Possible Mechanism of *Aframomum Sceptrum* Extracts Mediated Modulation of Renal Function after Monosodium Glutamate Exposure

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Abstract
The objective of the research was to explain the possible mechanism of an earlier reported role of *Aframomum sceptrum* extract in the modulation of renal function parameters in monosodium glutamate-induced toxicity.

Materials and Methods. Similar experimental methods previously reported by us in Ogbeke et al., (2016) were maintained.

Results. Monosodium glutamate administration led to a significant elevation of levels of serum and kidney lipid peroxidation due to decrease in the levels of serum and kidney antioxidant enzyme, super oxide dismutase, catalase, glutathione peroxidase and glutathione. There was observed increase in oxidative enzyme, aldehyde oxidase, sulphite oxidase, xanthine oxidase and monoamine oxidase activities in serum and kidney after monosodium glutamate consumption. *Aframomum sceptrum* treatment significantly regulated all altered indices.

Conclusions. The study concluded that the ability of *Aframomum sceptrum* extract to modulate renal function parameters in monosodium glutamate-induced toxicity is dependent on its efficacy in the induction and mobilization of antioxidant defense armory via the increased synthesis of tissue and serum enzymatic and non-enzymatic antioxidants, as well as improved oxidative enzyme activities that mediates the quenching of rising aldehydes and sulfides, N-oxides and aromatic oxides within the kidney.

Keywords
*Aframomum sceptrum*; oxidative stress; monosodium glutamate; mechanism of kidney function

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Problem statement and analysis of the latest research
Monosodium glutamate (MSG) is known for its ability to enhance palatability and appetite in diets; however, several indicators suggest that it is toxic to humans and experimental animals [1, 2, 3]. Particularly, there are studies indicating negative outcomes on the hypothalamus-pituitary axis of the brain which have led to neuroexcitatory/neuroendocrine effects and induction of obesity [4, 5, 6]. In addition, earlier and very recent studies have examined other metabolic and toxicological indices and reported the induction of oxidative stress through lipid peroxidation (LPO) in different tissues of experimental animals after administration of chronic doses [7, 8, 9, 10, 11].

*Aframomum sceptrum* is a well-known spice among southerners in Nigeria. It is popularly called ataiko and is known for its ability to enhance taste and food aroma and improve several alcoholic and non-alcoholic beverages among Urhobos and Uk-
wuapis of Delta State Nigeria [12, 13]. It has been widely researched and reported to be rich in phytochemicals and possess several ethnopharmacological properties; thus, it is reported for its efficacy in the traditional herbal management of malaria [14], wound healing, management of postnatal malignancies after delivery [15] and the treatment of several models of diabetes mellitus [16, 17]. The efficacy of A. sceptrum extracts has been explored in the preservation of food products like meat and the oxidative deterioration of palm oil [18, 19]. Its efficacy in the prevention of cyanide toxicity in Wistar rats has been reported by Atinaya, D.U et al., [20].

In our earlier report, Ogbeke G.I et al., [21], there was observed a decrease in renal function signified by increased serum urea, creatinine and electrolyte imbalance induced by MSG, while the administration of Aframomum sceptrum contributed to the restoration of these renal malfunctions.

The objective of the research was to explain the possible mechanism of action exerted by Aframomum sceptrum extracts in the modulation of renal malfunction induced by monosodium glutamate toxicity.

1. Materials and Methods

The details of the plant collection and extraction, monosodium glutamate purchase and preparation have been published earlier [21]. Thus, experimental design and protocol for animal handling was the same as published by us earlier [21]; the dose of MSG was the same as in the study published by Farombi and Onyema [22] who reported negative effects on selected biochemical parameters. The dose used for the study, therefore, was a single dose of 4g/g body weight of MSG administered intraperitoneally. This paper is a continuation of our research published earlier to explain the possible underlying mechanism for the observations and reports made by us [21].

1.1 Sample Collection

At the end of the experimental period, rats were sacrificed via cardiac puncture after which blood and kidney samples collected were prepared as described in our previous report [21].

1.2 Biochemical Analysis

Biochemical analysis was carried out following standard protocols and all reagents used were of analytical grade. Based on this, the assay of level of lipid peroxidation (MDA) was carried out by method of Gutteridge and Wilkins [23] and oxidative enzymes was carried out as follows; Aldehyde oxidase (AO) [24], Sulphite oxidase (SO) [25]; Monoamine Oxidase (MO) and Xanthine oxidase (XO) [26]. Ellman [27] for assay of reduced glutathione (GSH). Assay for specific activities of enzymatic antioxidants was done using the methods of Misra and Fridovich [28] for superoxide dismutase (SOD), Cohen et al. [29] for catalase (CAT), Habig et al. [30] and Khan et al. [31] for glutathione peroxidase (GPx).

1.3 Statistical Analysis

Results are presented as means ± standard deviation and analyzed using the analysis of variance (ANOVA), while comparisons were made using least significant difference (LSD) at p < 0.05 level of significance.

2. Results

According to Table 1, MSG administration significantly reduced antioxidant enzyme (SOD, CAT, GPx) activities and levels of GSH in the serum and liver, while the administration of both doses of A. sceptrum extract increased the activities of serum and kidney SOD and CAT, whereas only 350 mgKg⁻¹ increased Gpx activities, and GSH was not reversed.

According to Table 2, all kidney antioxidant activities increased significantly due to the administration of both doses of A. sceptrum (groups C and D) as compared to group B and reduced as compared to group A. The administration of only both doses of A. sceptrum (groups E and F) reduced antioxidant enzyme activities and levels of GSH.

Table 3 and Table 4 show that there were significantly increased MDA levels in the serum and kidney of rats administered only MSG (group B) as
Table 1. Effect of *A. sceptrum* extract on serum antioxidant activities.

<table>
<thead>
<tr>
<th>Groups</th>
<th>SOD (Unitsml⁻¹)</th>
<th>CAT (µmolmin⁻¹ml⁻¹)</th>
<th>GPx (µmolml⁻¹)</th>
<th>GSH (µmolml⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>44.75±2.44ᵃ</td>
<td>56.52±0.85ᵃ</td>
<td>12.08±1.24ᵃ</td>
<td>14.33±1.58ᵃ</td>
</tr>
<tr>
<td>B</td>
<td>21.72±1.73ᵇ</td>
<td>29.74±1.29ᵇ</td>
<td>7.03±0.91ᵇ</td>
<td>7.08±0.84ᵇ</td>
</tr>
<tr>
<td>C</td>
<td>34.56±2.33ᶜ</td>
<td>34.65±1.83ᶜ</td>
<td>6.14±3.14ᵇ</td>
<td>6.05±0.96ᶜ</td>
</tr>
<tr>
<td>D</td>
<td>35.37±3.15ᶜ</td>
<td>42.74±1.59ᵈ</td>
<td>10.08±2.07ᵇ</td>
<td>6.50±1.01ᵃ</td>
</tr>
<tr>
<td>E</td>
<td>37.37±1.15ᶜ</td>
<td>50.19±2.76ᵃ</td>
<td>9.84±1.74ᵇ</td>
<td>9.25±1.81ᵃ</td>
</tr>
<tr>
<td>F</td>
<td>42.70±1.67ᵃᶜ</td>
<td>46.58±2.00ᵈ</td>
<td>8.03±1.06ᵇ</td>
<td>8.03±1.25ᵈ</td>
</tr>
</tbody>
</table>

Note: Values are given as mean ± standard deviation; values not sharing a common superscript alphabet letter in the same column differ significantly at (p < 0.05).
- A = Normal Control;
- B = MSG Control;
- C = MSG+250mg/Kg⁻¹;
- D = MSG+350mg/Kg⁻¹ A. *sceptrum* extract;
- E = 250mg/Kg⁻¹ A. *sceptrum* extract;
- F = 350mg/Kg⁻¹ A. *sceptrum* extract

Table 2. Effect of *A. sceptrum* on kidney antioxidant activities.

<table>
<thead>
<tr>
<th>Groups</th>
<th>SOD (Unitsg⁻¹tissue)</th>
<th>CAT (µmolmin⁻¹g⁻¹ protein)</th>
<th>GSH (µmolg⁻¹ protein)</th>
<th>GPx (µmolmg⁻¹ protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>30.52±0.85ᵃ</td>
<td>42.15±6.23ᵃ</td>
<td>11.33±2.35ᵃ</td>
<td>15.28±2.14ᵃ</td>
</tr>
<tr>
<td>B</td>
<td>20.73±1.05ᵇ</td>
<td>18.38±0.91ᵇ</td>
<td>5.51±0.99ᵇ</td>
<td>6.23±1.08ᵇ</td>
</tr>
<tr>
<td>C</td>
<td>22.11±1.81ᵃ</td>
<td>22.20±9.22ᶜ</td>
<td>7.55±0.69ᶜ</td>
<td>7.04±2.04ᵇ</td>
</tr>
<tr>
<td>D</td>
<td>23.35±1.66ᵃ</td>
<td>25.50±1.83ᵈ</td>
<td>9.50±1.05ᵃ</td>
<td>12.11±1.27ᵃ</td>
</tr>
<tr>
<td>E</td>
<td>26.47±0.96ᵇ</td>
<td>30.05±2.13ᶜ</td>
<td>7.70±0.80ᵃ</td>
<td>14.48±1.64ᵃ</td>
</tr>
<tr>
<td>F</td>
<td>27.79±0.86ᵃ</td>
<td>25.50±1.83ᵃ</td>
<td>5.83±0.75ᵈ</td>
<td>13.98±0.96ᵃ</td>
</tr>
</tbody>
</table>

Note: Values are given as mean ± standard deviation, n = 6; values not sharing a common superscript alphabet letter in the same column differ significantly at (p < 0.05).

Table 3. Effect of *A. sceptrum* on activities of serum lipid peroxidation and oxidative enzymes.

<table>
<thead>
<tr>
<th>Groups</th>
<th>MDA (µmolml⁻¹)</th>
<th>AO (Unitsml⁻¹)</th>
<th>SO (Unitsml⁻¹)</th>
<th>MO (Unitsml⁻¹)</th>
<th>XO (Unitsml⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2.14±0.85ᵃ</td>
<td>4.95±1.26ᵃ</td>
<td>2.84±0.85ᵃ</td>
<td>10.71±1.06ᵇ</td>
<td>8.32±0.95ᵃ</td>
</tr>
<tr>
<td>B</td>
<td>6.77±0.64ᵇ</td>
<td>14.22±0.98ᵇ</td>
<td>8.88±1.09ᵇ</td>
<td>13.14±1.52ᵃ</td>
<td>9.84±1.24ᵃ</td>
</tr>
<tr>
<td>C</td>
<td>6.03±0.87ᵇ</td>
<td>11.20±0.78ᶜ</td>
<td>10.02±0.78ᵇ</td>
<td>11.22±0.78ᵃ</td>
<td>7.40±0.98ᵃ</td>
</tr>
<tr>
<td>D</td>
<td>5.28±1.59ᵇᶜ</td>
<td>13.58±1.88ᶜ</td>
<td>8.04±0.48ᵇᶜ</td>
<td>8.09±1.02ᶜ</td>
<td>7.84±0.58ᵃ</td>
</tr>
<tr>
<td>E</td>
<td>3.60±1.03ᵃᶜ</td>
<td>8.15±1.52ᵈ</td>
<td>6.88±0.96ᵈᶜ</td>
<td>7.28±2.67ᶜ</td>
<td>7.56±0.06ᵃ</td>
</tr>
<tr>
<td>F</td>
<td>3.55±0.67ᵃᶜ</td>
<td>7.63±1.80ᵈ</td>
<td>4.86±0.18ˢ</td>
<td>12.04±2.05ᵇ</td>
<td>9.01±1.40ᵃ</td>
</tr>
</tbody>
</table>

Note: Values are given as mean ± standard deviation, n = 6; values not sharing a common superscript alphabet letter in the same column differ significantly at (p < 0.05).
Table 4. Effect of A. scepbrum on renal oxidative enzyme activities.

<table>
<thead>
<tr>
<th>Groups</th>
<th>MDA (µmol·ml⁻¹)</th>
<th>AO (Units·g⁻¹·tissue)</th>
<th>SO (Units·g⁻¹·tissue)</th>
<th>MO (Units·g⁻¹·tissue)</th>
<th>XO (Units·g⁻¹·tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2.22±1.01 a</td>
<td>3.92±0.68 a</td>
<td>1.88±0.03 a</td>
<td>12.18±2.66 a</td>
<td>10.73±1.15 a</td>
</tr>
<tr>
<td>B</td>
<td>6.44±1.10 b</td>
<td>15.72±1.44 b</td>
<td>10.78±1.17 b</td>
<td>22.08±2.25 b</td>
<td>18.14±2.42 b</td>
</tr>
<tr>
<td>C</td>
<td>5.97±0.76 b</td>
<td>12.08±1.18 bc</td>
<td>9.40±2.34 bc</td>
<td>17.58±2.56 c</td>
<td>11.24±1.14 a</td>
</tr>
<tr>
<td>D</td>
<td>5.59±0.93 b</td>
<td>11.78±3.22 bc</td>
<td>7.24±1.11 c</td>
<td>16.92±1.22 ac</td>
<td>12.46±0.98 a</td>
</tr>
<tr>
<td>E</td>
<td>3.55±0.78 c</td>
<td>9.74±2.06 c</td>
<td>8.32±2.08 bc</td>
<td>14.18±1.98 ac</td>
<td>8.72±1.18 c</td>
</tr>
<tr>
<td>F</td>
<td>3.95±1.02 c</td>
<td>9.88±2.37 c</td>
<td>7.94±1.05 c</td>
<td>13.64±2.05 ac</td>
<td>9.41±3.4 c</td>
</tr>
</tbody>
</table>

Note: Values are given as mean ± standard deviation, n = 6; values not sharing a common superscript alphabet letter in the same column differ significantly at (p < 0.05).

compared to the control group. However, the administration of both doses of A. sceptrum (groups C and D) did not significantly reverse rising MDA. Only A. sceptrum treatment (groups E and F) did not increase MDA levels significantly. Oxidative enzymes (AO, SO, MO) were observed to increase in the serum and kidney of rats treated with MSG only (group B) as compared to the control group; serum XO activities remained significantly unaltered across all groups. Kidney XO significantly increased only in group B and reduced in groups E and F as compared to the control group. Serum AO and SO of rats in Group C reduced significantly as compared to group B, while kidney AO and SO did not reduce significantly. Treatment with A. sceptrum extracts reversed increasing trend of serum and kidney AO in groups D-F except for group D AO which was not significant as compared to group B in the kidney. MSG elevated serum and renal MO activities in group B as compared to the control group, while the administration of A. sceptrum significantly reduced this trend in other groups close to control values.

comes mediated by MSG administration. In our earlier report [21], we hypothesized that the decrease in serum creatinine/urea clearance might be a result of glomerular filtration functionality loss that led to the increase in generation capacities of oxidative stressors. This hypothesis was thus given a level of confirmatory insight owing to the increase in MDA in serum/kidney. Increased LPO is an established attribute for noxiousness and boost in ROS, RNS, superoxide anion (O₂⁻) hydroxyls (OH⁻) and peroxides synthesis capable of compromising tissue architecture [35, 36, 37, 38, 39, 40]. Similarly, the findings in this study are in agreement with earlier studies that were obtained in MDA which gave rise to increased AO, SO, MO and XO enzyme activities and this could also result from their activation by beneficial components inherent in plant extracts [12, 41].

The ability of A. sceptrum extracts to contribute to amplification of antioxidant enzyme activities, a decrease in LPO and oxidative enzymes activities confirms our previous statement [21] about its ability to protect the kidney against MSG-induced oxidative organ deterioration and loss of functional capabilities. This action could become possible due to the high content of phytochemicals such as polyphenols, flavonoids and catechins which were previously used to induce defense against toxic substances. Therefore, it is important to state that the possible mechanism used by MSG to exert its threatening effects on renal function is the constant release of reactive radicals, depletion of antioxidants,

3. Discussion

Perturbations in enzyme activities responsible for systemic defense are established biomarkers of normal responses to the management of negative outcomes due to toxins [32, 33, 34, 35]. The observed decrease in serum and renal antioxidant enzymes (Tables 1, 2) in group B might be a result of compromise of tissue defense against the pernicious out-
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Figure 1. Proposed possible mechanism of *Aframomum sceptrum* modulation of renal function in MSG-induced toxicity.

Concurrent inhibition of oxidative enzymes (AO, SO, MO, XO) which further mediates the gradual loss of kidney architecture (Fig. 1) leading to its inability to successfully filter urea/creatinine in serum, loss of electrolytes and maintenance of proper acid-base balance under normal body functioning as we reported earlier [21]. Similarly, another possible mechanism for the intervention of *A. sceptrum* extract may be due to its ability to influence positively increased synthesis of several component antioxidants against several trespassing toxicants capable of promoting MDA generation (Fig. 1). This is consistent with similar reports of the ability of some plant materials (*Piper longum* Linn and *Moringa oleifera*) to mitigate renal and hepatic malfunction induced by MSG [42, 43].

4. Conclusions

Based on the evidence mentioned above, it is concluded that the ability of *Aframomum sceptrum* extract to modulate renal function parameters in MSG-induced toxicity is dependent on its efficacy in the induction and mobilization of antioxidant defense armory via the increased synthesis of tissue and serum antioxidant and non-antioxidant enzymes, as well as improved oxidative enzyme activities that contributes to the quenching of the negative effects of rising MDA levels within the kidney.
Declaration

The authors declare that there is no conflict of interest and that there was no external source of funding or sponsorship for this study.

References


George BO, Osioma E, Falodun A. Effect of Atiko (Aframomum sceptrum) and African nutmeg (Monodora myristica) on reduced glutathione, uric acid levels and liver marker enzymes in streptozotocin-induced diabetic rats. Egyptian Journal of Biochemistry and Molecular Biology. 2010;28(2). DOI: https://doi.org/10.4314/ejbmb.v28i2.60794


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[37] Asagba SO. Cadmium in our food and drinking water - should we be worried? 70th in the series of inaugural lectures of the Delta State University, Abraka. 2019;14th February, Delsu Press.


[42] Thomas M., Sujatha KS, George S. Protective effect of Piper longum Linn. on monosodium glutamate induced alteration of liver enzymes in Wistar rats.


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