

Research Article

Antioxidant and Nephroprotective Studies on *Telfairia occidentalis* Pod in Experimental Rats

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OPEN ACCESS

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ARTICLE HISTORY

Received: 15/08/2023
Reviewed: 24/11/2023
Revised: 20/03/2024
Accepted: 05/05/2024
Published: 30/06/2024

CITATION

Egbuonu A. C. C., Alaabo P. O., Obike C. A., Atasi O. C., Njoku C. J., Iwuagwu C. J., Akujiobi M. E., Ovuta M. N. and Stanley C. E (2024). Antioxidant and Renal Function Studies on *Telfairia occidentalis* Pod in Experimental Rats. *Nigerian Journal of Biochemistry and Molecular Biology*. 39(2), 99-105
<https://doi.org/10.4314/njbmb.v39i2.9>

ABSTRACT

Monosodium glutamate (MSG) induces nephrotoxicity accompanied with oxidative stress at high dose (8000 mg/kg). Medicinal prospects of underutilized *Telfairia occidentalis* pod, TOP was suggested recently. This study investigated the *in vitro* antioxidant potentials, and *in vivo* antioxidant, renal function and histologic outcomes of TOP extract, TOPE, in MSG-challenged rats after oral exposure for 14 days. *In vitro*, ferric reducing antioxidant power (FRAP), total antioxidant capacity (TAC) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging activity of TOPE concentration-dependently peaked at the highest tested concentration. *In vivo*, MSG caused marked and significant ($p < 0.05$) alterations of the investigated antioxidant and renal function parameters. TOPE either improved, or elicited similar response on these parameters compared to the control, and dose-dependently ($p < 0.05$) diminished the MSG-induced effects. Histologic data revealed that the multifocal degeneration of the renal tubular epithelial cells of MSG-induced rats were absent in the control and others indicating significant degree of repair by TOPE in TOPE co-treatment groups. Thus, TOPE has demonstrated *in vitro* antioxidant capacity and *in vivo* protective inhibition against nephrotoxicity induced by administration of MSG in rats *via* probable antioxidant balancing mechanism.

Keywords: Antioxidant balance, monosodium glutamate, nephroprotective, nephrotoxic response, medicinal prospects

INTRODUCTION

Typical functions of the kidneys include detoxification, homeostasis of body fluids and electrolytes and excretion of toxic metabolic wastes (Ogoburo and Tuma, 2022; Kellum *et al.*, 2021), and production of enzymes and hormones (Puelles and Huber 2022). Thus, toxic assault on the kidneys by xenobiotics affecting any or all of these kidney functions is known as nephrotoxic response. Various mechanisms leading to nephrotoxic response result to the degeneration of the renal tubular epithelial cells and ultimately chronic kidney diseases (Kwiatkowska *et al.*, 2021) and oxidative stress (Ranasinghe *et al.*, 2023). Disruption in host antioxidant balance mechanism leading

to oxidative stress occurs due to up-regulation in molecular oxidation resulting in increased generation of free radicals and consequent stimulation of the membrane lipid peroxidation (Ranasinghe *et al.*, 2023). Such disruptive mechanisms could be triggered by food-borne chemicals, including MSG, a popular food flavour enhancer, and a sodium derivative of the acidic amino acid, glutamate with potential toxic manifestations (Kianifard *et al.*, 2019).

Nephrotoxicity due to monosodium glutamate (MSG) at low dose is not common (Egbuonu *et al.*, 2009). Consistent evidence, however, indicated nephrotoxicity due to a high dose of MSG via selective accumulation of toxic metabolites of MSG by the kidney (Eiya and Inneh 2022; Thongsepee *et al.*, 2022). Possible unintended overdose

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consumption of MSG has been highlighted (Egbuonu and Amadi 2021). Mechanistically, MSG causes overt toxicity by increasing the generation of free radicals through increased oxidative phosphorylation which results to oxidative stress (Banerjee *et al.*, 2020). This implies that restoration of antioxidant balance mechanism would be fundamental to combating MSG-induced intoxication and associated diseased responses on the kidneys either by preventing imbalance of free radicals and oxidants or by inhibiting the generation and accumulation of free radicals using defensive antioxidant system (Egbuonu, 2021; Egbuonu *et al.*, 2022a). Clinical procedures to achieve or manage these are costly, leading to a heightened search for cheap alternatives notably natural products sourced from underutilized plant parts. Recent studies explored the prospects of using fruited pumpkin (common name for *T. occidentalis*) and other plant-based sources to counter MSG-related adverse effect in animal models (Hajihassani *et al.*, 2020; Egbuonu *et al.*, 2022b).

The leaf and seed of *T. occidentalis* (genus of *Cucurbita* and family of *cucurbitaceae*) are consumed the world over (Omimakinde *et al.*, 2018). Fruited pumpkin has diverse natural antioxidant phytochemicals and medicinal properties relevant to combating toxic responses (Ntinya *et al.*, 2019; Kulczyński *et al.*, 2020; Hussain *et al.*, 2023). The fruit pod of *T. occidentalis*, which contains the pumpkin seeds is underutilized (Nyong *et al.*, 2021) and understudied. To the best of our knowledge, the antioxidant and renal function outcomes of *T. occidentalis* pod in MSG-compromised rats to ascertain the possible protection of *T. occidentalis* pod (TOP) on antioxidant, renal function and histopathologic changes in MSG-induced nephrotoxicity have not been reported. Therefore, this study investigated the in vitro antioxidant potential of *T. occidentalis* pod extract (TOPE), as well as its effect on some in vivo antioxidant and kidney function parameters and histopathologic outcomes in MSG-challenged rats.

MATERIALS AND METHODS

Study design and location

Plant material

Fresh pods of *Telfairia occidentalis* (fruited pumpkin) without the seeds were collected in the month of April, 2016 from Ndioro district of Ikwuano, Abia state, Nigeria. Running water was carefully used to rinse the pods which were then dried under room temperature (25 °C), milled, and weighed before extraction.

Assay kits and chemicals

Commercial kits for serum urea and creatinine determination were purchased from Randox Laboratories Ltd., Co-Atrim, UK. A popular commercial brand of MSG was bought from Ubani industrial market in Umuahia, Nigeria. All other reagents used were of analytical grade and were prepared using distilled water.

Experimental animals

Male Wistar rats weighing between 120 to 175 ± 0.5 g were obtained from the animal house unit of the Department of Biochemistry, University of Nigeria, Nsukka Enugu State, Nigeria. The animals were kept in clean aluminum cages under standard environmental conditions. Rats were allowed to acclimatize for 7 days before experiment commenced. They were allowed free access to drinking water and standard rats feed. Protocols of the experiment were approved according to the Guide for the Care and Use of Laboratory Animals by the Animal Ethics Committee, College of Natural Science, Michael Okpara University of Agriculture Umudike, Abia State, Nigeria.

Preparation of extract

Exactly, 200 g of milled *T. occidentalis* pod was extracted in 1.2 L ethanol (99.8 % purity; BDH, UK) for 72 h at 30 °C on a mechanical shaker (Stuart Scientific Orbital Shaker, UK) at room temperature. This was centrifuged at two hundred rpm for 10 min, and the supernatant filtered with Whatman No. 1(125 mm) filter paper and concentrated using a rotary evaporator at 40 °C. In order to achieve the required higher concentrations of 200 and 400 mg/kg body weight used in the animal study, the sample was reconstituted in distilled water before use.

Experimental design

In vitro study

The in vitro antioxidant potentials of TOPE was investigated by determining the ferric reducing antioxidant power (FRAP) against gallic acid equivalent (GAE), total antioxidant capacity (TAC) against ascorbic acid equivalent (AAE) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging activity against that of ascorbic acid equivalent (AAE).

In vivo (animal) study

Twenty male Wistar rats were allotted into five groups of four rats each (n = 4): (1) received 1 mL of normal saline daily, normal control; (2) 8000 mg/kg MSG only; (3) 8000 mg/kg MSG + 200 mg/kg of TOPE; (4) 8000 mg/kg MSG + 400 mg /kg of TOPE; (5) 200 mg/kg of TOPE. Extract and MSG were administered orally once daily for 14 consecutive days. Nephrotoxic response in the rats was evaluated biochemically and histopathologically.

Preparation of serum and tissues

After 14 days of treatment, rats were sacrificed under anesthesia, blood samples were collected by cardiac puncture and transferred into sterilized and properly labeled sample bottles. The blood samples were allowed to stand for 10 minutes at ambient temperature to clot before centrifuging (model SM800B, Surgifriend Medicals, Essex, England) at 3000 rpm for 15 minutes. Sera were obtained for the determination of the parameters. Rats were thereafter quickly dissected, and their kidneys were excised

and transferred into 10 % formalin solution for the histological study.

Determination of *in vitro* antioxidant properties

The FRAP was determined based on the reduction of Fe³⁺ to Fe²⁺ by antioxidant in acidic medium (Benzie and Strain, 1996), total antioxidant capacity (TAC) of the extract was determined by the phosphomolybdate assay method (Umamaheswari and Chatterjee 2007) and scavenging activity on DPPH free radicals was determined using the method of Gyamfi *et al.* (1999).

Determination of serum biochemical parameters

The serum sodium ion (Na⁺) concentration was estimated using colorimetric method based on modified method as described by Trinder (1951) while that of potassium ion (K⁺) concentration was determined using the turbidometric method as described by Henry *et al.* (1974). The serum calcium ion (Ca²⁺) concentration was determined using the colorimetric method as described by Faulker and Meites (1982) while bicarbonate ion (HCO³⁻) was determined using enzyme spectrophotometric procedures as described by Forrester *et al.* (1976). The serum urea concentration was determined using Urease-Berthelot reaction according to Fawcett (1960) while creatinine concentration was determined with Randox commercial kit based on direct endpoint method as described recently (Anuforo *et al.*, 2020).

The lipid peroxidation was estimated by measuring spectrophotometrically the level of the lipid peroxidation product, malondialdehyde (MDA) as described by Wallin *et al.* (1993). The reduced glutathione (GSH) concentration was determined with Randox kit based on the method of Goldberg and Spooner (1983). Activity of catalase (CAT) was determined by the method of Johansson and Borg (1988) whereas the glutathione peroxidase (GPX) activity was determined according to the method of Paglia and Valentine (1967). As contained in the Randox kit, the superoxide dismutase (SOD) activity was assayed by the method of Madesh and Balasubramanian (1998) while uric acid (UA) concentration was determined based on Trinder reaction (Prencipe *et al.*, 1978).

Histological preparation and examination of the kidney

The kidney was prepared and examined for histological alterations as reported recently (Egbonu *et al.*, 2022b). The prepared slides were examined with a Motic™ compound light microscope using × 40 objective lens. The photomicrographs of selected images were captured using a Motic™ 9.0 megapixels microscope camera at × 400 magnification.

Statistical analysis

The descriptive statistics and test for significance in mean of the data were by one-way analysis of variance (ANOVA) with the statistical package for social sciences (SPSS)

version 16. The Duncan's multiple range tests were used to identify the means that differ significantly at $p < 0.05$. Results were expressed as mean ± standard error of mean, SEM ($n = 4$).

RESULTS

In vitro antioxidant properties of *T. occidentalis* pod extract

In vitro, ferric reducing antioxidant power (FRAP) and Total antioxidant capacity (TAC) of TOPE increased with increasing concentration (Table 1). The 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging activity against ascorbic acid equivalent of TOPE peaked at the highest tested concentration (Table 1).

Effect of *T. Occidentalis* extract on some *in vivo* antioxidant parameters

In vivo, MSG increased ($p < 0.05$) levels of MDA, GPX, CAT and SOD but decreased ($p < 0.05$) uric acid and GSH compared to rats in control and other groups. Administration of TOPE altered the antioxidant parameters in a dose-dependent manner compared to rats in the control and those given MSG alone. The GPX and CAT activities significantly ($p < 0.05$) reduced in rats across the test groups compared to those in the control group. The uric acid (UA) and GSH levels significantly ($p < 0.05$) increased while MDA decreased ($p < 0.05$ with little variations of SOD in group 5, 3 and 4 as against group 2 (Table 2).

As depicted on Table 3, MSG only significantly increased ($p < 0.05$) HCO³⁻, Ca²⁺, creatinine and urea but decreased K⁺ and Na⁺ compared to control and others. Similarly, TOPE compared with the control and dose dependently countered the MSG-induced effect on the tested nephritic profiles in rats. Urea and creatinine concentrations were significantly decreased ($p < 0.05$) across the test groups as against group 2 while responses on the serum electrolytes (Ca²⁺, Na⁺, K⁺ and HCO³⁻) in rats across test groups varied significantly ($p < 0.05$) against group 2 rats.

Changes in renal histomorphology

As shown in Figure 1, plates 1, 3, 4 and 5, sections of the kidney collected from the animals in group 1 (control) and groups 3 (MSG, 8000 mg/kg +TOPE, 200 mg/kg), 4 (MSG, 8000 mg/kg +TOPE, 400 mg/kg) and 5 (TOPE, 200 mg/kg only) showed the normal renal histo-architecture with normal Glomeruli (G) in their Bowman's capsules (white arrow) embedded in a framework of normal renal tubules, including proximal convoluted tubules, distal convoluted tubules, pars recta and collecting ducts, (T). However, sections of the kidney (plate 2) collected from the animals in group 2 (MSG, 8000 mg/kg), showed a mild to moderate multifocal degeneration of the renal tubular epithelial cells in the cortex and inner medulla. When compared with the normal tubules (NT), the affected tubules (AT) showed

Table 1. *In vitro* antioxidant capacity of *Telfairia occidentalis* pod extract

Concentration of TOPE ($\mu\text{g/ml}$)	15.63	31.25	62.50	125	250	500	1000
FRAP in GAE (%)	0.154 \pm 0.02	0.170 \pm 0.01	0.174 \pm 0.01	0.175 \pm 0.01	0.177 \pm 0.00	0.178 \pm 0.01	0.182 \pm 0.01
TAC in AAE (%)	0.027 \pm 0.00	0.27 \pm 0.00	0.324 \pm 0.01	0.531 \pm 0.00	0.703 \pm 0.00	1.874 \pm 0.01	3.838 \pm 0.01
% DPPH Inhibition (TOPE)	66.82 \pm 0.04	64.77 \pm 0.03	65.40 \pm 0.05	65.97 \pm 0.04	67.67 \pm 0.10	70.45 \pm 0.01	75.22 \pm 0.03
% DPPH Inhibition (Ascorbic acid)	78.25 \pm 0.02	73.92 \pm 0.04	82.27 \pm 0.03	78.87 \pm 0.06	77.42 \pm 0.12	75.36 \pm 0.10	95.86 \pm 0.05

Results are mean \pm standard error of mean, SEM (n = triplicate determinations)

Table 2. Effect of *T. occidentalis* pod extract on some serum antioxidant status indicators

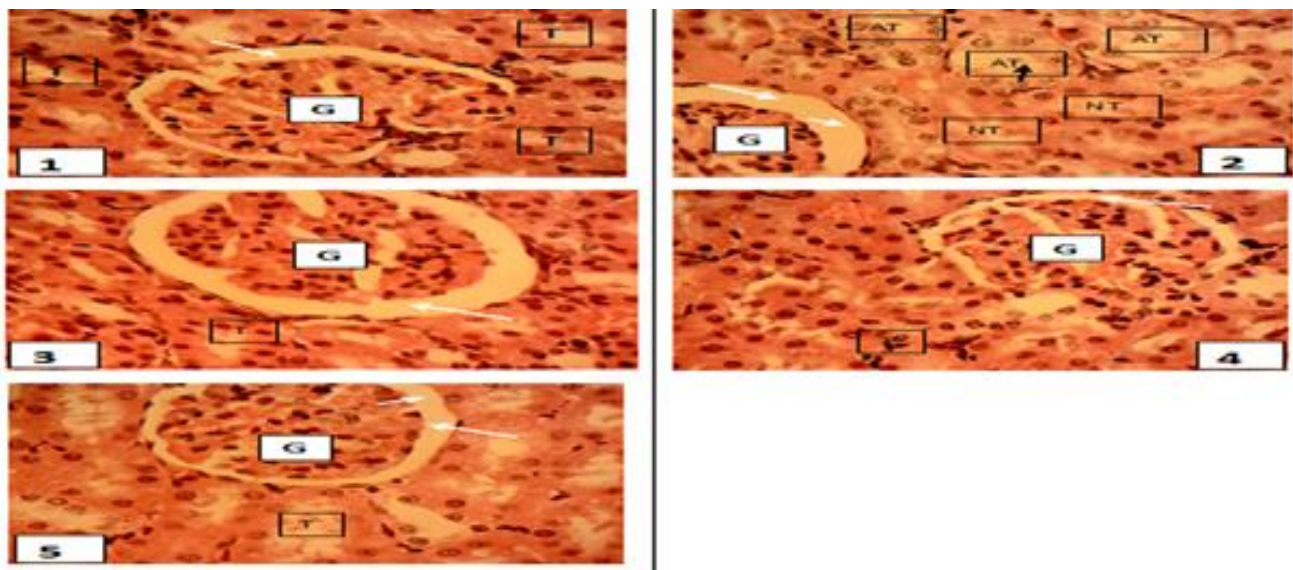
Groups	GPx (IU/L)	CAT (IU/L)	MDA (mg/dl)	SOD (IU/L)	GSH (mg/dl)
1	35.69 \pm 0.62 ^d	1.72 \pm 0.07 ^d	5.11 \pm 0.01 ^b	10.98 \pm 0.13 ^d	3.81 \pm 0.07 ^b
2	62.92 \pm 0.86 ^e	1.97 \pm 0.26 ^e	5.59 \pm 0.07 ^e	11.35 \pm 0.01 ^e	3.26 \pm 0.01 ^a
3	26.89 \pm 1.15 ^b	1.24 \pm 0.25 ^b	5.14 \pm 0.09 ^c	10.45 \pm 0.65 ^a	4.54 \pm 0.05 ^c
4	33.84 \pm 0.40 ^c	0.91 \pm 0.08 ^a	5.16 \pm 0.22 ^d	10.80 \pm 0.09 ^c	4.89 \pm 0.07 ^d
5	24.99 \pm 1.22 ^a	1.55 \pm 0.17 ^c	4.58 \pm 0.14 ^a	10.78 \pm 0.12 ^b	7.70 \pm 0.11 ^e

Results represent mean \pm S.E.M of group serum results obtained (n = 4). Mean values in the same column having different letters of the alphabet, are statistically significant at p < 0.05. Control group (1), MSG group (2), MSG + TOPE (200 mg/kg) group (3), MSG + TOPE (400 mg/kg) group (4) and TOPE (200 mg/kg) group (5)

Table 3. Effect of *T. occidentalis* pod extract on some serum renal function indicators

Groups	HCO ³⁻ (mmol/l)	K ⁺ (mmol/l)	Na ⁺ (mmol/l)	Ca ²⁺ (mmol/l)	Creatinine (mmol/l)	Urea (mmol/l)	UA (mg/dl)
1	29.03 \pm 0.81 ^c	4.58 \pm 0.03 ^e	124.60 \pm 1.37 ^b	4.79 \pm 0.22 ^b	1.32 \pm 0.09 ^d	35.85 \pm 0.61 ^a	6.85 \pm 0.04 ^c
2	32.50 \pm 1.04 ^e	3.79 \pm 0.07 ^a	101.60 \pm 2.26 ^a	5.01 \pm 0.40 ^e	1.47 \pm 0.06 ^e	68.50 \pm 1.85 ^e	6.54 \pm 0.25 ^a
3	31.25 \pm 1.11 ^d	4.46 \pm 0.52 ^d	145.00 \pm 1.22 ^e	4.81 \pm 0.31 ^c	1.14 \pm 0.04 ^a	54.50 \pm 1.04 ^c	6.57 \pm 0.20 ^b
4	28.75 \pm 0.48 ^b	3.94 \pm 0.29 ^b	131.25 \pm 1.03 ^c	5.00 \pm 0.37 ^d	1.25 \pm 0.01 ^c	59.75 \pm 0.48 ^d	6.88 \pm 0.29 ^d
5	22.50 \pm 0.29 ^a	4.20 \pm 0.16 ^c	143.50 \pm 0.29 ^d	4.60 \pm 0.23 ^a	1.21 \pm 0.01 ^b	53.00 \pm 1.15 ^b	7.01 \pm 0.42 ^e

Results represent mean \pm S.E.M of group serum results obtained (n = 4). Mean values in the same column having different letters of the alphabet, are statistically significant at p < 0.05. Control group (1), MSG group (2), MSG + TOPE (200 mg/kg) group (3), MSG + TOPE (400 mg/kg) group (4) and TOPE (200 mg/kg) group (5)

**Figure 1.** Photomicrographs of the effects of *T. occidentalis* pod extract on the renal histomorphology.

Note: Plate 1. Group 1 (Control); Plate 2. Group 2 (MSG only, 8000 mg/kg); Plate 3. (MSG + TOPE, 200 mg/kg); Plate 4. (MSG + TOPE, 400 mg/kg); Plate 5. (TOPE only, 200 mg/kg); Affected tubules = AT; Normal tubules = NT; Glomerulus = G; Bowman's capsule = white arrow; Clear cytoplasmic vacuoles = black arrow

DISCUSSION

This study investigated the *in vitro* antioxidant potentials, and *in vivo* antioxidant, renal function and histologic outcomes of *T. occidentalis* extract, in MSG-compromised rats. This was sequel to the medicinal prospects of underutilized *Telfairia occidentalis* pod, TOP suggested recently (Egbuonu *et al.*, 2022b). It is well established that antioxidant balance mechanism is fundamental to combating oxidative stress and nephrotoxic responses. MSG on the other hand has been shown to induce nephrotoxicity and oxidative stress at doses at and above 8000 mg/kg (Eiya and Inneh 2022; Thongsepee *et al.*, 2022). *In vitro*, ferric reducing antioxidant power (FRAP) in gallic acid equivalent (GAE), total antioxidant capacity (TAC) in GAE and 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging activity in ascorbic acid equivalent (AAE) of TOPE increased with increasing concentration of TOPE and peaked at the highest tested concentration. This indicated that TOPE exhibited concentration dependent *in vitro* antioxidant activity or significant hydrogen donating property. This implies that TOPE could donate hydrogen to pair up with lone pair of the free radicals and as such could act as an antioxidant *in vivo* by scavenging (mopping up) or breaking the free radical chains (Jan *et al.*, 2013; Mbinda and Musangi 2019). The antioxidant activity of TOPE is as expected and could have resulted from various antioxidant activity boosting phytochemicals, including phenols, vitamin C and phytic acid, known to be high in fruited pumpkin (Hussain *et al.*, 2023; Ntinya *et al.*, 2019). This study did not compute the IC₅₀ of TOPE from various concentrations for comparison with that of the respective standards. This is a notable shortcoming that needs to be addressed in future studies.

In vivo, MSG caused marked and significant effect on the assessed renal function parameters (serum urea, creatinine and electrolytes; potassium, sodium, calcium and hydrogen carbonate ions) compared to others. TOPE significantly improved on these assessed parameters compared to the control, and dose-dependently diminished the MSG-induced effects against the control. These indicated the induction of oxidative stress and nephrotoxic responses by MSG in the rats and consistent mitigation of the MSG-induced oxidative and nephrotoxic responses in the rats by TOPE. Increased serum MDA, GP_x, urea and creatinine as recorded herein reflected nephrotoxicity and oxidative stress in rats and humans (Ranasinghe *et al.*, 2023) while variations in sodium and potassium levels were generally attributed to decreased kidney function. Nephrotoxicity is a consistent outcome of MSG at high dose as in this study. In conformity with this research, significant increase ($p < 0.05$) in urea and creatinine levels and variations in serum electrolytes indicators of renal function were observed in the MSG only rats as against the control and others. This confirmed the role of MSG in inducing nephrotoxicity in the rats as earlier reported (Wu *et al.*, 2022). The parameters assessed are acceptable indicators that are relevant to achieving the study aim as entitled and designed. For instance, serum creatinine and urea are direct markers of nephrotoxicity and renal dysfunction used in the

detection of early renal damage (Campos *et al.*, 2018). Treatment with TOPE significantly reversed effect on the renal function parameters caused by MSG. This could be attributed to the inhibition of oxidative phosphorylation by TOPE and mopping up of the free radicals induced by MSG *via* probable up-regulation in the activities of defensive antioxidant enzymes including SOD, GP_x and CAT in the TOPE-treated experimental rats. This is a typical antioxidant balance mechanism suggesting antioxidant balancing capacity as a mechanistic route for the apparent nephroprotective role of TOPE. Consistent and dose-dependent effects of this position were recorded throughout the experiment as confirmed by the indices of kidney and antioxidant markers investigated. The *in vivo* outcome of this study and the suggestion thereto conformed to the significant *in vitro* antioxidant potential of TOPE reported herein.

Furthermore, MSG-induced oxidative response was mitigated by TOPE irrespective of dose. This aligned with the suggested significant antioxidant potential of TOPE and further confirmed the oxidant effect of MSG and antioxidant balancing response of TOPE on the MSG-related nephrotoxicity response. Generally, a notable mechanism through which MSG causes over toxicity is by inducing the generation of free radicals through oxidative phosphorylation (Banerjee *et al.*, 2020). Mechanistically, TOPE through antioxidant balance mechanism which is fundamental to combating toxic and associated diseased responses on the kidneys and other major organs may have mitigated the MSG related effects leading to the observed responses. To support this, the observed elevation of MDA in kidneys of group 2 rats (MSG only) in this study, indicates an MSG-related induction of oxidative stress or increased lipid peroxidation (Thongsepee *et al.*, 2022) which probably resulted from or to a collapse in the antioxidant defence mechanism (Egbuonu *et al.*, 2022a). In further support, TOPE in contrast to MSG only prevented lipid peroxidation in MSG-induced nephrotoxicity in this study. The result agreed with several others which reported that fruited pumpkin has diverse natural antioxidant phytochemicals and medicinal properties relevant to combating toxic responses, including lipid peroxidation inhibition and radical scavenging activity (Ntinya *et al.*, 2019; Kulczyński *et al.*, 2020; Hussain *et al.*, 2023). Also, administration of TOPE increased GSH concentration supporting its nephroprotective role in rats. Increase in GSH concentration as in this study is among the fundamental first line metabolic regulatory pathways essential for homeostasis and protection from oxidative stress (Banerjee *et al.*, 2020).

Histologic results revealed that the multifocal degeneration of the renal tubular epithelial cells of MSG-induced rats (group 2) were absent in the control and others. Unlike those of control and TOPE-treated groups (1, 3, 4 and 5), the lesions observed in group 2 were consistent with nephrotoxicity (Eiya and Inneh, 2022). The histologic outcome of group 2 rats is consistent with the significant

MSG-induced nephrotoxicity and oxidative stress in the rats reported herein. This was as expected. MSG is potentially toxic and could trigger membrane lipid peroxidation while the resultant lipid peroxidation-associated oxidative stress has been strongly associated with nephrotoxicity (Ranasinghe *et al.*, 2023; Kianifard *et al.*, 2019), as evidenced herein by degeneration of the renal tubular epithelial cells in the rats' histology. The histologic outcome also showed that TOPE caused responses comparable to that of the control and mitigated the MSG-induced histomorphologic changes in rats. This suggests that TOPE at the selected dose may not have any adverse effect on the renal function of rats and that the TOPE at the test doses, have an ameliorative effect on MSG-induced nephrotoxicity and oxidative stress. This indicates significant degree of repair by TOPE in TOPE co-treatment groups *via* probable antioxidant balancing effects

CONCLUSION

In this study, the results showed that *T. occidentalis* pod extract, TOPE, has *in vitro* antioxidant capacity. *In vivo*, TOPE exerted a protective effect against nephrotoxicity induced by the administration of MSG in rats possibly by antioxidant balancing mechanism. Thus, TOPE may possess a promising medicinal/therapeutic effect on the antioxidant, renal function and histopathologic outcomes in MSG-compromised rats. Elucidation of the bioactive contents in TOPE is an important step and a guide to discover novel drug hence is recommended for further study.

AUTHORS' CONTRIBUTIONS

Conceptualization, methodology, supervision and writing final review and edition, ACCE; investigation and formal analysis, CJI, MEA, MNO and SCE; writing original draft preparation, POA, CAO, OCA and CJN. All authors have read and agreed to the published version of the manuscript.

FUNDING STATEMENT

The research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

ACKNOWLEDGEMENT

The authors appreciate all that provided technical support for the successful completion of this study.

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