

Mechanistic Insights into Phytotherapeutic Interventions for Renal Protection and Disease Attenuation

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Abstract

Renal diseases such as acute kidney injury and chronic kidney disease have emerged as an escalating global health problem owing to metabolic complications, increasing age groups, and drug-induced nephrotoxicity caused by drugs such as cisplatin, gentamicin, and paracetamol. Overproduction of reactive oxygen species, sustained inflammation through the action of nuclear factor-kappa B (NF- κ B), mitochondrial dysfunction, and progressive tubulointerstitial fibrosis are some of the interlinked pathological processes. Herbal medicine and phytochemicals have emerged as potential multi-target therapeutics owing to shortcomings of conventional medicine.

The preclinical evaluation of diverse plant varieties including *Nigella sativa*, *Zingiber officinale*, curcumin, silymarin, epigallocatechin-3-gallate, carnosic acid, and ginsenoside Re has demonstrated remarkable nephroprotective effect through numerous models of experimental investigation. The effect is achieved by activating the cytoprotective Nrf2/HO-1 antioxidative system, replenishing endogenous supplies of glutathione and superoxide dismutase, inhibiting the expression of pro-inflammatory cytokines, and regulating the pathways of apoptosis. Therefore, the administration of herbal remedies both in pre-and concurrent treatment modes prevents injury to the proximal tubular brush borders, preserves renal morphology, and normalizes the values of blood urea nitrogen and serum creatinine. It will be necessary to standardize botanical extracts and develop innovative techniques for drug delivery using nanocarriers.

Keywords: Salvia Nephroprotection; Phytotherapy; Drug-induced nephrotoxicity; Oxidative stress; Nrf2/HO-1 pathway

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Introduction

1.1 Epidemiology and pathophysiology of Kidney diseases:

Renal diseases affect more than 10% of adults across the globe, meaning that about 850 million people are afflicted with various kidney problems, with the most common kidney disease being chronic kidney disease (CKD), which is rapidly becoming a major global public health crisis. The rising numbers of patients with type 2 diabetes mellitus, systemic hypertension, metabolic syndrome, and aging have largely contributed to the rising numbers of kidney failures across the globe in recent decades. Kidney diseases are some of the primary reasons for morbidity across the globe and are the cause of cardiovascular deaths (Kovesdy et al., 2022; Francis et al., 2024).

The pathophysiology of progressive renal decline is controlled at the cellular and molecular level by a self-sustaining network of oxidative stress, chronic inflammation, and hemodynamic disturbance. Due in great part to abnormal renin-angiotensin-aldosterone system (RAAS) activation, initial nephron loss causes compensatory intraglomerular hypertension and single-nephron hyperfiltration. In addition to causing podocyte separation and glomerular shear damage, this continuous mechanical stress also causes mitochondrial dysfunction and an excess of reactive oxygen species in tubular epithelial cells. The ensuing oxidative imbalance stimulates the recruitment of macrophages and the long-term release of pro-inflammatory cytokines (such as TNF- α and IL-1 β) by activating transcription factors like NF- κ B (Ma et al., 2023).

Inflammation in its chronic form leads to profibrotic events mediated primarily through TGF- β /Smad pathways towards the end stage of disease progression, thus inducing myofibroblast activation and epithelial to mesenchymal transformation. These processes lead to extensive tubulointerstitial fibrosis, glomerulosclerosis, and extracellular matrix accumulation. Rarefaction of microvasculature and hypoxia of the tubules become worse as fibrotic tissue takes the place of functional parenchyma tissue in a continuous loop of loss of nephrons leading to end-stage renal disease (Francis et al., 2024).

A number of diseases that affect the kidneys include acute kidney injury, drug nephrotoxicity, diabetic nephropathy, chronic kidney disease, among others, where herbal products and natural phytochemicals have proven effective as both main therapies and adjuncts in treatment. Oxidative stress, chronic inflammation, and interstitial fibrosis are the main factors responsible for the development of such diseases. The plants and phytochemical drugs help decrease these factors through multifunctional biological mechanisms (Daoud et al., 2026; Khan et al., 2022)).

Decreasing oxidative stress and cell damage constitute an important mechanism of action for nephroprotective herbs. The reactive oxygen species are efficiently scavenged by the bioactive components of phytochemicals, such as

terpenoids, polyphenols including curcumin and resveratrol, and flavonoids like quercetin and rutin. Besides being potent radical scavengers, these phytochemicals have the ability to activate the Nrf2/HO-1 signaling pathway, which leads to enhanced transcription of antioxidant enzymes like glutathione peroxidase, catalase, and superoxide dismutase. The glomerular podocytes and tubular epithelial cells are thus protected against lipid peroxidation, mitochondrial dysfunction, and apoptosis (Liu et al., 2026).

1.2 Herbs and Kidney diseases:

Herbal medications possess powerful anti-inflammatory action in the renal microenvironment. The NF- κ B pathway is an important participant in the macrophage accumulation and excessive production of inflammatory cytokines in response to renal pathological stress. Plant-derived molecules inhibit the expression of NF- κ B, hence downregulating other inflammatory mediators including inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2), interleukin-1 beta (IL-1 β), and tumor necrosis factor-alpha (TNF- α). These plant components efficiently prevent the cellular necrosis and microvascular injury in the renal parenchyma through suppressing this inflammatory pathway (Rapa et al., 2019).

Herbal formulations play an important role not only in immediate protection but also in the prevention of renal fibrogenesis and organ remodeling. The TGF- β /Smad pathway and RAAS dysregulation lead to epithelial-mesenchymal transformation, resulting in excessive accumulation of the extracellular matrix that results in terminal renal failure. Some examples of herbal medicines used traditionally for the protection of the kidney include *Boerhavia diffusa* (Punarnava), *Astragalus membranaceus*, and *Tribulus terrestris*. They prevent the fibrogenic collagen synthesis and expression of TGF- β 1 (Lee et al., 2024; AlAhmad et al., 2024).

Examples of serum markers of kidney function that are always improved after phytotherapy include blood urea nitrogen (BUN), serum creatinine levels, and proteinuria in preclinical models of kidney injury such as those caused by cisplatin, gentamicin, and ischemia-reperfusion injuries in mice. Histopathological analyses usually show the presence of low interstitial fibrosis and integrity of tubular brush borders after phytotherapy. In general, natural products are promising sources for the development of new kidney protective drugs and supplements because of their complicated pharmacodynamics, including antioxidative, anti-inflammatory, anti-apoptotic, and anti-fibrotic activities (Asgharpour et al., 2021).

1.3 Molecular mechanism of herbs to treat kidney disease:

1.3.1 Herbal as Antioxidant:

MDA and/or TBARS in the kidney represent markers of the inhibition of the lipid peroxidation cascade, which represents the first important criterion. The proximal tubular epithelium and glomerular podocytes cells are more vulnerable to damage from ROS due to an abundance of polyunsaturated fatty acids in the cellular membranes following toxic or ischemic injuries. This free radical cascade leads to injury to the intracellular structures and breakdown of the structural lipids in the membranes, resulting in necrotic or apoptotic cell death. Phytoconstituents such as flavonoids, polyphenols, and terpenoids prevent this cascade by neutralizing the hydroxyl and peroxy radicals and inhibiting the accumulation of kidney MDA in a dose-dependent way as shown in Figure 1 (Sujana et al., 2021).

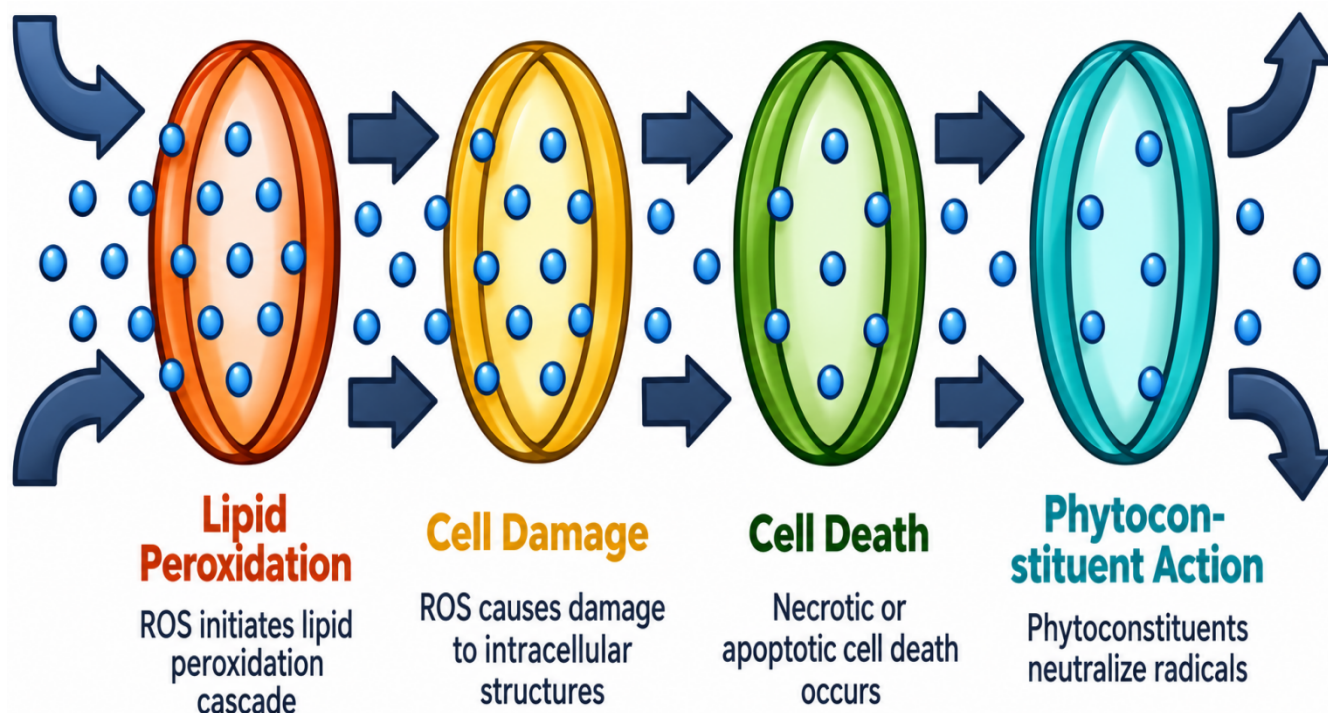
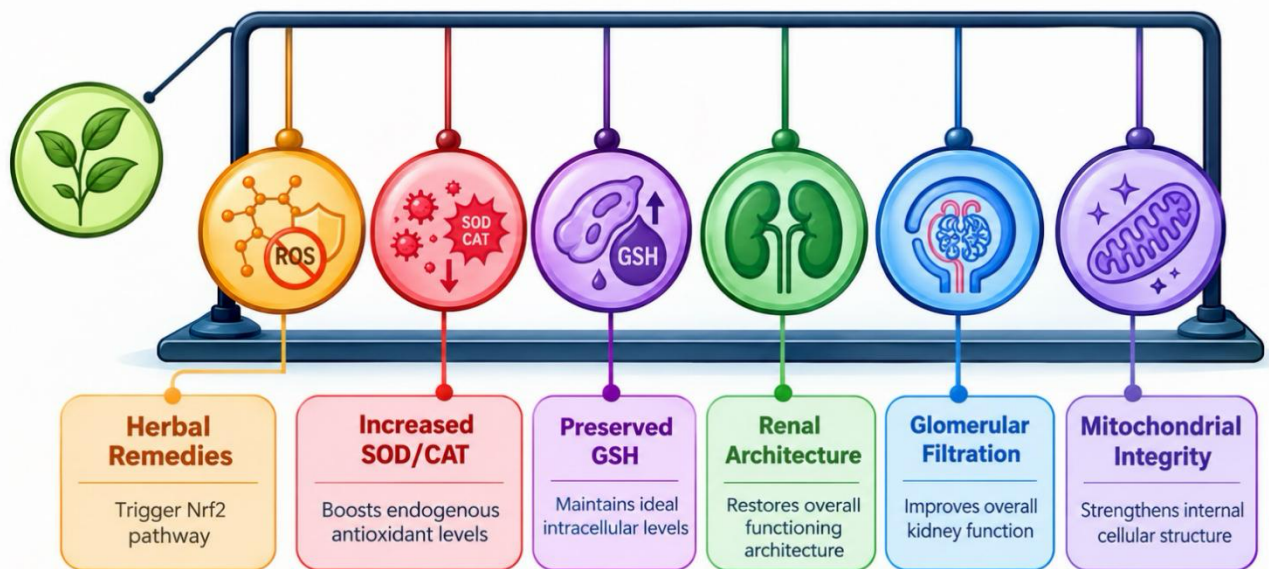


Figure 1: Phytoconstituents and Neuroprotection

Superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) levels are the main indicators of the second important parameter, which is the restoration of endogenous enzymatic and non-enzymatic antioxidant reserves. The physiological pool of these endogenous scavengers is quickly exhausted under prolonged nephropathological stress, rendering the renal parenchyma vulnerable to increasing oxidative damage. By triggering the nuclear factor erythroid 2-related factor 2 (Nrf2) transcriptional pathway, which increases the production of SOD and CAT and preserves ideal intracellular GSH levels, herbal remedies combat this fatigue. Restoring this internal enzymatic defense maintains overall functioning renal architecture, improves glomerular filtration, and strengthens mitochondrial integrity as depicted in Figure 2.

**Figure 2: Antioxidant and phytoconstituents to protect Kidney**

1.4 Benefits of herbals in kidney diseases:

By counteracting the early oxidative, inflammatory, and apoptotic processes caused within the kidney parenchyma, herbs offer substantial protection against the nephrotoxic effects of medications and chemicals. Metabolically active proximal tubular epithelial cells are mainly affected due to exposure to commonly used nephrotoxic medications like cisplatin, aminoglycosides, contrast agents, and heavy metals because of excessive free radical generation and mitochondrial dysfunction. By removing reactive oxygen species, activating the cytoprotective Nrf2/HO-1 antioxidant mechanism, and decreasing pro-inflammatory NF-kappa B pathways, bioactive plant constituents like flavonoids, polyphenols, and saponins protect the body from these effects. The prophylactic use or simultaneous use of herbs helps reduce the necrosis of the cells, maintain the integrity of the brush border of the tubules, and greatly restore the serum markers of renal function, such as serum creatinine and blood urea nitrogen. Various herbals are reported as antioxidant nephro-protector as shown in table 1.

I'll research real, verifiable studies for each herb from PubMed/Google Scholar. Let me search for nephroprotective antioxidant studies for each. Confirmed: Sahu BD, Rentam KKR, Putcha UK, Kuncha M, Vegi GMN, Sistla R. 2011. Food Chem Toxicol 49(12):3090-3097. PMID 21930180.

I now have all 15 verified references. Let me compile the final table.

Herbal Antioxidant Mechanisms in Nephroprotection — Evidence Table

Sr. No.	Herb Used	Molecular Mechanism for Nephroprotection	Reference
1	Nigella sativa (Black seed)	Ethanollic extract restored renal glutathione (GSH) and superoxide dismutase (SOD), lowered malondialdehyde (MDA), and attenuated paracetamol-induced tubular damage via anti-inflammatory/antioxidant action	Canayakin et al., 2016.
2	Curcuma longa (Curcumin)	Restored renal SOD/catalase and GSH, reduced lipid peroxidation and TNF- α , protecting against cisplatin-induced experimental nephrotoxicity	Kuhad A, et al., 2007.

3	<i>Zingiber officinale</i> (Ginger)	Ethanol extract (alone/with α -tocopherol) scavenged reactive oxygen molecules (ROM), preserving renal antioxidant status against cisplatin-induced acute renal failure	Ajith et al., 2007.
4	<i>Vitis vinifera</i> (Grape seed proanthocyanidin)	GSPE restored renal GSH, SH-groups, SOD and GST while lowering MDA, H ₂ O ₂ , NO and DNA damage in cisplatin nephrotoxicity	Hassan et al., 2013
5	<i>Silybum marianum</i> (Silymarin)	Decreased oxidative tissue damage and serum creatinine/urea in gentamicin-induced nephrotoxicity via membrane-stabilizing antioxidant flavonolignans	Varzi HN, et al., 2007.
6	<i>Allium sativum</i> (Garlic – Allicin)	Reduced renal MDA, MPO, NOx and TNF- α while increasing GSH and SOD, protecting against gentamicin-induced oxidative nephrotoxicity	El-Kashef et al, 2015.
7	<i>Camellia sinensis</i> (Green tea – EGCG)	Activated the Nrf2/HO-1 antioxidant signaling pathway and suppressed NF- κ B, restoring catalase, SOD, GPx and glutathione in cisplatin nephrotoxicity	Sahin et al., 2010.
8	<i>Rosmarinus officinalis</i> (Rosemary – Carnosic acid)	Potent antioxidant action attenuated oxidative stress markers and renal injury in cisplatin-induced nephrotoxicity	Sahu et al., 2011.
9	<i>Punica granatum</i> (Pomegranate)	Methanolic leaf extract preserved GSH, catalase and SOD activities and reduced lipid peroxidation in gentamicin-induced nephropathy	Mestry et al., 2020.
10	<i>Panax ginseng</i> (Ginsenoside Re)	Attenuated renal oxidative stress (MDA), inflammatory cytokines and apoptosis (Bax/Bcl-2, caspase pathway) in cisplatin-induced kidney injury	Wang et al., 2018.
11	<i>Withania somnifera</i> (Ashwagandha)	Root powder enhanced natural antioxidant defenses and scavenged free radicals, reducing lipid peroxidation in gentamicin-induced nephrotoxic rats	Jeyanthi and Subramanian 2009.
12	<i>Glycyrrhiza glabra</i> (Licorice)	Root extract (glycyrrhizin, glabridin, liquiritin) exerted antioxidant, anti-inflammatory and anti-apoptotic effects against cisplatin-induced nephrotoxicity in vitro/in vivo	Basist et al., 2022.
13	<i>Moringa oleifera</i> (Seed oil)	Modulated antioxidant, anti-inflammatory and antiapoptotic pathways to counter gentamicin-induced nephrotoxicity	Edeogu et al., 2020.
14	<i>Crocus sativus</i> (Saffron – Crocin)	Reduced renal MDA and elevated total thiol/glutathione peroxidase, lowering blood urea/creatinine in cisplatin-induced renal oxidative stress	Naghizadeh et al., 2010.

In a study on rats, Canayakin et al. found that the protective role of *Nigella sativa* seeds in preventing acute kidney injuries resulting from paracetamol intoxication. In response to acute tubular injury, serum urea, creatinine and tissue lipoperoxidation showed a significant rise in toxic doses of paracetamol. There was an increase in reduced glutathione, superoxide dismutase activity and restoration of renal functions with the use of the herbal extract orally prior to intoxication. Tubular structure maintenance and prevention of cell death occurred with histopathological analysis. Thus, the protective properties of *Nigella sativa* seeds are attributed to their antioxidant and membranous stabilizing properties.

Curcumin was found to be efficacious for acute renal damage and inflammation due to cisplatin in experimental mice according to the findings of Kuhad et

al. The administration of cisplatin led to nephrotoxicity, which is confirmed by increased levels of serum creatinine, morphological changes, and elevated levels of TNF- α . Curcumin was able to reduce the levels of TNF- α systemically and in the tissues on a dose-dependent basis, thus inhibiting the subsequent inflammation. Curcumin was further seen to significantly decrease lipid peroxidation in renal tissue and replenish glutathione, catalase, and superoxide dismutase stores.

The toxicity of cisplatin to the kidneys of rats was prevented by the ethanolic extract of *Zingiber officinale* (ginger), alone or together with alpha-tocopherol, as described by Ajith et al. Glomerular filtration rate and oxidative disturbance were significantly decreased because of cisplatin treatment. The ethanolic extract of ginger lowered serum creatinine and blood urea nitrogen

levels back to physiological state before and during the course of treatment. Moreover, the extract lowered the formation of lipid peroxide in renal tissue homogenate and increased the activity of antioxidants in the kidney. Thus, the authors concluded that ginger polyphenols are useful phytotherapy for preventing platinum-induced nephropathy.

According to Hassan et al., in experimental models, grape seed extract both by itself and in combination with fish oil provided protection against kidney damage caused by cisplatin. Exposure to cisplatin caused genotoxic DNA breakage in tubular cells and significant oxidative degradation of membrane lipids. Malondialdehyde concentrations were lowered and renal tissue's enzymatic defense capacity was restored when grape seed extract was administered concurrently. Additionally, the proanthocyanidin-rich extract attenuated acute tubular necrosis and decreased genomic damage. The authors stressed that supplementing with botanical polyphenols prevents oxidative damage and renal cell apoptosis brought on by chemotherapy.

It is through Varzi et al. that the nephroprotective activity of silymarin and vitamin E on tubular injury brought about by gentamicin was revealed in dogs. The exposure to gentamicin led to functional disturbances characterized by excessive loss of proteins, increased levels of blood urea nitrogen and hypercreatininemia. The functional deficits were attenuated through further silymarin treatment and maintenance of normal glomerular filtration rates. In silymarin-treated animals, histology revealed reduced tubular epithelial cell shedding, low cast production and preservation of brush-border membranes.

The authors El-Kashef et al. explained the role of allicin, which is a compound derived from the organosulfur group of *Allium sativum*, in protecting rats against nephrotoxicity due to gentamicin. There was renal dysfunction, oxidative stress, and increased levels of pro-inflammatory cytokines in the kidney tissues due to gentamicin treatment. Treatment with allicin resulted in increased activity of glutathione peroxidase and superoxide dismutase and decreased lipid peroxidation. Allicin also prevented inflammation and nitric oxide generation.

Epigallocatechin-3-gallate (EGCG), an important compound from green tea polyphenols, is noted for its ability to ameliorate nephrotoxic effects of cisplatin in rats through the activation of the Nrf2/HO-1 pathway as suggested by Sahin et al. Antioxidant systems of kidneys were downregulated due to cisplatin exposure, causing oxidative stress and considerable histological damage. EGCG intake resulted in upregulation of the nuclear factor erythroid 2-related factor 2 (Nrf2) as well as synthesis of downstream heme oxygenase-1 (HO-1). Besides correction of high levels of blood urea and serum creatinine, transcription activation also normalized redox balance in cells.

Sahu et al. identified the renoprotective action of carnosic acid in a cisplatin-induced nephropathy rat model. The consequences of cisplatin toxicity included acute renal failure, intracellular glutathione depletion, and higher lipid peroxidation. Carnosic acid

administration kept the activity of antioxidant enzymes intact and minimized the signs of kidney damage through the serum markers, thereby keeping the renal function parameters normal. Furthermore, the researchers noted that carnosic acid decreased the production of pro-inflammatory cytokines in renal parenchyma and inhibited the nuclear translocation of NF- κ B. It was concluded that carnosic acid keeps the tubules intact through reduction in oxidative and inflammatory damages.

Extract of *Punica granatum* (pomegranate) safeguards the structure of renal function against gentamicin nephrotoxicity in rodents, according to Mestry et al. In addition to elevated serum levels of creatinine, urea, and malondialdehyde, the aminoglycoside therapy led to lesions in the proximal tubules. Catalase, superoxide dismutase, and glutathione were replenished in renal tissue homogenates by pomegranate extract administration every day. Histopathological observations showed reduced tubular vacuolation, interstitial edema, and desquamation of the epithelium. The authors report that pomegranate has nephroprotective effects because of its high polyphenols and punicalagin content.

In an experimental model of renal damage induced by cisplatin, the protective actions of ginsenoside Re, which is one of the major saponins of *Panax ginseng*, were outlined by Wang et al. The treatment with cisplatin resulted in cell apoptosis, mitochondrial damage, and severe declines in renal excretory functions. Pre-treatment with ginsenoside Re lowered the markers of oxidative stress and serum urea nitrogen, as well as blood creatinine levels. Moreover, the saponin regulated the protein mediators of apoptosis by preserving Bcl-2 concentrations and suppressing the expression of Bax and caspase-3.

Ginsenoside Re, a major saponin constituent of *Panax ginseng*, exhibited its protective role in an experimentally-induced cisplatin-induced renal injury in rats. Exposure to cisplatin led to cellular apoptosis, mitochondrial toxicity, and severe impairment in renal excretory capacity. Ginsenoside Re decreased markers of oxidative stress and blood urea nitrogen and serum creatinine levels. Moreover, the saponin regulated apoptotic protein signaling, maintaining Bcl-2 expression and decreasing expression of pro-apoptotic Bax and caspase-3. It was thus concluded that the compound inhibited oxidative cell death and tubular apoptosis induced by cisplatin. The nephroprotective efficacy of root extract of *Withania somnifera* (Ashwagandha) was determined by Jeyanthi et al., who demonstrated a dose-dependent preservation of kidneys in rats. The harmful substance decreased the activity of native antioxidant enzymes in the kidney and led to significant lipid peroxidation. Co-administration of *Withania somnifera* restored the levels of glutathione peroxidase, catalase, and superoxide dismutase to physiological levels. Alongside with this, the extract maintained the glomerular architecture and reduced nitrogenous metabolites. It was revealed that the membrane-stabilizing and adaptogenic properties of the herb were due to withanolides.

The metabolic analysis and renoprotective effects of licorice root extract of *Glycyrrhiza glabra* against cisplatin induced toxicity have been studied in vivo and in vitro conditions by Basist et al. Cisplatin in animal studies induced increased levels of biomarkers, decrease in tubular epithelial cell viability, and excess formation of reactive oxygen species. The free radicals were scavenged, lipid peroxidation was decreased, and antioxidants were enhanced in the standardized *Glycyrrhiza glabra* extract. These renoprotective effects of *Glycyrrhiza glabra* are attributed to glycyrrhizin, isoliquiritigenin, and other flavonoids glycosides via chemical analysis.

In a study conducted by Edeogu et al., the role of *Moringa oleifera* seed oil for protection from gentamicin-induced kidney dysfunction in Wistar rats was explored. Oxidative stress, inflammation, and structural damage occurred in the cortical nephron cells due to the action of gentamicin. With the use of *Moringa oleifera* seed oil, endogenous enzymatic mechanisms were potentiated, while the levels of serum urea and creatinine were decreased. In the renal tubular cells, the oil inhibited the apoptosis cascade and downregulated the expression of pro-inflammatory markers. The scientists concluded that the protection from aminoglycoside nephropathy occurs through the anti-inflammatory, anti-apoptotic, and antioxidant activities of the *Moringa* oil.

As mentioned by Naghizadeh et al., crocin, which is a carotenoid that is obtained from *Crocus sativus*, protects rat kidneys against oxidative toxicity induced by cisplatin. Cisplatin-induced intoxication in renal homogenates resulted in depletion of glutathione levels, increase in lipid peroxidation, and decrease in total thiol levels. Treatment with crocin at a dose-dependent level reversed the biochemical changes and regained renal clearance ability. The presence of casts and tubular dilatation were not seen in the rats treated with crocin according to the histology.

Discussion:

More than 10% of adults in the world are affected by kidney disorders including acute renal failure and chronic kidney disease. This makes a serious threat to global public health. An increase in cases of diabetes mellitus, hypertension, metabolic disorders, and aging is closely related to the increase in prevalence of renal failure. Iatrogenic drug-induced nephrotoxicity, where life-saving drugs like antineoplastics such as cisplatin, aminoglycoside antibiotics such as gentamicin, and wrongly used painkillers such as paracetamol often induce further renal failure, is another issue. The importance of having safe multi-target renoprotective agents is stressed by morbidity, cardiovascular deaths, and high costs related to chronic renal failure (Mohandes et al., 2023).

This self-perpetuating cascade of hemodynamic disturbance, oxidative stress, inflammation, and apoptosis-mediated tissue remodeling is involved in the regulation of progressive renal failure pathogenesis at cellular and molecular levels. The accumulation of xenobiotics in the proximal tubular epithelial cells results in the overproduction of ROS and mitochondria

malfunction. One of these mechanisms includes depletion of natural antioxidants such as superoxide dismutase, catalase, and reduced glutathione caused by free radical overproduction as well as lipid peroxidation and damage to membranes. On the other hand, long-term oxidative stress activates NF- κ B transcription resulting in an increase in the pro-inflammatory cytokines TNF- α and IL-1 β . TGF- β /Smad pathway is triggered during chronic phases of the disease due to the inflammatory environment leading to ECM deposition and tubulointerstitial fibrosis and epithelial-to-mesenchymal transition (Kuhad et al., 2007).

In order to disrupt this complex pathogenic cascade, herbal medicines as well as isolated phytoconstituents have shown impressive efficacy in various experimental models of nephrotoxicity. With their ability to directly neutralize free radicals and restore cellular redox equilibrium, herbal preparations as well as biological active compounds such as curcumin, *Zingiber officinale*, grape seed proanthocyanidins, *Nigella sativa*, and *Glycyrrhiza glabra* are able to mitigate the oxidative stress induced by pharmaceutical compounds. Furthermore, some phytochemical compounds such as epigallocatechin-3-gallate (EGCG), carnolic acid, and crocin are able to promote the expression of the cytoprotective pathway of nuclear factor erythroid 2-related factor 2 (Nrf2)/ heme oxygenase-1 (HO-1), thus replenishing the enzymatic antioxidative pool and inhibiting lipid peroxidation (Canayakin et al., 2016).

Moreover, herbal therapies offer excellent anti-inflammatory and anti-apoptotic activities that protect the kidney from inflammation and redox modulation. Some natural compounds that prevent the nuclear translocation of NF- κ B are allicin, carnolic acid, and *Moringa oleifera* seed oil. They decrease the influx of leukocytes into the kidney and suppress the subsequent release of inflammatory cytokines. Also, through the inhibition of caspase-3 and Bax along with Bcl-2 activity, secondary metabolites like ginsenoside Re and the active ingredients in *Punica granatum*, *Withania somnifera*, and silymarin affect intrinsic apoptosis. These phytotherapeutics prevent the extensive shedding of tubular cells, cast formation, and parenchymal necrosis due to apoptotic processes and inflammation.

The significant reduction in blood urea nitrogen, serum creatinine, and proteinuria in preclinical mice clearly demonstrates that the physiological and cellular benefits derived lead to significant functional improvements. These chemical recovery processes are also proven by histopathology, demonstrating reduced fibrogenesis, reduced interstitial edema, and preservation of tubular structures. The combination of radical scavenging, Nrf2 activation, NF- κ B inhibition, and anti-apoptosis signals in these fourteen studies collectively prove that herbal supplements have provided valuable leads for the development of standard adjunct treatments for chronic and acute kidney conditions.

Conclusion:

In conclusion, the necessity for efficient, multitarget cytoprotective methods is highlighted by the rising global prevalence of renal diseases, which are caused by

metabolic comorbidities and drug-induced nephrotoxicity. Single-target synthetic medicines cannot readily address the intricate pathophysiology of kidney disease, which includes overlapping cycles of oxidative stress, persistent inflammation, mitochondrial failure, and increasing parenchymal fibrosis. By scavenging free radicals, activating Nrf2/HO-1 defense pathways, suppressing NF- κ B-mediated inflammation, and preventing apoptotic cell death, botanical extracts and isolated phytochemicals—such as curcumin, *Nigella sativa*, silymarin, epigallocatechin-3-gallate, and ginsenosides—counteract these pathological cascades, according to the experimental results compiled across the assessed studies.

Consequently, the two processes are highly effective in maintaining the integrity of the tubules, reducing interstitial fibrosis, and bringing back the renal function markers like blood urea nitrogen and serum creatinine levels. Despite the fact that preclinical studies suggest the nephroprotective nature of these herbal drugs, there is a need for extensive research to fully exploit their potential. The future efforts should focus on the standardization of phytoconstituent extracts, overcoming the pharmacokinetics and bioavailability challenges with advanced drug delivery systems, and establishing the safety and efficacy through human trials.

Reference:

1. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. *Kidney Int Suppl* (2011). 2022 Apr;12(1):7-11. doi: 10.1016/j.kisu.2021.11.003. Epub 2022 Mar 18. PMID: 35529086; PMCID: PMC9073222.
2. Francis, A., Harhay, M.N., Ong, A.C.M. et al. Chronic kidney disease and the global public health agenda: an international consensus. *Nat Rev Nephrol* 20, 473–485 (2024). <https://doi.org/10.1038/s41581-024-00820-6>.
3. Ma K, Zheng ZR, Meng Y. Pathogenesis of Chronic Kidney Disease Is Closely Bound up with Alzheimer's Disease, Especially via the Renin-Angiotensin System. *J Clin Med*. 2023 Feb 12;12(4):1459. doi: 10.3390/jcm12041459. PMID: 36835994; PMCID: PMC9966558.
4. Daoud, G., Ahsan, F., Mahmood, T. et al. Plant-based nephroprotective agents: a review of strategies to combat drug-induced kidney damage. *Clin Phytosci* 12, 1 (2026). <https://doi.org/10.1186/s40816-026-00417-5>.
5. Khan MA, Kassianos AJ, Hoy WE, Alam AK, Healy HG, Gobe GC. Promoting Plant-Based Therapies for Chronic Kidney Disease. *Journal of Evidence-Based Integrative Medicine*. 2022;27. doi:10.1177/2515690X221079688.
6. Liu H, Huang S, Chen S, Liang S, Huang M, Li S, Xu Y and Xie B (2026) Pharmacological potential of Chinese botanical drugs in managing chronic kidney disease by targeting mitochondrial quality control. *Front. Pharmacol.* 16:1725842. doi: 10.3389/fphar.2025.1725842.
7. Rapa SF, Di Iorio BR, Campiglia P, Heidland A, Marzocco S. Inflammation and Oxidative Stress in Chronic Kidney Disease-Potential Therapeutic Role of Minerals, Vitamins and Plant-Derived Metabolites. *Int J Mol Sci*. 2019 Dec 30;21(1):263. doi: 10.3390/ijms21010263. PMID: 31906008; PMCID: PMC6981831.
8. Lee OYA, Wong ANN, Ho CY, Tse KW, Chan AZ, Leung GP, Kwan YW, Yeung MHY. Potentials of Natural Antioxidants in Reducing Inflammation and Oxidative Stress in Chronic Kidney Disease. *Antioxidants* (Basel). 2024 Jun 20;13(6):751. doi: 10.3390/antiox13060751. PMID: 38929190; PMCID: PMC11201162.
9. AlAhmad, M. M., Al Namer, Y., Palaian, S., & Alomar, M. J. (2024). A nephrological perspective of herbal remedies on the progression of chronic kidney disease: A systematic review. *Journal of Applied Pharmaceutical Science*, 14(03).
10. Asgharpour, M., & Alirezaei, A. (2021). Herbal antioxidants in dialysis patients: a review of potential mechanisms and medical implications. *Renal Failure*, 43(1), 351–361. <https://doi.org/10.1080/0886022X.2021.1880939>.
11. 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. *J Appl Pharm Sci*, 2021; 11(10):113–127.
12. Canayakin D, Bayir Y, Kilic Baygutalp N, Sezen Karaoglan E, Atmaca HT, Kocak Ozgeris FB, et al. Paracetamol-induced nephrotoxicity and oxidative stress in rats: the protective role of *Nigella sativa*. *Pharm Biol*. 2016;54(10):2082–91.
13. Kuhad A, Pilkhwai S, Sharma S, Tirkey N, Chopra K. Effect of curcumin on inflammation and oxidative stress in cisplatin-induced experimental nephrotoxicity. *J Agric Food Chem*. 2007 Dec 12;55(25):10150-5. doi: 10.1021/jf0723965. Epub 2007 Nov 15. PMID: 18001039.
14. Ajith TA, Nivitha V, Usha S. Zingiber officinale Roscoe alone and in combination with alpha-tocopherol protect the kidney against cisplatin-induced acute renal failure. *Food Chem Toxicol*. 2007 Jun;45(6):921-7. doi: 10.1016/j.fct.2006.11.014. Epub 2006 Nov 29. PMID: 17210214.
15. Hassan HA, Edrees GM, El-Gamel EM, El-Sayed EA. Amelioration of cisplatin-induced nephrotoxicity by grape seed extract and fish oil is mediated by lowering oxidative stress and DNA damage. *Cytotechnology*. 2014 May;66(3):419-29. doi: 10.1007/s10616-013-9589-8. Epub 2013 Jun 13. PMID: 23761012; PMCID: PMC3973798.

16. Varzi HN, Esmailzadeh S, Morovvati H, Avizeh R, Shahriari A, Givi ME. Effect of silymarin and vitamin E on gentamicin-induced nephrotoxicity in dogs. *J Vet Pharmacol Ther.* 2007 Oct;30(5):477-81. doi: 10.1111/j.1365-2885.2007.00901.x. PMID: 17803742.
17. El-Kashef DH, El-Kenawi AE, Suddek GM, Salem HA. Protective effect of allicin against gentamicin-induced nephrotoxicity in rats. *Int Immunopharmacol.* 2015 Dec;29(2):679-686. doi: 10.1016/j.intimp.2015.09.010. Epub 2015 Sep 29. PMID: 26391062.
18. Sahin K, Tuzcu M, Gencoglu H, Dogukan A, Timurkan M, Sahin N, Aslan A, Kucuk O. Epigallocatechin-3-gallate activates Nrf2/HO-1 signaling pathway in cisplatin-induced nephrotoxicity in rats. *Life Sci.* 2010 Aug 14;87(7-8):240-5. doi: 10.1016/j.lfs.2010.06.014. Epub 2010 Jul 6. PMID: 20619277.
19. Sahu BD, Rentam KK, Putcha UK, Kuncha M, Vegi GM, Sistla R. Carnosic acid attenuates renal injury in an experimental model of rat cisplatin-induced nephrotoxicity. *Food Chem Toxicol.* 2011 Dec;49(12):3090-7. doi: 10.1016/j.fct.2011.08.018. Epub 2011 Sep 6. PMID: 21930180.
20. Mestry SN, Gawali NB, Pai SA, Gursahani MS, Dhodi JB, Munshi R, Juvekar AR. Punica granatum improves renal function in gentamicin-induced nephropathy in rats via attenuation of oxidative stress. *J Ayurveda Integr Med.* 2020 Jan-Mar;11(1):16-23. doi: 10.1016/j.jaim.2017.09.006. Epub 2018 Mar 17. PMID: 29555255; PMCID: PMC7125389.
21. Wang Z, Li YF, Han XY, Sun YS, Zhang LX, Liu W, Liu XX, Li W, Liu YY. Kidney Protection Effect of Ginsenoside Re and Its Underlying Mechanisms on Cisplatin-Induced Kidney Injury. *Cell Physiol Biochem.* 2018;48(5):2219-2229. doi: 10.1159/000492562. Epub 2018 Aug 15. PMID: 30110677.
22. Jeyanthi T, Subramanian P. Nephroprotective effect of *Withania somnifera*: a dose-dependent study. *Ren Fail.* 2009;31(9):814-21. doi: 10.3109/08860220903150320. PMID: 19925290.
23. Basist P, Zahiruddin S, Khan MU, Gautam G, Jan B, Khan MA, Parveen R, Ahmad S. Metabolite profiling and nephroprotective potential of *Glycyrrhiza glabra* L. roots against cisplatin-induced nephrotoxicity in vitro and in vivo. *Iran J Basic Med Sci.* 2022 Nov;25(11):1286-1298. doi: 10.22038/IJBMS.2022.65478.14404. PMID: 36474572; PMCID: PMC9699950.
24. Edeogu CO, Kalu ME, Famurewa AC, Asogwa NT, Onyeji GN, Ikpemo KO. Nephroprotective Effect of *Moringa Oleifera* Seed Oil on Gentamicin-Induced Nephrotoxicity in Rats: Biochemical Evaluation of Antioxidant, Anti-inflammatory, and Antiapoptotic Pathways. *J Am Coll Nutr.* 2020 May-Jun;39(4):307-315. doi: 10.1080/07315724.2019.1649218. Epub 2019 Aug 12. PMID: 31403889.
25. Naghizadeh B, Mansouri SM, Mashhadian NV. Crocin attenuates cisplatin-induced renal oxidative stress in rats. *Food Chem Toxicol.* 2010 Oct;48(10):2650-5. doi: 10.1016/j.fct.2010.06.035. Epub 2010 Jun 27. PMID: 20600529.
26. Mohandes S, Doke T, Hu H, Mukhi D, Dhillon P, Susztak K. Molecular pathways that drive diabetic kidney disease. *J Clin Invest.* 2023 Feb 15;133(4):e165654. doi: 10.1172/JCI165654. PMID: 36787250; PMCID: PMC9927939.