INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Targeting Oxidative Stress and Inflammation in Nephrotoxicity: Evidence from Euphorbia Neriifolia Research

K. Saimahesh [1]*, Keshava murthy S.G [2], Niharika C.P [3], likitha V [4], Preethi S.M [5]

East point college of pharmacy pharmacology. Bangalore Karnataka, India.

ARTICLE INFO

Published: 17 Jun. 2026
Keywords:
Nephrotoxicity; Oxidative stress; Inflammation; Euphorbia neriifolia; Reactive oxygen species; Antioxidants; Cytokines; NF-κB; Renal protection
DOI:
10.5281/zenodo.20731513

ABSTRACT

Nephrotoxicity is a clinically significant complication arising from exposure to a range of therapeutic agents, among them cisplatin, aminoglycoside antibiotics, and radiopharmaceuticals. The underlying pathology is driven principally by oxidative stress, inflammatory cascades, mitochondrial dysfunction, apoptosis, and cytokine-mediated injury. Despite growing awareness of these mechanisms, current nephroprotective options remain constrained by limited efficacy and non-trivial adverse effect profiles, leaving a clear therapeutic gap for safer alternatives. Medicinal plants have attracted increasing attention in this context, particularly those with documented antioxidant and anti-inflammatory activity. Euphorbia neriifolia, a member of the Euphorbiaceae family with a long history in traditional medicine, contains a diverse array of secondary metabolites — triterpenoids, flavonoids, phenolics, sterols, saponins, alkaloids, and glycosides — that collectively confer broad pharmacological activity. Evidence from related plant species suggests that such phytoconstituents protect the kidney by scavenging reactive oxygen species (ROS), attenuating lipid peroxidation, suppressing pro-inflammatory cytokines, modulating NF-κB signalling, restoring antioxidant enzyme activity, and limiting mitochondrial injury. This review examines the global burden of nephrotoxicity and the principal mechanisms through which renal injury develops, with particular attention to oxidative stress, inflammation, and cytokine dysregulation. It also consolidates available evidence on the phytochemistry and pharmacological properties of E. neriifolia, and discusses how widely used experimental models cisplatin- and gentamicin-induced nephrotoxicity have informed our understanding of antioxidant and anti-inflammatory renoprotection. Although direct nephroprotective data for E. neriifolia remain sparse, the cumulative phytochemical and pharmacological evidence strongly supports further targeted investigation

***Corresponding Author:** K. Saimahesh
Address: *East point college of pharmacy pharmacology. Bangalore Karnataka, India*
Email ✉: saimaheshsai2233@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

INTRODUCTION

Nephrotoxicity constitutes a major and persistent challenge in clinical medicine, arising frequently from therapeutic agents including cisplatin, aminoglycoside antibiotics, radiopharmaceuticals, and various other drugs [1,3]. Patients with pre-existing renal impairment carry a disproportionately high burden of nephrotoxic drug exposure, underscoring the critical importance of vigilant monitoring and preventive strategies [1]. Chronic kidney disease and urinary tract infections further heighten susceptibility to antibiotic-associated renal injury [2]. At a mechanistic level, nephrotoxic agents act primarily through oxidative stress, mitochondrial dysfunction, inflammation, and apoptosis — processes that converge to initiate and sustain kidney damage [3].

Among these, oxidative stress occupies a central position. Unchecked generation of reactive oxygen species (ROS) triggers lipid peroxidation, damages proteins and nucleic acids, and disrupts the normal physiology of renal tubular cells [6,7]. The link between ROS accumulation and chronic kidney disease progression is well established, and experimental work has demonstrated that antioxidant agents such as curcumin can meaningfully improve renal function and reduce oxidative markers in disease models [4,5].

Current therapeutic strategies, however, fall short of adequate nephroprotection. Cisplatin-induced oxidative injury remains a dose-limiting obstacle in oncology, while newer antibiotic classes and radioligand therapies continue to carry clinically relevant nephrotoxic risks [8,11]. Advances in kidney microphysiological systems have refined preclinical assessment, yet effective renoprotective interventions are still lacking [11]. Against this background, medicinal plants particularly those with documented antioxidant and anti-inflammatory properties represent a promising avenue of investigation.

Euphorbia neriifolia, commonly referred to as the Indian spurge tree, has a well-documented place in traditional medical systems across South Asia. Earlier work has characterised its ethnobotanical significance, phytochemical composition, and pharmacological activities including antioxidant, anti-inflammatory, antimicrobial, and cytoprotective effects [12,13] and these findings provide a credible foundation for exploring its nephroprotective potential.

2. GLOBAL BURDEN OF NEPHROTOXICITY

Drug-induced nephrotoxicity is a leading cause of both acute kidney injury and chronic kidney disease worldwide [1,3]. Its prevalence is especially pronounced in hospitalised patients, particularly those receiving nephrotoxic agents in the setting of already compromised renal function, where careful drug selection and monitoring become essential [1]. Antibiotic-associated renal injury is of particular concern in patients with urinary tract infections and underlying nephropathy [2].

The mechanisms through which nephrotoxic agents damage the kidney are varied and often intersecting, encompassing oxidative stress, ischaemia, inflammation, tubular obstruction, and direct tubular cytotoxicity [3]. Agents such as cisplatin, aminoglycosides, and radiotherapeutic compounds preferentially injure renal tubular epithelial cells [3,4], while the long-term renal sequelae of radioligand therapies and newer antibiotics add further to the overall clinical burden [5,6]. The emergence of kidney microphysiological models offers improved tools for predicting nephrotoxic risk and evaluating candidate protective interventions [6].

3. ROLE OF OXIDATIVE STRESS AND INFLAMMATION IN KIDNEY DAMAGE

Oxidative stress arises when ROS production outstrips the capacity of the endogenous antioxidant defence system, generating damage across cellular lipids, proteins, and nucleic acids and ultimately impairing renal function [6,7]. Its involvement in the development and progression of chronic kidney disease is firmly established, and there is growing evidence that ROS-driven injury feeds into inflammatory signalling pathways, creating a self-reinforcing cycle of renal fibrosis and tissue destruction [7,8].

Inflammation compounds nephrotoxic injury through the actions of pro-inflammatory cytokines, notably TNF-α, IL-1β, and IL-6, which promote inflammatory cell infiltration, cellular apoptosis, and fibrotic remodelling [8,9]. Compounds that reduce oxidative burden while simultaneously curtailing cytokine production have been shown to substantially improve renal functional parameters and limit the histopathological damage characteristic of established nephrotoxicity [4,5,9].

4. Mechanisms Of Nephrotoxicity

4.1 OXIDATIVE STRESS AND ROS PRODUCTION

Nephrotoxic agents including cisplatin, gentamicin, arsenic, and certain environmental toxins drive oxidative injury in renal tubular cells primarily through excessive ROS generation [38]. The downstream consequences of this ROS burden are wide-ranging: mitochondrial injury, apoptosis, inflammatory signalling, autophagy, and pyroptosis have all been implicated in the progression of drug-induced nephrotoxicity [38].

Natural antioxidants counter these effects by scavenging ROS, bolstering the intrinsic antioxidant defences, and limiting the oxidative cascades that propagate cellular damage in cisplatin-treated kidneys [32]. Polysulfide compounds show notable renoprotective activity through similar mechanisms. When concurrent exposure to toxic elements such as arsenic and antimony occurs, ROS-mediated autophagy and pyroptotic pathways are activated, intensifying the overall renal injury [33].

4.2 LIPID PEROXIDATION

Lipid peroxidation is a direct consequence of oxidative stress, degrading cellular membranes and eroding the structural and functional integrity of the renal tubule [34]. This process perpetuates oxidative damage and is closely linked to the emergence of renal cellular dysfunction and tissue injury. Therapeutic agents capable of interrupting lipid peroxidation including vitamin E and α-lipoic acid have demonstrated protective effects in nephrotoxicity models, in part by limiting oxidative and inflammatory injury [34]. Flavonoid-rich plant extracts have also shown benefit in gentamicin-induced nephrotoxicity, while cilastatin has been reported to attenuate cisplatin-induced lipid alterations and associated tubular damage [35,37].

4.3 CYTOKINE-MEDIATED INFLAMMATION

The pro-inflammatory cytokines TNF-α, IL-1β, and IL-6 are central mediators of nephrotoxic injury, promoting inflammatory infiltration, apoptosis, fibrosis, and through their positive feedback on ROS generation further oxidative damage [38,40]. A growing body of evidence demonstrates that natural bioactive compounds can interrupt these inflammatory pathways. Ursolic acid reduces circulating levels of IL-1β,

IL-6, and TNF-α and attenuates apoptosis and oxidative stress in cisplatin-treated animals . Diosmin exerts comparable renoprotective effects through cytokine modulation and oxidative damage reduction , while phenolic compounds isolated from Tamarix honey alleviate nephrotoxicity by suppressing the IL-6/STAT3/TNF-α axis and blocking oxidative stress-driven apoptosis [40].

4.4 NF-KB SIGNALLING PATHWAY

NF-κB occupies a central regulatory node in the inflammatory and oxidative stress response and plays a well-documented role in nephrotoxicity pathogenesis. Its activation drives renal injury by promoting inflammatory gene expression, apoptosis, and oxidative cellular damage [41]. Natural compounds have proven effective at targeting this pathway: kaempferol attenuates cisplatin-induced nephrotoxicity by modulating NF-κB alongside oxidative stress, inflammation, and apoptosis [41]; umbelliferone protects against gentamicin-induced renal toxicity through suppression of the TLR4/NF-κB-p65/NLRP3 pathway; and apocynin reduces methotrexate-induced nephrotoxicity by inhibiting both NF-κB-p65 activity and the downstream p38-MAPK and IL-6/STAT-3 signalling cascades.

4.5 MITOCHONDRIAL DYSFUNCTION

Mitochondrial integrity is essential for maintaining ATP production and limiting ROS generation within the kidney, and its disruption is an early and important feature of nephrotoxicity [44]. Mitochondrial injury both arises from and amplifies oxidative stress, creating a damaging feedback loop that promotes inflammation and further cellular damage within renal tissues [44]. Leonurine, a natural compound, has been shown to protect against cisplatin-induced nephrotoxicity by simultaneously inhibiting mitochondrial dysfunction, suppressing NLRP3 inflammasome activation, and reducing endoplasmic reticulum stress, demonstrating the therapeutic value of multi-target mitochondrial protection [45].

5. LIMITATIONS OF CURRENT THERAPIES

Despite meaningful advances in our understanding of nephrotoxicity, the therapeutic options currently available remain inadequate. Cisplatin-induced oxidative injury continues to be a major dose-limiting factor in cancer treatment, and newer agents including certain antibiotics and radioligand therapeutics carry their own clinically significant nephrotoxic risks. Existing nephroprotective strategies are often hampered by limited efficacy, adverse effect profiles, or the risk of interfering with the pharmacological action of the primary drug. There is therefore a genuine and pressing need for safer, more effective agents that combine antioxidant and anti-inflammatory activity without compromising therapeutic outcomes.

6. BOTANICAL PROFILE OF EUPHORBIA NERIIFOLIA

Euphorbia neriifolia Linn. (family Euphorbiaceae), commonly known as the Indian spurge tree, is a xerophytic succulent shrub distributed across tropical and subtropical regions [46]. Its distinctive morphology thick fleshy stems, spines, latex-containing tissues,and simple leaves reflects adaptation to arid conditions. Across traditional medicine systems, various parts of the plant (leaves, stems, latex, and roots) have been employed for centuries in the management of inflammatory conditions, respiratory ailments, skin diseases, pain, and infectious diseases. Pharmacological investigation has since validated a broad spectrum of biological activities, including antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, wound-healing, and immunomodulatory effects [13,16,47].

7. PHYTOCHEMICAL CONSTITUENTS RELEVANT TO RENAL PROTECTION

Phytochemical studies of *E. neriifolia* have identified a rich array of bioactive constituents, including triterpenoids, flavonoids, phenolics, sterols, alkaloids, saponins, glycosides, and diterpenes, a profile broadly consistent with the secondary metabolite diversity seen across the genus *Euphorbia*. These compounds account for the plant's antioxidant and anti-inflammatory activities and underpin its overall therapeutic value. Among them, phenolic compounds and flavonoids are of particular relevance to renal protection: they are potent scavengers of ROS generated during oxidative stress, inhibit lipid peroxidation, and modulate key inflammatory mediators. More broadly, phytoconstituents derived from medicinal plants have demonstrated nephroprotective effects by enhancing antioxidant enzyme activity and downregulating inflammatory signalling pathways.

8. TRITERPENOIDS (EUPHOL) AND RENAL PROTECTION

Euphol, the principal triterpenoid of Euphorbia species, possesses well-characterised antioxidant, anti-inflammatory, and cytoprotective properties [52]. Triterpenes from this genus attenuate inflammatory responses through modulation of the PI3K/AKT/Bax and NF-κB/NLRP3 signalling pathways. Euphol has additionally been reported to modulate TGF-β signalling, suggesting a potential anti-fibrotic dimension to its renoprotective activity. Taken together, these properties indicate that the triterpenoid fraction of E. neriifolia may contribute to kidney protection through complementary antioxidant, anti-inflammatory, and anti-fibrotic mechanisms.

9. PHENOLICS AND RENAL PROTECTION

Phenolic compounds are among the most potent natural antioxidants, protecting tissues from

oxidative damage by maintaining redox homeostasis and strengthening cellular defence mechanisms. Polyphenols and their metabolites have been specifically recognised for their nephroprotective effects, reducing oxidative stress and dampening inflammatory signalling in the kidney. Experimental models of chemically induced renal injury have demonstrated that phenolic acids can significantly attenuate nephrotoxic damage, and dietary polyphenols have shown benefit in chronic kidney disease management by supporting antioxidant defences and reducing inflammation. The phenolic fraction of *E. neriifolia* is therefore well positioned to contribute to renal protection through ROS scavenging, inhibition of lipid peroxidation, and modulation of inflammatory cytokine activity.

10. STEROLS AND RENAL PROTECTION

Sterols regulate lipid metabolism and may influence the onset and trajectory of renal disease. Sterol regulatory element-binding proteins (SREBPs) are particularly relevant to diabetic nephropathy, and modulating their activity has been associated with improved renal outcomes and decelerated disease progression. Disruptions in lipid homeostasis are recognised as drivers of renal dysfunction and inflammation, making the maintenance of sterol balance an important consideration in nephroprotection. The sterol constituents of *E. neriifolia* may therefore contribute to kidney health by supporting lipid metabolic homeostasis and modulating inflammatory signalling pathways.

11. EXPERIMENTAL MODELS OF NEPHROTOXICITY

11.1 CISPLATIN-INDUCED NEPHROTOXICITY

Cisplatin-induced nephrotoxicity is the most widely employed experimental model for evaluating nephroprotective interventions. Cisplatin accumulates selectively in renal proximal tubular cells, producing substantial and reproducible kidney injury that closely mirrors the clinical nephrotoxicity observed during chemotherapy, lending the model high translational relevance. Injury develops through overlapping pathological mechanisms: oxidative stress, inflammation, apoptosis, mitochondrial dysfunction, and vascular damage each contribute to the overall picture [62,64]. Natural antioxidants have consistently shown capacity to alleviate cisplatin-induced renal injury by enhancing endogenous antioxidant defences and reducing oxidative damage, and compounds with combined antioxidant and anti-inflammatory activity are increasingly recognised as the most promising candidates for nephroprotection [62,64].

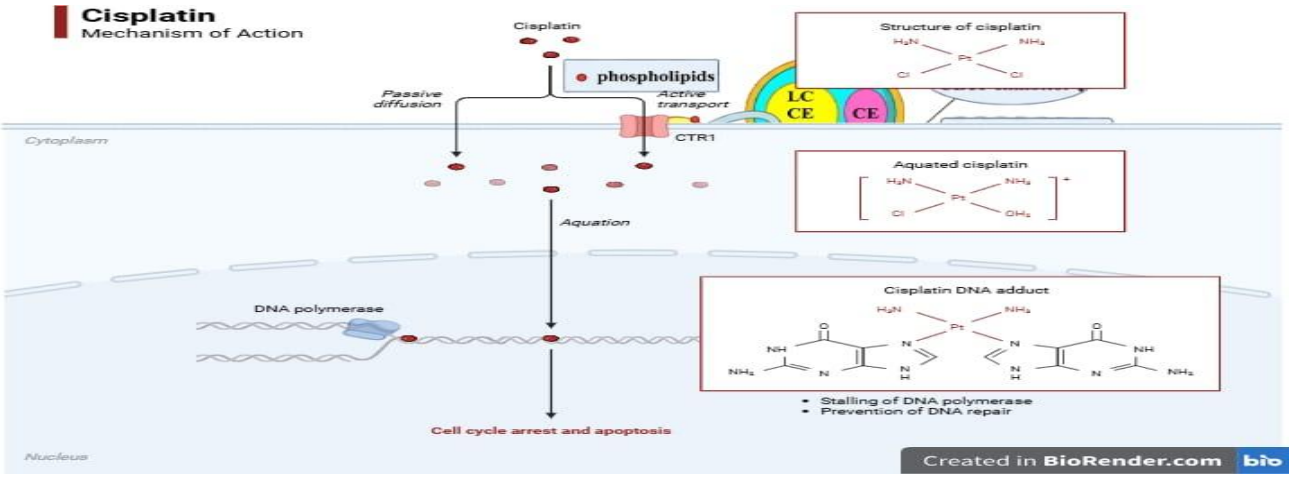

FIG 1: Cisplatin enters renal tubular cells via passive diffusion and transporter-mediated uptake. Once internalised, it undergoes aquation to its active form, which binds DNA and forms adducts, disrupting replication and transcription. The resulting DNA damage triggers cell cycle arrest and initiates apoptotic signalling (Biorender).

11.2 GENTAMICIN-INDUCED RENAL DAMAGE

Gentamicin-induced nephrotoxicity serves as a complementary experimental model for investigating acute kidney injury and assessing candidate renoprotective agents. The injury is characterised by oxidative stress, mitochondrial dysfunction, inflammation, and programmed cell death [65,66]. Programmed necrosis of tubular and collecting duct cells is a notable histopathological feature, contributing substantially to progressive renal tissue loss [65]. Oxidative stress and inflammatory signalling pathways are central to the progression of this injury pattern, culminating in structural damage and functional impairment [66].

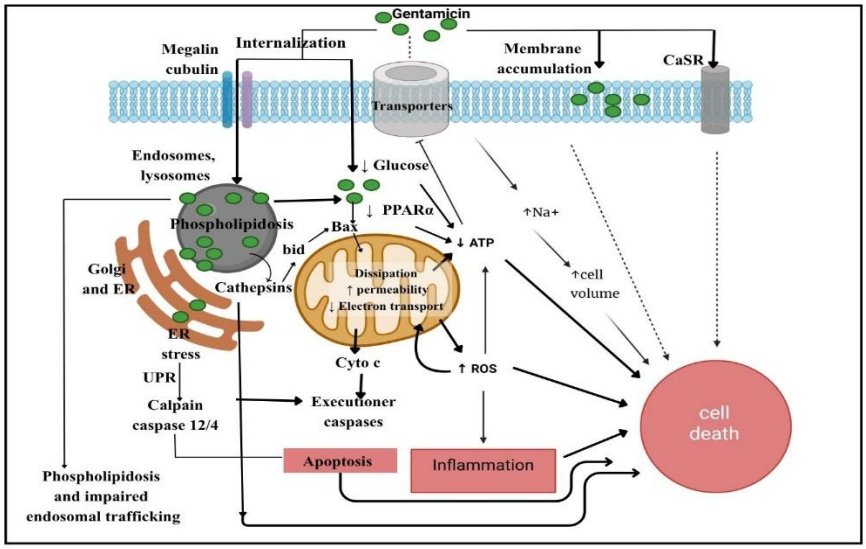

FIG 2: Gentamicin cytotoxicity is initiated by megalin/cubilin-mediated internalisation and membrane accumulation. This triggers endoplasmic reticulum stress, mitochondrial dysfunction via cytochrome c release, impaired ATP synthesis, and elevated ROS production, with apoptotic and inflammatory cell death as the final outcome (Biorender).

12. ANTIOXIDANT ENZYME MODULATION

The kidney's intrinsic antioxidant system centred on superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH) constitutes the primary enzymatic defence against oxidative injury. Preserving the activity of these enzymes is fundamental to redox homeostasis and renal tissue protection. Natural compounds such as quercetin, catechin, and genistein restore these enzyme activities in cisplatin-treated animals, meaningfully reducing oxidative stress-related damage [67]. Natural antioxidants more broadly have been shown to reinforce endogenous defence mechanisms and limit ROS-driven renal injury [63,68]. The bioactive phytochemicals of *E. neriifolia* are thus well placed to support

nephroprotection through enhanced antioxidant enzyme activity and reduced oxidative burden in renal tissues [12,13,68].

13. IN VITRO AND IN VIVO EVIDENCE FOR NEPHROPROTECTION

The nephroprotective potential of *E. neriifolia* is likely to operate through mechanisms comparable to those characterised in other nephroprotective medicinal plants principally antioxidant and anti-inflammatory actions. Medicinal plants assessed in in silico, in vitro, and in vivo nephrotoxicity models have consistently demonstrated kidney-protective effects by reducing oxidative stress and suppressing inflammatory responses [20]. More specifically, certain plant extracts have been shown to protect against cisplatin-induced nephrotoxicity by alleviating oxidative stress and improving renal function markers [21], providing scientific precedent for this class of intervention. Given its rich antioxidant and anti-inflammatory phytoconstituent profile, *E. neriifolia* represents a credible candidate for direct nephroprotective investigation [12,22].

14. FUTURE PERSPECTIVES

While the antioxidant and anti-inflammatory activity of *E. neriifolia* is reasonably well supported, its specific nephroprotective potential requires more systematic investigation. Priority areas for future research include the isolation and structural characterisation of the individual phytoconstituents responsible for renal protection; detailed in vitro and in vivo evaluation across diverse kidney injury models; and mechanistic work focused on the key signalling pathways implicated in nephroprotection, particularly NF-κB, Nrf2, inflammatory cytokines, oxidative stress, and mitochondrial dysfunction. Comprehensive histopathological and biochemical assessment will be essential to substantiate any observed protective effects. Ultimately, rigorous clinical evaluation of safety, tolerability, and therapeutic efficacy will be required before *E. neriifolia* can be considered for application as a nephroprotective agent in human medicine.

15. CONCLUSION

Nephrotoxicity is a clinically important complication driven by converging pathological mechanisms — oxidative stress, inflammation, apoptosis, and mitochondrial dysfunction — that collectively impair renal function. Excess ROS production and heightened inflammatory signalling are the primary engines of kidney injury, and the therapeutic options currently available remain limited and burdened by adverse effects. Cisplatin- and gentamicin-induced experimental models have been instrumental in delineating these mechanisms and in identifying candidate protective interventions. Within this landscape, medicinal plants have emerged as a promising class of nephroprotective agents. *Euphorbia neriifolia*, with its triterpenoids, flavonoids, phenolic compounds, and sterols, possesses the pharmacological profile necessary to protect the kidney through free radical scavenging, inhibition of lipid peroxidation, and modulation of inflammatory signalling pathways. Direct experimental evidence for its nephroprotective activity remains limited, and targeted in vitro, in vivo, and clinical studies are essential to validate this potential and elucidate the molecular mechanisms underlying its renoprotective effects.

REFERENCES

1. Zeleke TK, Kemal LK, Mehari EA, Sema FD, Seid AM, Mekonnen GA, Abebe RB. Nephrotoxic drug burden and predictors of exposure among patients with renal impairment in Ethiopia: a multi-center study. Heliyon. 2024 Jan 30;10(2).

2. Dicu-Andreescu I, Penescu MN, Căpușă C, Verzan C. Chronic kidney disease, urinary tract infections and antibiotic nephrotoxicity: are there any relationships?. Medicina. 2022 Dec 27;59(1):49.
3. Kwiatkowska E, Domański L, Dziedziejko V, Kajdy A, Stefańska K, Kwiatkowski S. The mechanism of drug nephrotoxicity and the methods for preventing kidney damage. International Journal of Molecular Sciences. 2021 Jun 6;22(11):6109.
4. 9.Ali BH, Al‐Salam S, Al Suleimani Y, Al Kalbani J, Al Bahlani S, Ashique M, Manoj P, Al Dhahli B, Al Abri N, Naser HT, Yasin J. Curcumin ameliorates kidney function and oxidative stress in experimental chronic kidney disease. Basic & Clinical Pharmacology & Toxicology. 2018 Jan;122(1):65-73.
5. Ali BH, Al‐Salam S, Al Suleimani Y, Al Kalbani J, Al Bahlani S, Ashique M, Manoj P, Al Dhahli B, Al Abri N, Naser HT, Yasin J. Curcumin ameliorates kidney function and oxidative stress in experimental chronic kidney disease. Basic & Clinical Pharmacology & Toxicology. 2018 Jan;122(1):65-73.
6. Ling XC, Kuo KL. Oxidative stress in chronic kidney disease. Renal Replacement Therapy. 2018 Dec;4(1):1-9.
7. Duni A, Liakopoulos V, Roumeliotis S, Peschos D, Dounousi E. Oxidative stress in the pathogenesis and evolution of chronic kidney disease: untangling Ariadne's thread. International journal of molecular sciences. 2019 Jul 29;20(15):3711.
8. Katanić Stanković JS, Selaković D, Rosić G. Oxidative damage as a fundament of systemic toxicities induced by cisplatin—the crucial limitation or potential therapeutic target?. International Journal of Molecular Sciences. 2023 Sep 26;24(19):14574.
9. Stathopoulos P, Romanos LT, Loutradis C, Falagas ME. Nephrotoxicity of New Antibiotics: A Systematic Review. Toxics. 2025 Jul 19;13(7):606.
10. Steinhelfer L, Lunger L, Cala L, Pfob CH, Lapa C, Hartrampf PE, Buck AK, Schäfer H, Schmaderer C, Tauber R, Brosch-Lenz J. Long-term nephrotoxicity of 177Lu-PSMA radioligand therapy. Journal of Nuclear Medicine. 2024 Jan 1;65(1):79-84.
11. Mahadeo A, Yeung CK, Himmelfarb J, Kelly EJ. Kidney microphysiological models for nephrotoxicity assessment. Current opinion in toxicology. 2022 Jun 1;30:100341.
12. Sultana A, Hossain MJ, Kuddus MR, Rashid MA, Zahan MS, Mitra S, Roy A, Alam S, Sarker MM, Naina Mohamed I. Ethnobotanical Uses, Phytochemistry, toxicology, and pharmacological properties of Euphorbia neriifolia Linn. against infectious diseases: A comprehensive review. Molecules. 2022 Jul 8;27(14):4374.
13. Chaudhary P, Singh D, Swapnil P, Meena M, Janmeda P. Euphorbia neriifolia (Indian spurge tree): A plant of multiple biological and pharmacological activities. Sustainability. 2023 Jan 9;15(2):1225.
14. Gadekar MG, Kathar MN, Sanap GS. Therapeutic Role of Euphorbia Nerifolia their Active Constituents and Pharmacological Activity in Disease prevention and Treatment.
15. Chaudhary P, Meena M, Janmeda P. Microscopic characterization, TLC fingerprinting and optimization of total lipid content from Euphorbia neriifolia (L.) using response surface methodology. Microscopy Research and Technique. 2024 Mar;87(3):565-90.
16. Chaudhary P, Singh D, Swapnil P, Meena M, Janmeda P. Euphorbia neriifolia (Indian spurge tree): A plant of multiple biological and

pharmacological activities. Sustainability. 2023 Jan 9;15(2):1225.
17. Sultana A, Hossain MJ, Kuddus MR, Rashid MA, Zahan MS, Mitra S, Roy A, Alam S, Sarker MM, Naina Mohamed I. Ethnobotanical Uses, Phytochemistry, toxicology, and pharmacological properties of Euphorbia neriifolia Linn. against infectious diseases: A comprehensive review. Molecules. 2022 Jul 8;27(14):4374.
18. Benjamaa R, Moujanni A, Kaushik N, Choi EH, Essamadi AK, Kaushik NK. Euphorbia species latex: A comprehensive review on phytochemistry and biological activities. Frontiers in plant science. 2022 Oct 6;13:1008881.
19. Srivastava S, Panchani D, Modi N. PHYTOCHEMICAL ANALYSIS OF EUPHORBIA SPECIES OF GUJARAT, INDIA: A REVIEW. International Association of Biologicals and Computational Digest. 2024 Mar 27;3(1):22-33.
20. Sujana D, Saptarini NM, Sumiwi SA, Levita J. Nephroprotective activity of medicinal plants: A review on in silico-, in vitro-, and in vivo-based studies. Journal of Applied Pharmaceutical Science. 2021 Oct 3;11(10):113-27.
21. Kpemissi M, Eklu-Gadegbeku K, Veerapur VP, Negru M, Taulescu M, Chandramohan V, Hiriyan J, Banakar SM, Nv T, Suhas DS, Puneeth TA. Nephroprotective activity of Combretum micranthum G. Don in cisplatin induced nephrotoxicity in rats: In-vitro, in-vivo and in-silico experiments. Biomedicine & Pharmacotherapy. 2019 Aug 1;116:108961.
22. Kpemissi M, Eklu-Gadegbeku K, Veerapur VP, Potârniche AV, Adi K, Vijayakumar S, Banakar SM, Thimmaiah NV, Metowogo K, Aklikokou K. Antioxidant and nephroprotection activities of Combretum micranthum: A phytochemical, in-vitro and ex-vivo studies. Heliyon. 2019 Mar 1;5(3).
23. Rota C, Morigi M, Cerullo D, Introna M, Colpani O, Corna D, Capelli C, Rabelink TJ, Leuning DG, Rottoli D, Benigni A. Therapeutic potential of stromal cells of non-renal or renal origin in experimental chronic kidney disease. Stem cell research & therapy. 2018 Aug 14;9(1):220.
24. Rossing P, Hansen TW, Kuemler T. Cardiovascular and non‐renal complications of chronic kidney disease: Managing risk. Diabetes, Obesity and Metabolism. 2024 Nov;26:13-21.
25. Perez-Villa F, Lafage-Proust MH, Gielen E, Ortiz A, Spasovski G, Argiles A. The renal patient seen by non-renal physicians: the kidney embedded in the 'milieu intérieur'. Clinical kidney journal. 2021 Apr 1;14(4):1077-87.
26. Güntürk İ, Yazici C, Köse SK, Dağli F, Yücel B, Yay AH. The effect of N-acetylcysteine on inflammation and oxidative stress in cisplatin-induced nephrotoxicity: a rat model. Turkish Journal of Medical Sciences. 2019;49(6):1789-99.
27. Sengul E, Gelen V, Yildirim S, Tekin S, Dag Y. The effects of selenium in acrylamide-induced nephrotoxicity in rats: roles of oxidative stress, inflammation, apoptosis, and DNA damage. Biological trace element research. 2021 Jan;199(1):173-84.
28. Casanova AG, Harvat M, Vicente-Vicente L, Pellicer-Valero ÓJ, Morales AI, López-Hernández FJ, Martín-Guerrero JD. Regression modeling of the antioxidant-to-nephroprotective relation shows the pivotal role of oxidative stress in cisplatin nephrotoxicity. Antioxidants. 2021 Aug 26;10(9):1355.
29. Alibakhshi T, Khodayar MJ, Khorsandi L, Rashno M, Zeidooni L. Protective effects of

zingerone on oxidative stress and inflammation in cisplatin-induced rat nephrotoxicity. Biomedicine & Pharmacotherapy. 2018 Sep 1;105:225-32.
30. Zhou J, Nie RC, Yin YX, Cai XX, Xie D, Cai MY. Protective effect of natural antioxidants on reducing Cisplatin‐Induced nephrotoxicity. Disease markers. 2022;2022(1):1612348.
31. Cao X, Nie X, Xiong S, Cao L, Wu Z, Moore PK, Bian JS. Renal protective effect of polysulfide in cisplatin-induced nephrotoxicity. Redox biology. 2018 May 1;15:513-21.
32. Wu H, Huang J. Drug-induced nephrotoxicity: pathogenic mechanisms, biomarkers and prevention strategies. Current drug metabolism. 2018 Jun 1;19(7):559-67.
33. Wan F, Zhong G, Wu S, Jiang X, Liao J, Zhang X, Zhang H, Mehmood K, Tang Z, Hu L. Arsenic and antimony co-induced nephrotoxicity via autophagy and pyroptosis through ROS-mediated pathway in vivo and in vitro. Ecotoxicology and Environmental Safety. 2021 Sep 15;221:112442.
34. Abdelhalim MA, Qaid HA, Al-Mohy YH, Ghannam MM. The protective roles of vitamin E and α-lipoic acid against nephrotoxicity, lipid peroxidation, and inflammatory damage induced by gold nanoparticles. International journal of nanomedicine. 2020 Jan 31:729-34.
35. Ungur RA, Borda IM, Codea RA, Ciortea VM, Năsui BA, Muste S, Sarpataky O, Filip M, Irsay L, Crăciun EC, Căinap S. A flavonoid-rich extract of Sambucus nigra L. reduced lipid peroxidation in a rat experimental model of gentamicin nephrotoxicity. Materials. 2022 Jan 20;15(3):772.
36. Ranasinghe R, Mathai M, Zulli A. Cytoprotective remedies for ameliorating nephrotoxicity induced by renal oxidative stress. Life Sciences. 2023 Apr 1;318:121466.
37. Moreno-Gordaliza E, Esteban-Fernández D, Lázaro A, Aboulmagd S, Humanes B, Tejedor A, Linscheid MW, Gómez-Gómez MM. Lipid imaging for visualizing cilastatin amelioration of cisplatin-induced nephrotoxicity. Journal of Lipid Research. 2018 Sep 1;59(9):1561-74.
38. Tripathi P, Alshahrani S. Mitigation of IL-1β, IL-6, TNF-α, and markers of apoptosis by ursolic acid against cisplatin-induced oxidative stress and nephrotoxicity in rats. Human & Experimental Toxicology. 2021 Dec;40(12_suppl):S397-405.
39. Anwer T, Alshahrani S, Somaili AM, Khubrani AH, Ahmed RA, Jali AM, Alshamrani A, Rashid H, Nomeir Y, Khalid M, Alam MF. Nephroprotective effect of diosmin against cisplatin-induced kidney damage by modulating IL-1β, IL-6, TNFα and renal oxidative damage. Molecules. 2023 Jan 30;28(3):1302.
40. Aati H, Aati SY, Bahr HS, Abdel-Sattar AR, Embaby MA, Reda AM, Abdelmohsen UR, Bringmann G, Hassan HM, Darwish MA. Tamarix honey phenolics attenuate cisplatin-induced kidney toxicity by inhibition of inflammation mediated IL-6/STAT3/TNF-α and oxidative stress-dependent Nrf2/caspase-3 apoptotic signaling pathways. Frontiers in Pharmacology. 2025 Jul 4;16:1584832.
41. Wang Z, Sun W, Sun X, Wang Y, Zhou M. Kaempferol ameliorates Cisplatin induced nephrotoxicity by modulating oxidative stress, inflammation and apoptosis via ERK and NF-κB pathways. Amb Express. 2020 Mar 26;10(1):58.
42. Hassanein EH, Ali FE, Kozman MR, Abd El-Ghafar OA. Umbelliferone attenuates gentamicin-induced renal toxicity by suppression of TLR-4/NF-κB-p65/NLRP-3 and JAK1/STAT-3 signaling pathways. Environmental Science and Pollution Research. 2021 Mar;28(9):11558-71.

43. Hassanein EH, Sayed AM, El-Ghafar OA, Omar ZM, Rashwan EK, Mohammedsaleh ZM, Kyung SY, Park JH, Kim HS, Ali FE. Apocynin abrogates methotrexate-induced nephrotoxicity: role of TLR4/NF-κB-p65/p38-MAPK, IL-6/STAT-3, PPAR-γ, and SIRT1/FOXO3 signaling pathways. Archives of Pharmacal Research. 2023 Apr;46(4):339-59.
44. Fontecha-Barriuso M, Lopez-Diaz AM, Guerrero-Mauvecin J, Miguel V, Ramos AM, Sanchez-Niño MD, Ruiz-Ortega M, Ortiz A, Sanz AB. Tubular mitochondrial dysfunction, oxidative stress, and progression of chronic kidney disease. Antioxidants. 2022 Jul 12;11(7):1356.
45. Zhang Q, Sun Q, Tong Y, Bi X, Chen L, Lu J, Ding W. Leonurine attenuates cisplatin nephrotoxicity by suppressing the NLRP3 inflammasome, mitochondrial dysfunction, and endoplasmic reticulum stress. International Urology and Nephrology. 2022 Sep;54(9):2275-84.
46. Bigoniya P, Rana A. A comprehensive phyto-pharmacological review of Euphorbia neriifolia Linn. Pharmacognosy Reviews. 2008 Jul 1;2(4):57.
47. Chaudhary P, Singh D, Swapnil P, Meena M, Janmeda P. Euphorbia neriifolia (Indian spurge tree): A plant of multiple biological and pharmacological activities. Sustainability. 2023 Jan 9;15(2):1225.
48. Lien EJ, Lien LL, Wang R, Wang J. Phytochemical analysis of medicinal plants with kidney protective activities. Chinese journal of integrative medicine. 2012 Oct;18(10):790-800.
49. Sundararajan R, Bharampuram A, Koduru R. A review on phytoconstituents for nephroprotective activity. Pharmacophore. 2014;5(1-2014):160-82.
50. Rabizadeh F, Mirian MS, Doosti R, Kiani-Anbouhi R, Eftekhari E. Phytochemical classification of medicinal plants used in the treatment of kidney disease based on traditional Persian medicine. Evidence‐based Complementary and Alternative Medicine. 2022;2022(1):8022599.
51. Zrouri H, Elbouzidi A, Bouhrim M, Bencheikh N, Kharchoufa L, Ouahhoud S, Ouassou H, El Assri S, Choukri M. Phytochemical analysis, antioxidant activity, and nephroprotective effect of the Raphanus sativus aqueous extract. Mediterr. J. Chem. 2021;11(84):10-3171.
52. Shaban AF, Abd El Kawy MA, Hamed AR, Salama A. Euphol: chemical and biological aspects: A review. Egyptian Journal of Chemistry. 2025 Jun 1;68(6):705-26.
53. Zhou M, Tan W, Liu J, Gu Z, Zhao J. Euphorbium total triterpenes improve Freund's complete adjuvant-induced arthritis through PI3K/AKT/Bax and NF-κB/NLRP3 signaling pathways. Journal of Ethnopharmacology. 2023 Apr 24;306:116146.
54. Chen CL, Chen YP, Lin MW, Huang YB, Chang FR, Duh TH, Wu DC, Wu WC, Kao YC, Yang PH. Euphol from Euphorbia tirucalli negatively modulates TGF-β responsiveness via TGF-β receptor segregation inside membrane rafts. PloS one. 2015 Oct 8;10(10):e0140249.
55. Singh D, Kaur R, Chander V, Chopra K. Antioxidants in the prevention of renal disease. Journal of medicinal food. 2006 Dec 1;9(4):443-50.
56. Guerreiro Í, Ferreira-Pêgo C, Carregosa D, Santos CN, Menezes R, Fernandes AS, Costa JG. Polyphenols and their metabolites in renal diseases: An overview. Foods. 2022 Apr 6;11(7):1060.
57. Cariddi LN, Escobar FM, Sabini MC, Campra NA, Bagnis G, Decote-Ricardo D, Freire-de-Lima CG, Mañas F, Sabini LI, Dalcero AM.

Phenolic acid protects of renal damage induced by ochratoxin A in a 28-days-oral treatment in rats. Environmental Toxicology and Pharmacology. 2016 Apr 1;43:105-11.

58. Lobene AJ, Biruete A, Mirmohammadali SN, Ellis LM, Cladis DP. Dietary (Poly) phenols in the Management of Chronic Kidney Disease: A Narrative Review. Dietetics. 2025 Nov 7;4(4):51
59. Kandasamy N, Ashokkumar N. Renoprotective effect of myricetin restrains dyslipidemia and renal mesangial cell proliferation by the suppression of sterol regulatory element binding proteins in an experimental model of diabetic nephropathy. European journal of pharmacology. 2014 Nov 15;743:53-62.
60. Jiang T, Liebman SE, Lucia MS, Phillips CL, Levi M. Calorie restriction modulates renal expression of sterol regulatory element binding proteins, lipid accumulation, and age-related renal disease. Journal of the American Society of Nephrology. 2005 Aug 1;16(8):2385-94.
61. Wahl P, Ducasa GM, Fornoni A. Systemic and renal lipids in kidney disease development and progression. American Journal of Physiology-Renal Physiology. 2016 Mar 15;310(6):F433-45.
62. Volarevic V, Djokovic B, Jankovic MG, Harrell CR, Fellabaum C, Djonov V, Arsenijevic N. Molecular mechanisms of cisplatin-induced nephrotoxicity: a balance on the knife edge between renoprotection and tumor toxicity. Journal of biomedical science. 2019 Mar 13;26(1):25.
63. Zhou J, Nie RC, Yin YX, Cai XX, Xie D, Cai MY. Protective effect of natural antioxidants on reducing Cisplatin‐Induced nephrotoxicity. Disease markers. 2022;2022(1):1612348.
64. Zhang D, Luo G, Jin K, Bao X, Huang L, Ke J. The underlying mechanisms of cisplatin-induced nephrotoxicity and its therapeutic intervention using natural compounds. Naunyn-Schmiedeberg's archives of pharmacology. 2023 Nov;396(11):2925-41.
65. Huang H, Jin WW, Huang M, Ji H, Capen DE, Xia Y, Yuan J, Păunescu TG, Lu HA. Gentamicin-induced acute kidney injury in an animal model involves programmed necrosis of the collecting duct. Journal of the American Society of Nephrology. 2020 Sep 1;31(9):2097-115.
66. Gamaan MA, Zaky HS, Ahmed HI. Gentamicin-induced nephrotoxicity: A mechanistic approach. Azhar International Journal of Pharmaceutical and Medical Sciences. 2023 Jun 1;3(2):11-9.
67. Verma PK, Sharma P, Tukra S, Singh B, Sood S, Pankaj NK, Brahma B, Abdi G, Bhat ZF. Functional, Structural and Genetic Modulation in Plasma and Renal Antioxidant Systems by Quercetin, Catechin and Genistein in Cisplatin‐Induced Acute Nephrotoxicity in Wistar Rats. Food Science & Nutrition. 2025 Aug;13(8):e70680.
68. Zhou J, Nie RC, Yin YX, Cai XX, Xie D, Cai MY. Protective effect of natural antioxidants on reducing Cisplatin‐Induced nephrotoxicity. Disease markers. 2022;2022(1):1612348.

HOW TO CITE: K. Saimahesh *, Keshava murthy S.G, Niharika C.P, likitha V, Preethi S.M, Targeting Oxidative Stress and Inflammation in Nephrotoxicity: Evidence from Euphorbia Neriifolia Research, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 6, 4308-4320. https://doi.org/ 10.5281/zenodo.20731513