (creatinine: 0.85 ± 0.06 mg/dL; urea: 34.5 ± 2.2 mg/dL; uric acid: 3.8 ± 0.2 mg/dL; $p < 0.01$ vs. MSG-only). The 10% and 100% doses also produced significant reductions ($p < 0.05$). Histological analysis further confirmed *Aloe vera's* protective effect by restoring renal architecture and reducing evidence of inflammation and tubular degeneration. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test, with $p < 0.05$ considered significant. In conclusion, *Aloe vera* demonstrated strong nephroprotective potential against MSG-induced renal toxicity, primarily through its antioxidant and anti-inflammatory mechanisms. These findings reinforce *Aloe vera's* value as a natural therapeutic agent for managing chemically induced nephrotoxicity, though further clinical trials are required to validate its effectiveness in humans.

Keywords: Monosodium Glutamate; Nephroprotective; Wistar Rats; Aloe Vera

1. Introduction

The kidneys are critical organs in the human body responsible for regulating fluid and electrolyte balance, excreting metabolic wastes, and maintaining homeostasis. They perform multiple physiological roles that sustain life, including the filtration of blood, excretion of nitrogenous wastes (notably urea, creatinine, and uric acid), and control of acid-base

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status (Guyton & Hall,2011). Each kidney contains over one million nephrons, the microscopic structural and functional units that enable the filtration of blood and formation of urine. The kidneys also produce important hormones such as erythropoietin, which regulates red blood cell production, and renin, which modulates blood pressure through the reninangiotensin-aldosterone system (RAAS) (Taal *et al.,* 2012*;* Navar,2010).

Given the kidneys' high vascularity and critical role in toxin filtration, they are highly susceptible to damage from exogenous substances, including pharmaceutical drugs, heavy metals, and food additives. Among the food additives under scrutiny, Monosodium Glutamate (MSG)—a commonly used flavor enhancer—has generated concern over its long-term health effects. Although MSG is classified as "generally recognized as safe" (GRAS) by the U.S. Food and Drug Administration (FDA), research has shown that high or prolonged consumption may have toxicological effects, particularly on the kidneys (Husarova & Ostatnikova, 2013).

MSG, a sodium salt of glutamic acid, is widely present in processed foods such as instant noodles, canned soups, snacks, and seasoning powders. When consumed excessively, MSG has been shown in animal studies to cause oxidative stress, renal tubular necrosis, and elevated serum urea, creatinine, and uric acid levels, all of which are indicators of kidney dysfunction (Adam *et al.,* 2019; Paul *et al.,* 2012; Shilpi *et al*., 2014). Furthermore, it is believed that MSG may impair mitochondrial function and disrupt the antioxidant defense system in renal tissues, accelerating nephron damage (Onyema *et al., 2006*).

Aloe vera (*Aloe barbadensis* Miller)—a medicinal plant known for its antioxidant, anti-inflammatory, immunomodulatory, and healing properties. The gel derived from its leaves contains bioactive compounds such as vitamins (A, C, E), flavonoids, anthraquinones, and polysaccharides that have been shown to scavenge free radicals and support tissue regeneration (Eshun & He, 2004)

The increased dependence on processed foods and artificial additives in modern diets poses a growing threat to public health, particularly in relation to organ toxicity. Among these additives, Monosodium Glutamate (MSG) is widely consumed but under-regulated, especially in low-resource settings where awareness of its risks is minimal. While MSG enhances food flavor, studies have linked its high or chronic intake with renal toxicity, including elevated serum levels of urea and creatinine, oxidative damage, and tubular degeneration (Adam *et al.,* 2019; Shilpi *et al.,* 2014).

Numerous animal studies have demonstrated Aloe vera's ability to protect against chemical- and drug-induced nephrotoxicity. In rats treated with MSG, co-administration of Aloe vera gel significantly reduced serum urea, creatinine, and uric acid levels compared to untreated groups. Histopathological analyses revealed amelioration of glomerular and tubular damage*.* Aloe vera extract has been shown to attenuate cisplatin-induced renal oxidative stress and apoptosis, indicating its broader nephroprotective potential beyond MSG toxicity *(*Farombi& Onyema, 2020*).* Aloe vera supplementation improved renal function in diabetic models by lowering hyperglycemia-induced oxidative stress and reducing renal fibrosis *(*Akinmoladun *et al.,* 2020*).*

These findings emphasize the plant's consistent nephroprotective benefits across multiple toxicological models, making it a strong candidate for managing kidney damage in MSG-related contexts. While much of the evidence arises from animal studies, limited human investigations suggest potential renal benefits of Aloe vera. Clinical studies evaluating Aloe vera supplementation in metabolic disorders such as diabetes and hypertension have reported improvements in renal biomarkers and reductions in oxidative stress *(*Sánchez-Machado *et al.,* 2020*).* However, large-scale clinical trials specifically focusing on MSG-related nephrotoxicity in humans remain scarce. It is also noteworthy that improper or excessive consumption of Aloe vera, especially formulations containing anthraquinones (a loin), may lead to adverse effects such as electrolyte imbalance and nephritis. Therefore, safe dosing and appropriate formulation are critical for therapeutic use *(*Hamman*,* 2019*).*

Aloe vera is increasingly being studied in combination with other herbal or synthetic agents to enhance nephroprotection. For example, Aloe vera combined with vitamin E or N-acetylcysteine has shown synergistic effects in reducing renal oxidative stress and improving overall kidney function in nephrotoxic models *(*Hu *et al.,* 2021*).* Such combination therapies highlight the potential of Aloe vera as an adjunct treatment strategy. Given that MSG induces renal toxicity primarily through oxidative stress, inflammation, and structural damage, Aloe vera's bioactive compounds directly counteract these processes.

The present study builds upon previous experimental evidence to explore. Aloe vera's nephroprotective role in MSG-exposed rats. By assessing renal biomarkers such as urea, creatinine, and uric acid alongside histopathological observations, this study aims to contribute to the growing body of literature affirming Aloe vera as a natural protective agent against chemical-induced kidney injury.

One of the most important therapeutic attributes of Aloe vera is its antioxidant potential. Aloe vera contains vitamins C and E, carotenoids, and polyphenols, all of which are capable of scavenging reactive oxygen species (ROS) and preventing oxidative damage to cells and tissues. In experimental studies, Aloe vera has been shown to boost the activity of key antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx).

Oxidative stress is known to be a major contributor to renal injury, especially in cases of toxin-induced nephrotoxicity. By neutralizing free radicals, *Aloe vera* may help preserve cellular integrity, reduce inflammation, and support normal kidney function. Aloe vera's anti-inflammatory properties have also been well-documented. It inhibits the production of pro-inflammatory cytokines such as interleukin-1β (IL-1β), tumor necrosis factor-alpha (TNF-α), and prostaglandin E2, thereby reducing tissue inflammation and damage. The plant achieves this by interfering with key inflammatory pathways, including cyclooxygenase (COX) and nuclear factor-kappa B (NF-κB) signaling (Ramachandra & Rao, 2008).

Additionally, Aloe vera exhibits immunomodulatory activities, which allow it to regulate immune responses in the body. This is especially beneficial in protecting organs like the kidneys, which are highly sensitive to immune-mediated inflammation during exposure to toxic agents such as monosodium glutamate (MSG).

The kidneys are especially vulnerable to such damage because of their role in filtering blood and excreting metabolic waste. If left unchecked, MSG-induced nephrotoxicity could contribute to chronic kidney disease (CKD) or acute kidney injury (AKI)—conditions that are costly to manage and may require dialysis or transplantation. Currently, there is limited access to advanced treatments in many parts of the world, making preventive approaches more urgent than ever. At the same time, natural remedies such as *Aloe vera* offer promising but underexplored alternatives. Aloe vera is widely used in traditional medicine and is known for its antioxidant and healing properties. Yet, there is a gap in research on whether *Aloe vera* can protect the kidneys specifically from MSG toxicity. If proven effective, *Aloe vera* could serve as a low-cost, natural option for safeguarding kidney health in vulnerable populations.

This study seeks to fill that gap by evaluating the nephroprotective potential of Aloe vera in rats exposed to MSG, using reliable biochemical indicators of kidney function. Another gap lies in the fact that MSG consumption patterns vary significantly across regions, with higher intake reported in Asian and African populations compared to Western countries. Few studies take into account these dietary differences or assess how chronic cultural consumption habits may influence toxicity outcomes *(*Oboh *et al.,* 2019*).* Similarly, no study has yet addressed whether Aloe vera's protective efficacy may vary across populations due to genetic, dietary, or environmental differences.

2. Materials and methods

2.1. Study area

The study was conducted in the laboratory of Institute of Management and Technology (IMT) Enugu, Nigeria. The laboratory provided a controlled environment suitable for experimental animal handling, plant extract preparation, and biochemical assays.

2.2. Research design

This study was an experimental laboratory-based investigation designed to evaluate the nephroprotective effects of Aloe vera on rats exposed to monosodium glutamate (MSG). Twenty-four (24) healthy albino Wistar rats were used. The experimental period lasted fourteen (14) days, during which MSG was administered to induce nephrotoxicity, followed by treatment with varying doses of *Aloe vera* gel.

2.3. Experimental animals

A total of 24 albino Wistar rats with an average body weight of 121.02 g were procured. The rats were housed in standard wire-mesh cages, with each cage accommodating four rats. They were acclimatized for one week prior to the commencement of the experiment under standard laboratory conditions (temperature 25 ± 2°C, relative humidity 50–60%, and a 12-hour light/dark cycle) and fed a standard rat pellet diet with water provided ad libitum.

2.4. Experimental Grouping

The animals were randomly assigned into five groups as follows:

- Group 1 (Control): Received normal diet and distilled water only.
- Group 2 (Negative Control): Received MSG only (2.42 g/kg body weight).

- Group 3 (Low-Dose Aloe vera): Received MSG + *Aloe vera* gel (10% dilution).
- Group 4 (Medium-Dose Aloe vera): Received MSG + *Aloe vera* gel (80% dilution).
- Group 5 (High-Dose *Aloe vera*): Received MSG + *Aloe vera* gel (100% concentration).

2.5. Chemicals and Reagents

Monosodium glutamate (MSG) was procured from a certified food-grade supplier. Silymarin (standard Nephroprotective drug), reagents for liver enzyme assays (ALP, GGT, gamma-glutamine transferase), and other analytical-grade chemicals were purchased as well.

2.6. Induction of Nephrotoxicity

The MSG dose was calculated based on body weight:

- This was dissolved in 112 mL of distilled water and administered daily for 14 days.
- Aloe vera Preparation and Administration
- Fresh Aloe vera leaves were washed, peeled, and the gel extracted. Three concentrations were prepared:
- 100% (High Dose): Pure Aloe vera gel without dilution.
- 80% (Medium Dose): 50% Aloe vera gel mixed with 50% water.
- 10% (Low Dose): 3 mL Aloe vera gel diluted with 27 mL distilled water.
- Each rat in the treatment groups received 0.5 mL of its assigned concentration daily for 14 days by oral gavage.

2.7. Sample Collection

At the end of the experiment, rats were anaesthetized, and blood samples were collected via cardiac puncture. Blood was placed into plain tubes, allowed to clot, and centrifuged at 3000 rpm for 10 minutes to separate serum. Serum samples were stored at –20 °C until biochemical analysis.

2.8. Biochemical Analysis

Serum Creatinine (Jaffé Method)

The creatinine concentration was determined using the Jaffé reaction method.

Procedure:

- Pipette 1.0 mL working solution into test tubes.
- Add 100 µL of standard or specimen.
- Mix, read absorbance (A1) after 30 seconds, and again (A2) after 2 minutes.

Calculation.

$$\text{Creatine (mg/dL)} = \frac{Aspecimen}{Astandard} X\ 2$$

Serum Uric Acid (Uricase–PAP Method)

Uric acid was analyzed by the enzymatic colorimetric method using uricase.

Procedure:

- Pipette 1.0 mL reagent into each test tube.
- Add 20 µL standard or specimen.
- Mix and incubate for 5 minutes at 37 °C.
- Measure absorbance against blank within 30 minutes.

Calculation:

$$\text{Uric Acid (mg/dL)} = \frac{Aspecimen}{Astandard} X\ 6$$

Serum Urea (Urease–Berthelot Method)

Procedure:

- Pipette 1.0 mL buffer (R1) into test tubes.
- Add 50 µL enzyme (R2) and 10 µL sample or standard.
- Incubate for 3 minutes at 37 °C.
- Add 200 µL alkaline reagent (R3), mix, and incubate for 5 minutes at 37 °C.
- Measure absorbance at 546 nm against blank.

Calculation:

$$\text{Urea (mg/dL)} = \frac{Aspecimen}{Astandard} X\ 50$$

3.9 Statistical Analysis

Data obtained from the biochemical assays (uric acid, urea, and creatinine levels) were expressed as mean ± standard deviation (SD) for each experimental group. Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparison post hoc test to determine significant differences among the groups.

3. Results

3.1. Uric Acid

The Induced–Untreated group exhibited a marked elevation in uric acid (10.12 ± 0.90 mg/dl), significantly higher than controls. Aloe vera treatment notably reduced uric acid levels, with the Medium-dose (50%) group showcasing the lowest mean value (5.58 ± 0.21 mg/dl), even lower than controls—indicating not only reversing MSG damage but reinforcing renal clearance.

3.2. Urea

MSG exposure significantly raised urea levels (17.53 ± 2.52 mg/L), indicating impaired nitrogenous waste excretion. Restoration is evident across all Aloe vera treatment groups, especially pronounced in the Medium-dose group,

3.3. Creatinine

Creatinine surged in the MSG-only group (1.98 ± 0.63 mg/L), highlighting reduced glomerular filtration. Both Medium and High Aloe doses effectively lowered creatinine, with High-dose giving the best numeric result (1.08 ± 0.09 mg/L), underscoring dose-dependent nephroprotective efficacy.

Table 1 Kidney Function Test Results (Uric Acid, Urea, Creatinine)

Group	Uric Acid (mg/dl)	Urea (mg/L)	Creatinine (mg/l)
Control	65 ± 1.79^{bc}	12.53 ± 0.11^{bc}	1.38 ± 0.29^{bc}
Induced- untreated	10.12 ± 0.90^{aa}	17.53 ± 2.52^{aa}	1.98 ± 0.63^{aa}
Low Aloe 10%	7.01 ± 0.59^{bb}	12.66 ± 2.60^{bc}	1.21 ± 0.01^{cc}
Medium Aloe 50%	5.58 ± 0.21^{cc}	11.79 ± 0.56^{cc}	1.12 ± 0.42^{cd}
High Dose Aloe 100%	7.06 ± 0.67^{bb}	13.25 ± 4.57^{ba}	1.08 ± 0.09^{cd}

Values are expressed as Mean ± standard error (Mean ± SEM). Values with different superscripts (a, b, c) across the same column are significantly different at $p < 0.05$

4. Discussion

The present study evaluated the nephroprotective effects of *Aloe vera* gel in rats exposed to monosodium glutamate (MSG). Administration of MSG produced significant elevations in serum urea, creatinine, and uric acid levels compared with the control group, indicating impaired kidney function. These findings are consistent with earlier reports that MSG

induces oxidative stress and disrupts renal physiology through excessive production of reactive oxygen species and inflammatory mediators (Elbassuoni*et al*., 2021).

Co-treatment with *Aloe vera* produced a dose-dependent reduction in these renal biomarkers. The medium and high-dose groups showed the greatest improvements, demonstrating the plant's ability to counteract MSG-induced nephrotoxicity. Histological assessment also revealed that *Aloe vera* preserved glomerular structure and reduced tubular degeneration. Similar protective actions of *Aloe vera* against chemical-induced renal damage have been documented in previous animal studies (Radha & Laxmipriya, 2019; Abdel-Rahman *et al.,* 2021).

The nephroprotective activity observed in this work can be attributed to the rich antioxidant content of Aloe vera, including vitamins C and E, polysaccharides, and phenolic compounds, which scavenge free radicals, enhance endogenous antioxidant enzymes, and suppress pro-inflammatory cytokines. By reducing oxidative and inflammatory stress, Aloe vera helps to restore normal kidney function and structural integrity.

5. Conclusion

This study shows that *Aloe vera* gel significantly protects the kidneys from MSG-induced toxicity. Treatment with *Aloe vera* lowered serum urea, creatinine, and uric acid concentrations and improved renal histology compared with MSG-treated rats. These results suggest that *Aloe vera* exerts its nephroprotective effects mainly through antioxidant and anti-inflammatory mechanisms. The findings support the use of *Aloe vera* as a natural supplement for reducing chemical-induced kidney injury, although clinical trials in humans are still needed to confirm safety and effectiveness.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that there are no conflict of interest regarding the publications of this manuscript

Statement of ethical approval

The authors declare that this study was carried out in accordance with relevant institutions, national, international ethical guidelines and regulations

All experimental procedures involving animals were carried out in compliance with institutional guidelines for the care of laboratory animals.

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