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REVIEW ARTICLE

A Review on Herbal Therapeutics in Nephroprotection: Exploring Herbal Agents, Bioactive Compounds, Formulations, Mechanisms of Action, and Comparison with Conventional Treatments

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Abstract

Kidney damage caused by nephrotoxic substances remains a persistent challenge in modern healthcare, contributing significantly to the incidence of Acute Kidney Injury (AKI) and Chronic Kidney Disease (CKD). This review provides a comprehensive overview of the pathophysiological mechanisms underlying nephrotoxicity and explores the therapeutic potential of herbal agents in preventing and mitigating renal injury. Herbal nephroprotective agents are rich in polyphenols, flavonoids, and other phytochemicals which exert renoprotective effects through a range of molecular mechanisms. These include modulation of oxidative stress, inflammation, apoptosis, and fibrosis via signalling pathways such as PI3K/AKT/mTOR, Nrf2/HO-1, MAPK, and JAK/STAT. Through these actions, they help to maintain cellular integrity, reduce injury markers, and support renal recovery. Accumulating evidence suggests that these agents may offer substantial benefits in attenuating nephrotoxicity of various etiologies. As kidney diseases continue to rise globally, plant-based therapeutics present a promising adjunct to conventional care, potentially contributing to safer and more holistic nephroprotection. Therefore, this review further highlights the significant role of herbal agents and their formulations in the field of renal injury-associated mechanistic approaches.

Major Findings: Herbal agents containing bioactive phytoconstitutents demonstrate protective effects against nephrotoxicity through multiple mechanisms, including antioxidant activity, anti-inflammatory effects, anti-fibrotic action, and enhancement of detoxification pathways.

Keyword: Conventional Nephroprotective Approaches, Bioactive Compounds, Herbal Drugs, Herbal Formulations, Medicinal Plants, Nephrotoxicity

1. Introduction

Nephrotoxicity caused by exposure to harmful substances is a significant global health concern. The kidneys, being highly vascularized and responsible for filtering toxins, are particularly vulnerable to injury from nephrotoxic drugs, heavy metals, metabolic disorders, and environmental pollutants[1]. Common culprits include aminoglycoside antibiotics, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), chemotherapeutic agents like cisplatin, and contrast dyes used in medical imaging. Additionally, conditions such as diabetes and hypertension further exacerbate renal damage by inducing oxidative stress, inflammation, and fibrosis, leading to CKD or even end-stage renal failure. Despite advancements in conventional treatments, such as dialysis, corticosteroids, and reno-protective medications, these therapies often focus

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on managing symptoms rather than preventing or reversing kidney damage. Moreover, they can lead to significant side effects, creating a need for alternative and safer nephroprotective strategies[2].

In recent years, natural nephroprotective agents, particularly medicinal plants, have gained attention due to their antioxidant, anti-inflammatory, and detoxifying properties. Traditional healing systems, such as *Ayurveda*, Traditional Chinese Medicine (TCM), and Unani medicine, have long utilised herbs to support kidney function and counteract toxicity[3]. Scientific research is now validating the nephroprotective effects of several herbal agents, including *Curcuma longa* (turmeric), *Withania somnifera* (*ashwagandha*), *Nigella sativa* (black seed), *Silybum marianum* (milk thistle), and *Punica granatum* (pomegranate)[4]. These herbs offer multi-targeted protection by reducing oxidative stress, inhibiting inflammation, preventing fibrosis, and enhancing detoxification mechanisms. Given their natural origin and lower risk of adverse effects, these herbal interventions present a promising alternative to conventional nephroprotective therapies[5]. This review explores the mechanisms, efficacy, and potential integration of herbal medicine in nephrotoxicity management, emphasising the need for scientifically backed natural treatments to safeguard kidney health.

2. Pathophysiology of Nephrotoxicity

The kidneys are particularly susceptible to toxicants due to their essential role in filtering blood, excreting metabolic waste, and maintaining fluid and electrolyte homeostasis[6]. Exposure to nephrotoxic agents, including pharmaceutical drugs, heavy metals, and environmental pollutants, can result in both structural and functional impairment by increasing the risk of AKI and CKD[7,8]. Many pharmaceutical drugs, while essential for treating diseases that can inadvertently harm kidney tissues[9]. These drugs interfere with key renal functions, including glomerular filtration, tubular reabsorption, and renal blood flow regulation[10,11]. A prime examples are aminoglycoside antibiotics, NSAIDs and cisplatin, which is also a chemotherapy drug[12]. Also, the exposure to heavy metals from industrial waste, contaminated water, and occupational hazards can result in severe and irreversible kidney damage. Metals like Uranium, Arsenic, and Lead are commonly found in polluted environments[13,14]. Beyond pharmaceutical drugs and heavy metals, various environmental and industrial chemicals contribute to nephrotoxicity. Contaminated grains and improperly stored food are major sources of mycotoxin exposure[15,16].

Nephrotoxicity arises from a complex interplay of molecular and cellular processes, primarily driven by oxidative stress, inflammation, apoptosis, fibrosis, and vascular dysfunction[17]. Among these, oxidative stress is a central initiating factor. Nephrotoxic agents trigger the overproduction of Reactive Oxygen Species (ROS), which lead to lipid peroxidation, mitochondrial damage, and DNA fragmentation[18,19]. These oxidative insults activate apoptotic signalling cascades, which is particularly caspase-mediated pathways resulting in the loss of functional renal tubular cells and contributing to tubular necrosis[20,21]. In parallel, inflammatory responses are initiated, characterised by the upregulation of pro-inflammatory cytokines such as TNF-α, IL-6, and TGF-β. These mediators recruit immune cells to renal tissues, amplifying cellular injury and promoting renal fibrosis, particularly through the induction of Epithelial-Mesenchymal Transition (EMT) and deposition of extracellular matrix proteins[22,23]. Over time, these fibrotic changes lead to glomerular and tubular scarring, culminating in a progressive decline in Glomerular Filtration Rate (GFR) and an elevated risk of developing CKD or End-Stage Renal Disease (ESRD)[24,25]. Vascular dysfunction further exacerbates renal injury. Impaired renal perfusion, endothelial cell damage, and afferent arteriole vasoconstriction compromise oxygen delivery, resulting in ischemic injury and further deterioration of renal function[26]. These interconnected pathological mechanisms reinforce one another, creating a vicious cycle of nephron loss and functional decline (Figure 1) Understanding these pathways is crucial for the development of effective therapeutic strategies aimed at halting or reversing nephrotoxicity. Early intervention targeting oxidative and inflammatory cascades may hold promise in preserving renal integrity and function[27].

3. Herbal Medicine in Nephroprotection

3.1 Traditional Use of Herbs for Kidney Health

For centuries, medicinal plants have been used in traditional healing systems, such as Ayurveda, TCM,

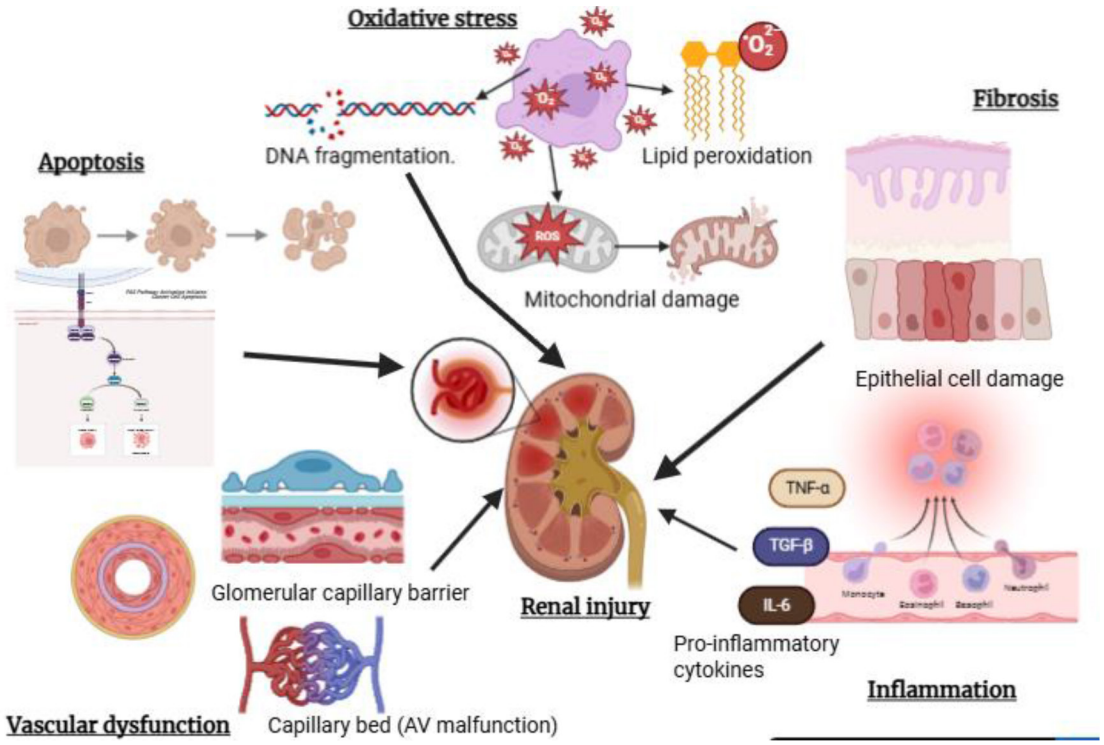


Figure 1. Molecular pathogenesis of nephrotoxicity.

and Unani medicine, to maintain kidney health and treat renal disorders. Ancient texts describe numerous herbs that were traditionally used to support urine production (diuretics), detoxification, and kidney regeneration[28]. For instance, Punarnava (*Boerhavia diffusa*) has been widely used in Ayurveda to treat fluid retention and kidney dysfunction, while Astragalus membranaceus in TCM is known for its nephroprotective and immune-boosting properties. These traditional practices laid the foundation for modern research into the effectiveness of herbal nephroprotective agents[29].

3.2 Scientific Basis for Herbal Nephroprotection

Recent scientific advancements have provided strong evidence supporting the nephroprotective potential of medicinal plants. Herbs contain bioactive compounds, such as flavonoids, alkaloids, polyphenols, and saponins, which exhibit antioxidant, anti-inflammatory, antifibrotic, and detoxifying properties[30]. Scientific studies have demonstrated that herbal agents can reduce oxidative stress by scavenging reactive oxygen species that contribute to kidney damage[31]. Suppress inflammatory pathways by inhibiting pro-inflammatory cytokines like TNF-α and IL-6. Prevent kidney fibrosis by regulating extracellular matrix deposition and epithelial-mesenchymal transition[32]. Enhance detoxification mechanisms by promoting renal clearance of toxins and heavy metals. Improve renal circulation and filtration by maintaining blood flow to the glomeruli[33].

Table 1 provides a comprehensive list of herbal medicines with scientific evidence for their nephroprotective properties, including their bioactive compounds, mechanisms of action, and therapeutic applications.

4. Bioactive Compounds in Nephroprotective Herbs

Nephroprotective herbs contain bioactive compounds that help prevent or mitigate kidney damage caused by oxidative stress, inflammation, fibrosis, and nephrotoxic agents. These bioactive compounds include antioxidants, anti-inflammatory agents, nephron regenerative molecules, and detoxifying compounds that support kidney function and promote renal repair. Understanding the mechanisms through which these

Table 1. List of herbal medicines used in preclinical study in nephrotoxicity

S. No.	Herbal medicine	Active compounds	Nephroprotective effects	References
1	*Tinospora cordifolia* (Guduchi)	Alkaloids, Terpenoids	Reduces kidney inflammation, supports immune function	34
2	*Eclipta alba* (False daisy)	Wedelolactone	Prevents kidney fibrosis	35
3	*Andrographis paniculata*	Andrographolides	Anti-inflammatory, immune-modulating	36
4	*Aloe vera*	Aloin	Reduces kidney damage, protects renal tissues	37
5	*Ocimum sanctum* (Holy basil)	Eugenol, ursolic acid	Anti-inflammatory, nephroprotective	38
6	*Berberis aristata* (Tree turmeric)	Berberine	Antioxidant, antifibrotic	39
7	*Lagerstroemia speciosa*	Corosolic acid	Improves glucose metabolism, prevents diabetic nephropathy	40
8	*Nelumbo nucifera* (Lotus seed)	Alkaloids, flavonoids	Antioxidant, kidney-protective	41
9	*Glycyrrhiza glabra* (Licorice)	Glycyrrhizin	Anti-inflammatory, prevents nephrotoxicity	42
10	*Urtica dioica* (Nettle)	Phenolic acids	Anti-inflammatory, nephroprotective	43
11	*Rubia cordifolia* (Manjistha)	Alkaloids, anthraquinones	Prevents kidney fibrosis	44
12	*Cinnamomum verum* (Cinnamon)	Cinnamaldehyde	Antioxidant protects renal function	45
13	*Solanum nigrum* (Black nightshade)	Glycoalkaloids	Diuretic, reduces nephrotoxicity	46
14	*Crataeva nurvala*	Lupeol	Improves kidney function, reduces urolithiasis	46
15	*Arctium lappa* (Burdock root)	Lignans, polyphenols	Detoxifying, anti-inflammatory	47
16	*Raphanus sativus* (Radish)	Glucosinolates	Diuretic, detoxifying	48
17	*Salvia miltiorrhiza* (Danshen)	Tanshinones	Improves renal blood flow, reduces oxidative stress	46
18	*Piper nigrum* (Black pepper)	Piperine	Enhances the bioavailability of nephroprotective compounds	36
19	*Alpinia galanga*	Galangin	Reduces nephrotoxicity in diabetic nephropathy	49
20	*Ficus racemosa*	Tannins, flavonoids	Protects against heavy metal nephrotoxicity	50
21	*Momordica charantia* (Bitter melon)	Charantin	Prevents oxidative stress in diabetic nephropathy	51
22	*Sapindus mukorossi*	Saponins	Protects against nephrotoxic compounds	52
23	*Eclipta prostrata*	Wedelolactone	Prevents nephrotoxicity and fibrosis	41
24	*Rosa damascena* (Damask rose)	Phenolics, flavonoids	Reduces inflammation, protects renal tissue	53
25	*Plumbago zeylanica*	Plumbagin	Prevents nephrotoxicity, supports kidney function	42
26	*Aegle marmelos* (Bael)	Marmelosin	Reduces oxidative stress, improves renal filtration	37
27	*Costus speciosus*	Diosgenin	Protects against nephrotoxic drugs	39
28	*Centella asiatica* (Gotu kola)	Asiaticoside	Reduces kidney inflammation, enhances repair	40
29	*Citrus limon* (Lemon)	Vitamin C, flavonoids	Protects against kidney stone formation	38
30	*Malva sylvestris*	Malvone, polyphenols	Anti-inflammatory, supports renal detoxification	45
31	*Ananas comosus* (Pineapple)	Bromelain	Anti-inflammatory, prevents fibrosis	46
32	*Panax ginseng*	Ginsenosides	Enhances renal function, prevents CKD	46

Table 1. Continued...

S. No.	Herbal medicine	Active compounds	Nephroprotective effects	References
33	*Coriandrum sativum* (Coriander)	Linalool, flavonoids	Detoxifying, protects against nephrotoxic agents	47
34	*Foeniculum vulgare* (Fennel)	Anethole	Diuretic, prevents urinary tract infections	48
35	*Achillea millefolium* (Yarrow)	Sesquiterpene lactones	Reduces inflammation, protects against nephrotoxicity	36
36	*Peganum harmala* (Syrian rue)	Harmine, harmaline	Protects against oxidative stress-induced nephrotoxicity	49
37	*Nigella sativa*	Antioxidant, anti-inflammatory	Prevents nephron apoptosis, reduces inflammation	54
38	*Moringa oleifera*	Antioxidant, nephroregenerative	Repairs damaged kidney cells, prevents tubular necrosis	52
39	*Pllanthus niruri*	Diuretic, detoxifying	Aids in kidney stone prevention, supports toxin elimination	55

compounds exert their protective effects is crucial for their integration into therapeutic strategies[56].

Table 2 provides a comprehensive list of some bioactive compounds used in nephrotoxicity, along with their herbal sources and potential nephroprotective benefits.

5. Evidence-Based Herbal Formulations for Nephroprotection

Nephrotoxicity, caused by drugs, toxins, and metabolic disorders, is a major contributor to kidney damage, often leading to CKD or AKI. Conventional treatments such as dialysis and pharmaceutical interventions provide symptomatic relief but do not effectively prevent or reverse kidney damage. As a result, there is growing interest in alternative nephroprotective strategies, particularly those based on herbal formulations[70].

Traditional medicinal systems, including *Ayurveda*, traditional Chinese medicine, and *Unani* medicine, have long utilised herbal combinations to support kidney health[71]. Modern scientific advancements have now validated the efficacy of many of these herbal formulations, demonstrating their potential in protecting against nephrotoxicity through mechanisms such as antioxidation, anti-inflammation, detoxification, and nephro regeneration[72].

Several evidence-based herbal formulations have shown promising nephroprotective effects in both preclinical and clinical studies. These formulations, often consisting of multiple bioactive herbs, work synergistically to protect renal tissues, enhance detoxification, reduce oxidative stress, and prevent fibrosis[73]. With increasing research supporting their efficacy, herbal formulations are emerging as a viable complementary approach to conventional nephroprotective therapies[74].

This document explores various herbal formulations with documented nephroprotective effects, highlighting their compositions, mechanisms of action, and supporting scientific evidence from preclinical and clinical studies.

Table 3 explores various herbal formulations with documented nephroprotective effects, highlighting their compositions, mechanisms of action, and supporting scientific evidence from preclinical and clinical studies.

6. Clinical Trials Validating Herbal Nephroprotective Formulations

Kidney damage caused by exposure to toxins, medications, or metabolic imbalances is a growing global health concern, often leading to AKI and CKD. Although conventional therapies are widely used to manage these conditions, they often come with significant side effects and offer limited efficacy in halting disease progression[85]. As a result, increasing attention has been directed toward herbal nephroprotective formulations, which demonstrate the ability to reduce oxidative stress, suppress inflammation, and enhance detoxification mechanisms and also offer a potentially

Table 2. List of bioactive compounds used in nephroprotoxity

S. No.	Bioactive compound	Herbal source	Nephroprotective benefits	References
1	Curcumin	*Curcuma longa* (Turmeric)	Scavenges ROS, inhibits TNF-α, reduces kidney fibrosis	57
2	Silymarin	*Silybum marianum* (Milk thistle)	Enhances heavy metal excretion, prevents drug-induced nephrotoxicity	58
3	Thymoquinone	*Nigella sativa* (Black seed)	Reduces inflammation, prevents nephron apoptosis	59
4	Ellagic Acid	*Punica granatum* (Pomegranate)	Prevents oxidative damage, reduces collagen deposition in renal tissue	60
5	Allicin	*Allium sativum* (Garlic)	Lowers renal inflammation, reduces oxidative stress in glomeruli	61
6	Quercetin	*Moringa oleifera* (Drumstick tree)	Repairs damaged kidney cells, prevents tubular necrosis	62
7	Gingerol and Shogaol	*Zingiber officinale* (Ginger)	Inhibits pro-inflammatory cytokines, reduces kidney fibrosis	63
8	Punarnavine	*Boerhavia diffusa* (Punarnava)	Supports kidney detoxification, prevents fluid retention	64
9	Astragalosides	*Astragalus membranaceus*	Enhances renal circulation, prevents CKD progression	65
10	Lignans and Flavonoids	*Phyllanthus niruri* (Stonebreaker)	Aids in kidney stone prevention, supports toxin elimination	66
11	Anthocyanins and Polyphenols	*Hibiscus sabdariffa* (Roselle)	Protects kidneys from hypertensive damage	67
12	Isothiocyanates	*Moringa oleifera*	Promotes kidney repair, reduces fibrosis progression	62
13	Saponins	*Tribulus terrestris* (Gokshura)	Enhances urine production, prevents urinary tract infections	68
14	Terpenoids and Alkaloids	*Tinospora cordifolia* (Guduchi)	Reduces kidney inflammation, supports immune function	56
15	Resveratrol	*Vitis vinifera* (Grapes)	Protects renal tubules from oxidative stress and ischemic injury	69

Table 3. Evidence-based herbal formulations for nephroprotection

S. No.	Herbal formulation	Composition	Mechanism of action	Preclinical/Clinical study references
1	NEERI-KFT	*Boerhavia diffusa*, *Crataeva nurvala*, *Tribulus terrestris*, *Ocimum sanctum*	Antioxidant, anti-inflammatory, nephroprotective	75
2	*Asarum europaeum* L. *Unani* Formulation	*Asarum europaeum*, *Punica granatum*, *Glycyrrhiza glabra*	Detoxifying, nephron-protective	76
3	Natural Coumarins	Scoparone, Fraxetin, Umbelliferone	Anti-inflammatory, protects against diabetic nephropathy	77
4	Traditional Urolithiasis Formula	*Phyllanthus niruri*, *Tribulus terrestris*, *Boerhavia diffusa*	Reduces kidney stone formation, improves urine output	78
5	Chamomile Extract (*Matricaria chamomilla*)	Apigenin, Luteolin	Antioxidant, reduces kidney inflammation	79
6	Pomegranate Extract (*Punica granatum*)	Ellagic acid, Punicalagin	Protects against nephrotoxicity from toxins	80
7	*Ayurvedic* Nephro protective Formula	*Tinospora cordifolia*, *Terminalia chebula*, *Boerhavia diffusa*	Supports kidney function, prevents CKD	81
8	Luteolin-Rich Extracts	Luteolin from celery, parsley	Anti-inflammatory, reduces kidney fibrosis	82
9	Multi-Herbal *Ayurvedic* Formulation	*Curcuma longa*, *Andrographis paniculata*, *Boerhavia diffusa*	Nephroprotective, reduces oxidative damage	83
10	Nephroprotective Nutraceuticals	Polyphenols, flavonoids, curcuminoids	Antioxidant, anti-inflammatory	84

safe and more holistic alternative. To validate these therapeutic claims there are numerous clinical studies have investigated the efficacy of herbal remedies in conditions such as CKD, drug-induced nephrotoxicity, and diabetic nephropathy. A recent meta-analysis by Zhou et al. reviewed 21 clinical trials involving 1,857 CKD patients in which 954 received treatment with *Salvia miltiorrhiza,* which is an herbal formulation. Results indicated that *Salvia miltiorrhiza* significantly reduced urine protein levels, improved kidney function, and helped attenuate CKD progression without notable side effects[86]. A retrospective analysis was conducted in South Korea involving data from six RCTs to assess the renal safety of four herbal formulations, which are commonly used in Traditional Korean Medicine (TKM). The study enrolled a total of 407 human participants. The participants included 142 males and 265 females, with a mean age of approximately 44 years. Treatment duration ranged from 4 to 12 weeks, depending on the specific trial and herbal formulation. In the study, CGX was administered to 65 participants (42 in the intervention group and 23 in the placebo group), BST to 79 participants (40 intervention, 39 placebo), Myelophil to 97 participants (48 intervention, 49 placebo), and Panax ginseng to 166 participants (110 intervention, 56 placebo). The study evaluated key renal function indicators, including Blood Urea Nitrogen (BUN), serum creatinine, and estimated glomerular filtration rate (eGFR), before and after treatment. Across all formulations, no statistically significant differences were observed between the herbal medicine and placebo groups for any of these renal markers. Furthermore, no participants in the herbal medicine group experienced a drop in eGFR below 60 mL/min post-treatment, a threshold commonly used to indicate kidney dysfunction. Only one participant, a 69-year-old male taking BST, had an eGFR below 60 after treatment, and this was not considered statistically significant. Also, no cases of acute kidney injury were reported based on established diagnostic criteria. These results suggest that short-term use of CGX, BST, Myelophil, and Panax ginseng extract is safe with respect to kidney function in healthy individuals or those with non-renal indications. Although none of the herbal medicines were prescribed specifically for kidney disorders, the findings are valuable in addressing safety concerns surrounding herbal nephrotoxicity[87].

These findings confirm that herbal formulations can effectively modulate key pathological mechanisms such as inflammation, oxidative stress, and fibrosis, offering renal protection through multi-targeted molecular pathways. After all these trials they provide compelling evidence for the nephroprotective potential of herbal medicines. However, larger and multicenter randomized controlled trials are still necessary to standardize dosing regimens, evaluate long-term safety, and confirm efficacy across diverse populations.

7. Mechanisms of Herbal Protection against Nephrotoxicity

Herbal medicines exert their nephroprotective effects through multiple mechanisms that work synergistically to prevent, mitigate, and reverse kidney damage caused by toxic drugs, heavy metals, oxidative stress, and inflammation (Figure 2)[88]. The three primary mechanisms through which nephroprotective herbs safeguard kidney function include antioxidant and free radical scavenging activity, anti-inflammatory and cytoprotective effects, and the enhancement of renal detoxification pathways[89]. These mechanisms help preserve renal tissue integrity, maintain normal kidney function, and prevent the progression of AKI and CKD[90].

8. Antioxidant and Free Radical Scavenging Activity

Oxidative stress plays a critical role in drug-induced nephrotoxicity, ischemic kidney injury, and metabolic disorders such as diabetes-related kidney damage. It results from an imbalance between the production of ROS and the body's antioxidant defence system[91]. Excessive ROS leads to lipid peroxidation, mitochondrial dysfunction, protein oxidation, and DNA damage, ultimately causing cell apoptosis and renal fibrosis[92].

Many nephroprotective herbs contain potent antioxidants such as flavonoids, polyphenols, alkaloids, carotenoids, and terpenoids, which help neutralise ROS and restore cellular redox balance[93]. For example, Curcumin from Curcuma longa (Turmeric) and Quercetin from Moringa oleifera have been shown to scavenge free radicals, upregulate endogenous

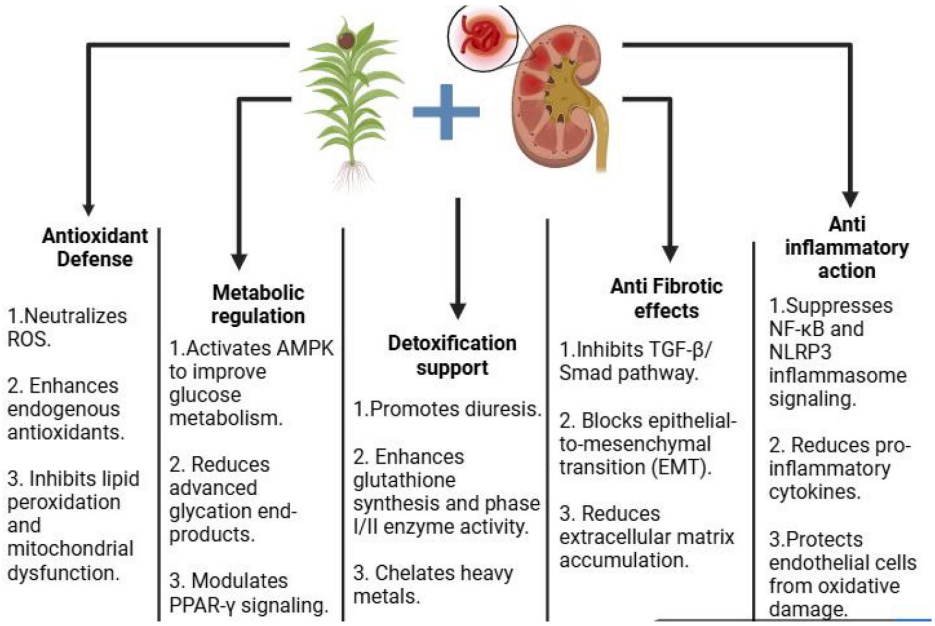


Figure 2. Various mechanisms of herbal agents and bioactive compounds against nephrotoxicity.

antioxidants like glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT), and inhibit lipid peroxidation in kidney tissues[94].

9. Anti-inflammatory and Cytoprotective Effects

Chronic inflammation is a significant contributor to nephrotoxicity, as it leads to immune cell infiltration, cytokine overproduction, endothelial dysfunction, and renal fibrosis. Pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β, along with activation of nuclear factor kappa B (NF-κB), contribute to renal cell apoptosis and tubular damage[95].

Many herbal compounds exert anti-inflammatory and cytoprotective effects by modulating immune responses, inhibiting inflammatory cytokines, and suppressing oxidative stress-induced damage[96]. Thymoquinone from *Nigella sativa* (Black Seed) and Allicin from *Allium sativum* (Garlic) have been found to inhibit NF-κB activation, suppress the release of inflammatory cytokines, and protect renal cells from apoptosis[97].

10. Enhancement of Renal Detoxification Pathways

The kidneys play a crucial role in detoxifying metabolic waste products, eliminating xenobiotics, and filtering toxins from the bloodstream. Nephrotoxic agents, such as heavy metals, pesticides, and pharmaceutical drugs, overload the kidneys' detoxification capacity, leading to renal impairment and oxidative stress[98,99].

Several herbs have been found to enhance renal detoxification pathways by promoting diuresis, increasing glutathione levels, and supporting phase I and phase II detoxification enzymes[100]. Saponins from *Tribulus terrestris* (Gokshura) and Punarnavine from *Boerhavia diffusa* (Punarnava) act as natural diuretics, helping in the excretion of toxins and preventing kidney stone formation[101].

11. Comparative Analysis: Herbal vs. Conventional Nephroprotective Approaches

Nephroprotective treatment is crucial in preventing and managing the prevalence of kidney damage, which is increasing rapidly with both herbal and conventional therapies. While conventional therapeutic approaches using pharmaceuticals offer targeted efficacy, but may pose risks to safety and efficacy comparatively herbal agents. However, limitations in standardisation, dosage regulation, and clinical validation hinder their throughout acceptance. Table 4 summarising the comparative analysis on the potential of herbal and conventional treatment for nephrotoxicity[102-105].

Table 4. Comparative analysis between herbal and conventional nephroprotective approaches

Aspect	Herbal nephroprotective treatments	Conventional nephroprotective treatments	Synergistic potential
Mechanism of action	Multi-targeted effects (antioxidant, anti-inflammatory, diuretic, antifibrotic, detoxifying)	Mostly single-targeted (*e.g.*, ACE inhibitors focus on blood pressure regulation)	Herbs like curcumin, quercetin, and silymarin can complement pharmaceutical nephroprotective effects.
Adverse effects	Generally lower toxicity compared to pharmaceuticals	Higher risk of nephrotoxicity (*e.g.*, NSAIDs, calcineurin inhibitors)	Herbs like silymarin and resveratrol can reduce drug-induced nephrotoxicity
Renal detoxification	Herbs like Punarnava (*Boerhavia diffusa*) and *Phyllanthus niruri* enhance toxin elimination	Dialysis is required in severe kidney damage	Herbal diuretics can improve kidney function alongside conventional diuretics
Cost and accessibility	More affordable and widely available, especially in rural areas	Expensive (especially dialysis and transplantation) and may not be accessible to all patients	Herbal medicine can reduce the economic burden in low-resource settings
Scientific evidence	Limited large-scale clinical trials, mostly preclinical studies	Well-established through RCTs and regulatory approvals	Combining herbal and conventional treatments may justify further clinical trials
Regulatory standards	Lack of standardisation, variable bioactive composition	Strictly regulated, ensuring consistent drug quality	HPLC and GMP standards can improve herbal product reliability
Drug-Herb interactions	Some herbs may alter drug metabolism (*e.g.*, Curcumin may affect blood thinners)	Defined interactions known for pharmaceutical drugs	Certain herbs (*e.g.*, Piperine from Black Pepper) can enhance drug absorption
Speed of action	Slower onset, requiring prolonged use	Faster action, but potential for side effects	Herbal treatments can be used for long-term kidney health alongside pharmaceuticals
Protection against Nephrotoxicity	Herbal antioxidants (*e.g.*, Silymarin, Curcumin, Resveratrol) can reduce drug-induced kidney damage	Drugs like Cisplatin and NSAIDs can cause nephrotoxicity	Herbal antioxidants can help counteract nephrotoxicity from drugs
Kidney function improvement	Herbs like Punarnava act as natural diuretics, improving urine output	Pharmaceutical diuretics help manage fluid overload	Combined use of herbal and conventional diuretics may optimise fluid balance
Inflammation and fibrosis reduction	Herbs like Nigella sativa and Gingerol reduce inflammation	Corticosteroids and immunosuppressants are used for inflammation control	Herbal anti-inflammatory effects may help reduce corticosteroid dependency
Bioavailability enhancement	Some herbs (*e.g.*, Piperine from Black Pepper) enhance drug absorption	Drug absorption may be limited due to metabolism and excretion	Herbal bioenhancers can increase drug efficacy
Long-term safety	Traditionally used in Ayurveda and TCM, culturally accepted	Long-term drug use may cause cumulative toxicity	Combining both can offer safer long-term nephroprotection

12. Challenges and Future Perspectives in Herbal Nephroprotection

Herbal nephroprotective agents are gaining attention as alternative or complementary therapies for kidney diseases due to their antioxidant, anti-inflammatory, and detoxifying properties. However, several challenges hinder their clinical adoption.

One major issue is the lack of standardisation in herbal formulations, leading to variability in bioactive compounds due to differences in plant cultivation, harvesting, and processing. This inconsistency makes dosage determination difficult and affects therapeutic efficacy. Implementing quality control techniques such as HPLC, Mass Spectrometry, and NMR can ensure purity and potency. Additionally, adulteration and contamination with heavy metals, pesticides, and synthetic additives pose safety risks, highlighting the need for Good Agricultural Practices (GAP) and Good Manufacturing Practices (GMP).

The absence of large-scale clinical trials remains a significant barrier. While preclinical studies show promising results, Randomised Controlled Trials (RCTs) are essential to establish safety, efficacy, and optimal dosing in humans. Limited research funding and variability in individual responses further complicate clinical studies. Moreover, long-term safety concerns arise as many herbal formulations require prolonged use for therapeutic benefits.

Regulatory challenges also restrict the integration of herbal nephroprotective treatments into mainstream medicine. Unlike pharmaceutical drugs, many herbal medicines are sold as dietary supplements with minimal oversight. The lack of global regulatory frameworks results in inconsistent safety standards. Furthermore, herb-drug interactions can alter the metabolism of conventional nephroprotective drugs, potentially leading to adverse effects.

To address these challenges, stricter regulatory guidelines from agencies like the FDA, EMA, and WHO are needed. Collaboration between traditional medicine practitioners, pharmaceutical researchers, and regulatory bodies can improve safety standards and clinical evaluation. Increased healthcare provider education on herbal nephroprotective agents will ensure informed decision-making in clinical practice.

13. Conclusion

Herbal nephroprotective agents have shown promising potential in managing nephrotoxicity through mechanisms such as antioxidation, anti-inflammation, detoxification, and nephron regeneration. Various herbal formulations have demonstrated efficacy in protecting kidney cells from oxidative stress, inflammation, and drug-induced toxicity. Preclinical studies have provided substantial evidence supporting the protective effects of herbs like *Curcuma longa*, *Silybum marianum*, *Phyllanthus niruri*, and *Astragalus membranaceus*. Additionally, some small-scale clinical trials suggest that herbal nephroprotective agents may complement conventional therapies in reducing nephrotoxicity and improving renal function. However, despite these promising findings, major challenges remain, including the lack of standardisation in herbal formulations, insufficient large-scale clinical trials, and the need for stricter regulatory frameworks to ensure safety and efficacy. To fully integrate herbal nephroprotective agents into modern clinical practice, future research should focus on conducting well-structured, large-scale Randomised Controlled Trials (RCTs) to validate their efficacy and safety. Standardisation of herbal formulations, including dosage optimisation, quality control, and regulatory approval, will be crucial for ensuring consistency and reliability. Advanced pharmacological studies are needed to elucidate the precise mechanisms of action of bioactive compounds and their interactions with conventional nephroprotective drugs. Additionally, the potential for personalised herbal medicine should be explored, considering genetic variations and individual metabolic responses to herbal treatments. By addressing these challenges, herbal nephroprotective agents can be established as viable therapeutic options for kidney disease management, either as standalone treatments or as adjuncts to conventional therapies.

14. Author Contribution

MA: literature search, manuscript drafting, and critical revision; PB: Conceptualization and contributed to writing and editing of the manuscript; BP: contributed to manuscript structure; AM: Supervision and approval of the version to be published. All authors have read and agreed to the published version of the manuscript.

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