Medicinal Plants in the Treatment of Kidney Disorders

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Abstract
Kidney disorders, encompassing acute kidney injury (AKI) and chronic kidney disease (CKD), represent a substantial and escalating global health burden, affecting an estimated 850 million individuals worldwide. Conventional pharmacological approaches, including angiotensin-converting enzyme inhibitors, diuretics, and immunosuppressants, while effective in disease management, are often associated with adverse effects such as nephrotoxicity, electrolyte imbalances, and progression to end-stage renal disease. These limitations have stimulated considerable scientific interest in medicinal plants as complementary or adjunctive therapeutic strategies. The present review critically examines the pharmacological basis of plant-based interventions in renal disorders, with particular emphasis on mechanisms including antioxidant defense through Nrf2 activation and reactive oxygen species scavenging, anti-inflammatory pathways via NF-κB suppression, diuretic modulation, nephroprotection against nephrotoxin-induced injury, and prevention of renal fibrosis through TGF-β1 inhibition. Bioactive phytochemical classes including flavonoids, alkaloids, terpenoids, saponins, and polyphenols are discussed in relation to their pharmacological targets within the kidney. Additionally, the review encompasses preclinical evidence from animal models of AKI and CKD, available clinical data, formulation strategies for improving bioavailability, and regulatory considerations for translating plant-based therapies. Collectively, current evidence supports the nephroprotective potential of several medicinal plants; however, rigorous, well-designed clinical trials and standardized phytochemical profiling remain essential prerequisites for their integration into mainstream renal therapeutics.

Keywords: Medicinal plants, Kidney disorders, Nephroprotection, Phytochemicals, Renal health, Translational research, Oxidative stress, Renal fibrosis

1. Introduction

Kidney disorders constitute one of the most pressing challenges in contemporary medicine, encompassing a spectrum of pathological conditions ranging from acute kidney injury to chronic kidney disease and end-stage renal failure. According to the Global Burden of Disease study, CKD alone accounts for over 1.2 million deaths annually, with projections indicating a significant increase in prevalence over the coming decades as a consequence of rising rates of diabetes mellitus, hypertension, and obesity [1, 2]. The kidneys perform indispensable physiological functions including glomerular filtration, tubular reabsorption and secretion, blood pressure regulation via the renin-angiotensin-aldosterone system, erythropoiesis through erythropoietin synthesis, and activation of vitamin D [3]. Disruption of these functions precipitates a cascade of systemic complications including fluid and electrolyte imbalances, cardiovascular disease, anaemia, and mineral-bone disorders.

Current first-line pharmacological management of kidney disorders relies heavily on agents such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, SGLT-2 inhibitors, and loop diuretics. While these drugs delay disease progression, they do not offer curative potential, and long-term use is associated with risks such as hyperkalaemia, acute kidney injury on chronic kidney disease, and drug-drug interactions [4, 5]. Renal replacement therapy through haemodialysis or kidney transplantation remains the definitive intervention for end-stage disease but is limited by availability, cost, and quality of life concerns. Against this clinical backdrop, there has been a renaissance of interest in medicinal plants as sources of bioactive compounds with nephroprotective potential [6, 7].

Ethnopharmacological traditions across South Asia, Africa, the Mediterranean, and East Asia have long incorporated plant-based remedies for renal disorders, including kidney stone dissolution, urinary tract infections, and renal edema [8]. Modern phytopharmacological research has begun to validate these traditional uses by elucidating molecular mechanisms of renal protection, conducting preclinical studies in validated animal models, and, increasingly, progressing selected candidates to clinical evaluation. The present review aims to provide a comprehensive and critically evaluated synthesis of the current evidence base for medicinal plants in renal therapeutics, covering pathophysiological targets, phytochemical classes, mechanisms of action, preclinical and clinical evidence, formulation innovations, and translational challenges.

2. Pathophysiology of Kidney Disorders

A thorough understanding of the pathophysiological mechanisms underlying kidney disorders is essential for rationalizing plant-based therapeutic interventions. Renal pathology, irrespective of the initiating cause, converges on several common cellular and molecular events: oxidative stress, chronic inflammation, tubular cell death, glomerulosclerosis, and interstitial fibrosis [9, 10]. These processes are interconnected and mutually reinforcing, creating a self-perpetuating cycle of nephron loss and functional deterioration.

Oxidative stress arises when the production of reactive oxygen species (ROS) exceeds the capacity of endogenous antioxidant defense systems, including superoxide dismutase (SOD), catalase, glutathione peroxidase, and the Nrf2-Keap1 pathway. In AKI, ischaemia-reperfusion injury, nephrotoxic drugs (e.g., cisplatin, gentamicin), and contrast agents are the principal inducers of ROS, causing mitochondrial dysfunction, lipid peroxidation, and tubular epithelial cell apoptosis [9, 11]. In CKD, sustained glomerular hypertension, hyperglycaemia, and accumulated uraemic toxins chronically activate NADPH oxidase and uncouple endothelial nitric oxide synthase, perpetuating oxidative injury [10].

Inflammatory mechanisms are equally central to renal pathology. Pro-inflammatory cytokines including tumour necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6), as well as the transcription factor NF-κB, orchestrate macrophage infiltration, complement activation, and upregulation of adhesion molecules in injured glomerular and tubular compartments [12]. These inflammatory cascades stimulate resident fibroblast activation and transdifferentiation of tubular epithelial cells into myofibroblasts through epithelial-to-mesenchymal transition (EMT), a process principally mediated by transforming growth factor-beta 1 (TGF-β1) and its downstream effector Smad2/3 signalling [13]. Progressive deposition of extracellular matrix components, including collagen types I, III, and IV, results in tubulointerstitial fibrosis — the pathological hallmark of advanced CKD and the strongest histological predictor of progression to end-stage renal failure [14].

The renin-angiotensin-aldosterone system (RAAS) plays a pivotal role in modulating renal haemodynamics and contributing to glomerular hypertension. Angiotensin II, acting through AT1 receptors, promotes afferent arteriole constriction, mesangial cell proliferation, podocyte injury, and direct fibrogenic signalling. Podocyte loss and dysfunction, resulting in proteinuria, serves as an early sentinel of glomerular damage in both diabetic nephropathy and immune-mediated glomerular diseases [15]. Nephrolithiasis, another prevalent renal disorder, arises from urinary supersaturation with calcium oxalate, uric acid, or calcium phosphate salts, with crystallization and aggregation in the renal collecting system promoting tubular obstruction, inflammation, and infection [16].

3. Medicinal Plants and Their Bioactive Compounds

The pharmacological richness of medicinal plants resides in their diverse secondary metabolite profiles, encompassing flavonoids, alkaloids, terpenoids, saponins, tannins, and polyphenols. Each class exhibits distinctive physicochemical and biological properties relevant to renal pharmacology. Understanding structure-activity relationships within these classes is fundamental to the rational development of plant-derived nephroprotective agents.

Flavonoids represent the most extensively studied class of plant polyphenols in the context of renal protection. Structurally characterized by a benzene ring fused to a gamma-pyrone ring, flavonoids encompass subclasses including flavones, flavonols, flavanones, isoflavones, and anthocyanidins. Quercetin, kaempferol, and luteolin have demonstrated capacity to scavenge free radicals, chelate redox-active metals, inhibit xanthine oxidase, and suppress NF-κB-dependent inflammatory gene expression [17]. Sinensetin and other polymethoxyflavones isolated from Orthosiphon stamineus (Java tea) exhibit potent diuretic effects and anti-inflammatory properties, with documented efficacy in preliminary clinical studies for urinary tract conditions and early-stage renal insufficiency [18].

Terpenoids, including monoterpenes, sesquiterpenes, diterpenes, and triterpenes, contribute diverse mechanisms relevant to renal pharmacology. Astragaloside IV, a triterpene saponin derived from Astragalus membranaceus, has emerged as a particularly promising nephroprotective agent. This compound activates telomerase reverse transcriptase (TERT), thereby protecting renal podocytes from oxidative and senescence-related injury, reduces proteinuria, and attenuates TGF-β1-driven fibrosis [19, 20]. The quinone-derived terpenoid thymoquinone from Nigella sativa seeds combines potent antioxidant activity with anti-apoptotic and anti-inflammatory actions, demonstrating protection against gentamicin-, cisplatin-, and contrast-induced nephropathy in experimental models [21].

Alkaloids derived from Berberis species, including berberine, modulate AMP-activated protein kinase (AMPK) signalling, thereby reducing lipid accumulation in tubular cells, diminishing ROS production, and attenuating diabetic nephropathy progression [22]. Punarnavine, an alkaloid constituent of Boerhavia diffusa (punarnava), exhibits pronounced anti-fibrotic activity alongside diuretic, anti-inflammatory, and immunomodulatory properties, making it a multitarget candidate for CKD management [23]. Saponins, particularly the steroidal glycoside protodioscin from Tribulus terrestris, modulate renal haemodynamics through diuretic mechanisms and protect tubular epithelial cells against nephrotoxin-induced apoptosis [24].

Polyphenolic compounds including curcumin from Curcuma longa and punicalagin from Punica granatum (pomegranate) represent additional high-priority candidates. Curcumin's capacity to simultaneously activate Nrf2-antioxidant response elements and suppress NF-κB, combined with direct inhibition of TGF-β1 and downstream Smad3 phosphorylation, positions it as a mechanistically comprehensive nephroprotective agent [25]. Ellagitannins from pomegranate, hydrolysed to ellagic acid and subsequently metabolized to urolithins by intestinal microbiota, demonstrate anti-inflammatory and anti-oxidative activity in experimental CKD models and in patients receiving haemodialysis [26].

4. Mechanisms of Action in Renal Protection

The nephroprotective actions of medicinal plant compounds operate through interconnected molecular pathways that collectively address the multifactorial nature of renal pathology. The principal mechanistic categories include antioxidant defense augmentation, anti-inflammatory pathway suppression, modulation of renal haemodynamics, and prevention of tubular and glomerular fibrosis.

Antioxidant defense is the most extensively characterized mechanism of plant-derived nephroprotective agents. The Keap1-Nrf2 pathway constitutes the master regulator of cellular antioxidant responses. Under oxidative stress conditions, curcumin, sulforaphane (from cruciferous vegetables), and quercetin facilitate nuclear translocation of Nrf2 by disrupting its cytoplasmic sequestration by Keap1, thereby inducing expression of antioxidant enzymes including heme oxygenase-1 (HO-1), NAD(P)H quinone oxidoreductase-1 (NQO1), and glutamate-cysteine ligase [17, 25]. Thymoquinone directly scavenges superoxide and hydroxyl radicals and augments intrinsic glutathione levels, attenuating lipid peroxidation in renal tubular mitochondria [21].

Anti-inflammatory mechanisms are equally critical. NF-κB inhibition by curcumin, geraniin, and rosmarinic acid blocks transcription of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), downregulates cyclooxygenase-2 (COX-2), and reduces monocyte chemoattractant protein-1 (MCP-1)-mediated macrophage infiltration into renal tissue [12, 25]. Inhibition of the inflammasome pathway, particularly NLRP3 activation which drives IL-1β maturation, has been documented for quercetin and berberine in models of AKI, adding a further layer of anti-inflammatory control [22]. Additionally, several flavonoids inhibit leukocyte adhesion to glomerular endothelium by downregulating intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) expression, limiting inflammatory cell recruitment [17].

Modulation of renal haemodynamics by plant-derived diuretics represents a clinically relevant mechanism. Orthosiphon stamineus aqueous extracts increase urinary volume and electrolyte excretion through mechanisms that involve inhibition of renal tubular sodium reabsorption and, independently, mild inhibition of carbonic anhydrase [18]. Tribulus terrestris saponins augment renal blood flow and glomerular filtration rate in experimental animals without inducing electrolyte imbalances comparable to loop diuretics, suggesting a favourable tolerability profile [24]. Modulation of the RAAS by phytochemicals such as ursolic acid and oleanolic acid, which act as natural ACE inhibitors, provides an additional mechanism through which plants may attenuate glomerular hypertension and proteinuria [26].

Anti-fibrotic mechanisms centre on suppression of TGF-β1-Smad2/3 signalling, the dominant pathway driving renal fibrogenesis. Astragaloside IV, boeravinone B, and curcumin inhibit TGF-β1 gene expression, prevent Smad2/3 nuclear translocation, and suppress connective tissue growth factor (CTGF), thereby reducing collagen synthesis and myofibroblast transdifferentiation [19, 23]. Additionally, matrix metalloproteinase (MMP) activation by certain phytochemicals promotes collagen degradation, and inhibition of tissue inhibitors of metalloproteinases (TIMPs) contributes to extracellular matrix resolution in early fibrotic states [13].

5. Preclinical and Translational Research

The preclinical evidence base for medicinal plants in renal disorders is extensive, generated across a variety of experimental models that recapitulate the pathophysiology of human renal disease. Rodent models of cisplatin-induced AKI, gentamicin nephrotoxicity, ischaemia-reperfusion injury, streptozotocin-induced diabetic nephropathy, adenine-induced CKD, and unilateral ureteral obstruction (UUO) have been extensively employed to characterize nephroprotective activity [9, 11]. These models, while imperfect surrogates for complex human disease, provide mechanistic insights and form the foundational evidentiary layer for subsequent clinical investigation.

Pharmacokinetic characterization represents a critical and often underemphasized component of translational research. Many phytochemicals exhibit poor oral bioavailability due to low aqueous solubility, limited membrane permeability, extensive first-pass metabolism, and rapid systemic clearance. Curcumin, the most extensively studied example, achieves plasma concentrations well below pharmacologically effective levels following conventional oral dosing, necessitating formulation strategies to enhance absorption [25]. In contrast, compounds such as rosmarinic acid and berberine demonstrate moderate oral bioavailability with adequate renal tissue penetration, facilitating more straightforward clinical development [22, 18]. The identification of metabolically active transformation products — for instance, the conversion of punicalagins to urolithins by gut microbiota — has introduced the concept of prodrug-like phytochemical activation and the relevance of inter-individual microbiome variation in therapeutic response [26].

The translation of preclinical findings to human clinical trials faces numerous challenges, including heterogeneity in plant material composition due to geographic, seasonal, and post-harvest variables; variability in extraction methods and standardization of bioactive content; absence of dose-finding studies in healthy volunteers prior to patient trials; and the methodological limitations of many available clinical studies, including small sample sizes, short follow-up durations, and inadequate blinding [6, 7]. The ethical and regulatory framework governing phytomedicines also varies substantially across jurisdictions, creating additional complexity for international clinical development programmes [27].

6. Clinical Applications

Despite these challenges, a meaningful body of clinical evidence supports the use of selected medicinal plants in specific renal conditions. Nephrolithiasis represents the condition with perhaps the strongest clinical evidence base for plant-based intervention. Phyllanthus niruri has been evaluated in multiple randomized controlled trials and systematic reviews, demonstrating consistent reductions in urinary calcium and oxalate excretion, inhibition of calcium oxalate crystal aggregation, and facilitation of stone passage [28]. Meta-analyses of available clinical data suggest superiority over placebo in reducing stone recurrence, though evidence is still insufficient for direct comparison with standard pharmacological interventions such as potassium citrate or thiazide diuretics.

In diabetic nephropathy, Astragalus membranaceus preparations have been most extensively studied, particularly in Asian clinical populations. A meta-analysis encompassing over twenty randomized trials demonstrated statistically significant reductions in 24-hour urinary protein excretion, serum creatinine, and blood urea nitrogen with Astragalus supplementation compared to standard therapy alone [20]. The effects were attributed principally to podocyte protection, RAAS modulation, and reduction of oxidative and inflammatory injury at the glomerular level. Curcumin formulations have also yielded promising results in pilot clinical trials of CKD patients, showing reductions in urinary TGF-β1 excretion and inflammatory biomarkers [25]. Orthosiphon stamineus preparations have been assessed in pilot studies and observational clinical data for their diuretic efficacy and tolerability in patients with mild renal impairment and urinary tract infections [18].

Safety considerations are paramount when applying plant-based therapies to patients with already compromised renal function. Several plants traditionally used for urinary disorders contain aristolochic acid derivatives — potent nephrotoxins implicated in aristolochic acid nephropathy — and strict regulatory scrutiny is required to exclude contamination or adulteration of herbal preparations with Aristolochia species [29]. The potential for pharmacokinetic interactions between phytochemicals and conventional renal medications, mediated through cytochrome P450 enzyme inhibition or induction, represents an additional safety consideration that requires systematic investigation [27].

7. Formulation Strategies and Advanced Delivery Systems

The limited bioavailability of many phytochemicals has driven substantial innovation in formulation science aimed at enhancing their therapeutic potential. Nanoparticle-based delivery systems, including polymeric nanoparticles, solid lipid nanoparticles (SLN), and nanostructured lipid carriers (NLC), have been employed to encapsulate hydrophobic compounds such as curcumin, thymoquinone, and quercetin, achieving markedly improved aqueous solubility, mucosal permeability, and plasma half-life [30]. Liposomal formulations of curcumin have demonstrated 30- to 40-fold improvements in oral bioavailability in preclinical studies compared to unformulated curcumin, while simultaneously enhancing renal tissue accumulation [25, 30].

Self-emulsifying drug delivery systems (SEDDS) represent another widely explored strategy for poorly water-soluble phytochemicals. These systems, consisting of oils, surfactants, and co-solvents, form fine oil-in-water emulsions spontaneously upon contact with gastrointestinal fluids, presenting dissolved drug for absorption at the intestinal epithelium. SEDDS formulations of astragaloside IV and quercetin have demonstrated significantly enhanced plasma Cmax and area-under-the-curve values in pharmacokinetic studies [19]. Cyclodextrin inclusion complexation, co-crystallization with pharmaceutical grade co-formers, and amorphous solid dispersion technologies have additionally been applied to improve the dissolution characteristics of crystalline phytochemicals.

Kidney-targeted drug delivery represents an advanced frontier in renal pharmacology. Folate receptor-targeted nanocarriers exploit the high expression of folate receptors on proximal tubular epithelial cells to achieve preferential renal accumulation of encapsulated phytochemicals. Receptor-mediated endocytosis via megalin and cubilin — multiligand endocytic receptors expressed on brush border membranes of proximal tubular cells — has been proposed as a pathway for tubule-targeted delivery of phytochemical-protein conjugates [31]. Such organ-targeted strategies hold the potential to reduce systemic drug exposure and associated off-target effects while concentrating therapeutic concentrations at the site of renal injury.

8. Regulatory, Safety, and Commercialization Challenges

The path from ethnobotanical observation to clinically approved phytomedicine is inherently complex, beset by regulatory, scientific, and commercial obstacles that are distinct from those encountered in the development of synthetic drugs. Regulatory agencies including the United States Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the World Health Organization (WHO) have developed dedicated guidelines for the evaluation of botanical drugs and herbal medicinal products, acknowledging both the unique nature of phytochemicals and the necessity for rigorous evidence standards [27, 32].

A fundamental challenge in phytomedicine development is the chemical complexity and variability of plant-derived preparations. Unlike single-entity synthetic drugs, botanical preparations may contain hundreds of biologically active constituents whose relative contributions to therapeutic activity and toxicity are incompletely understood. Ensuring batch-to-batch consistency in terms of the chemical fingerprint of botanical preparations requires sophisticated analytical methodologies, including high-performance liquid chromatography coupled with mass spectrometry (HPLC-MS) and nuclear magnetic resonance (NMR) spectroscopy, and implementation of good agricultural and collection practices (GACP) throughout the supply chain [33].

Intellectual property protection for naturally occurring phytochemicals is inherently limited, reducing commercial incentives for pharmaceutical industry investment in costly late-phase clinical trials. The novelty requirement for patent protection is difficult to satisfy for known natural compounds, though novel formulations, extraction processes, and specific therapeutic indications may be patentable [34]. Public funding of clinical research through academic consortia and national health research bodies therefore plays a vital role in advancing phytomedicine through late-phase clinical development. Post-market surveillance and pharmacovigilance systems specific to herbal medicines are also necessary to detect rare adverse effects and herb-drug interactions that may not be evident in pre-market trials [29, 35].

9. Conclusions and Future Directions

The evidence reviewed herein affirms that medicinal plants constitute a scientifically credible and pharmacologically diverse resource for the development of novel nephroprotective therapies. Compounds spanning multiple phytochemical classes — flavonoids, terpenoid saponins, polyphenols, alkaloids, and quinone derivatives — have demonstrated convergent activity against the principal pathophysiological mechanisms driving AKI and CKD, including oxidative stress, inflammatory cytokine cascades, TGF-β1-mediated fibrosis, and haemodynamic dysregulation. The most compelling clinical evidence currently exists for Phyllanthus niruri in nephrolithiasis, Astragalus membranaceus in diabetic nephropathy, and curcumin-based formulations in CKD, though all require larger, better-designed confirmatory trials to achieve definitive clinical integration.

Future directions in this field should prioritize several key areas. First, network pharmacology and systems biology approaches integrating genomics, transcriptomics, and metabolomics data are increasingly being applied to map phytochemical-target interaction networks in renal disease, enabling a more rational selection of plant candidates and prediction of synergistic combinations [36, 37]. Second, advanced formulation technologies — including kidney-targeted nanocarriers and stimuli-responsive drug delivery systems — should be further developed to overcome the bioavailability limitations that have historically impeded clinical translation. Third, standardization of botanical preparations using validated phytochemical fingerprinting methods and internationally recognized quality benchmarks is essential for ensuring reproducibility of clinical results [33, 38].

The integration of artificial intelligence in phytopharmacological research offers transformative potential, enabling high-throughput virtual screening of plant metabolite databases against validated renal disease targets, prediction of metabolic liabilities, and analysis of large-scale clinical and real-world evidence datasets [39]. Finally, collaborative engagement between traditional medicine systems, academic research institutions, regulatory agencies, and the pharmaceutical industry is essential to translate the ethnopharmacological heritage of medicinal plants into safe, effective, and accessible treatments for the substantial global population affected by kidney disorders [6, 40].

Figures

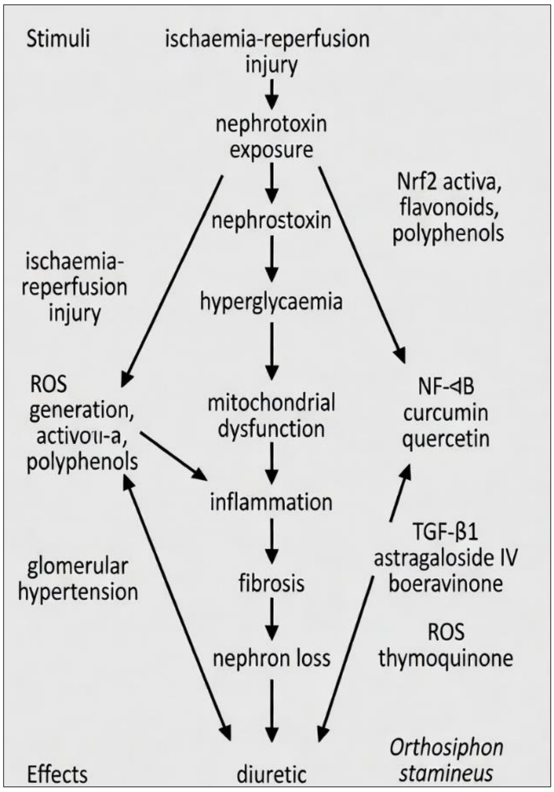

Fig 1: Pathophysiology of kidney disorders and molecular targets of medicinal plant compounds.

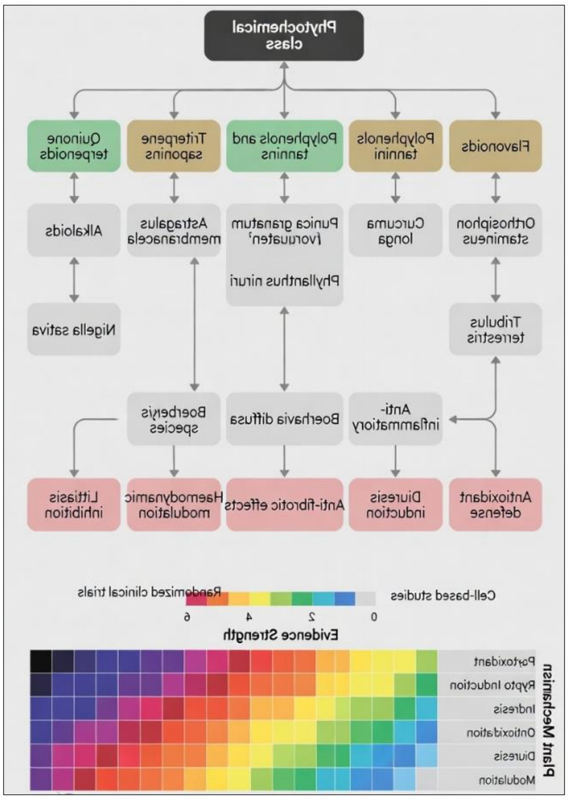

Fig 2: Classification of nephroprotective medicinal plants by phytochemical class and mechanisms of renal protection.

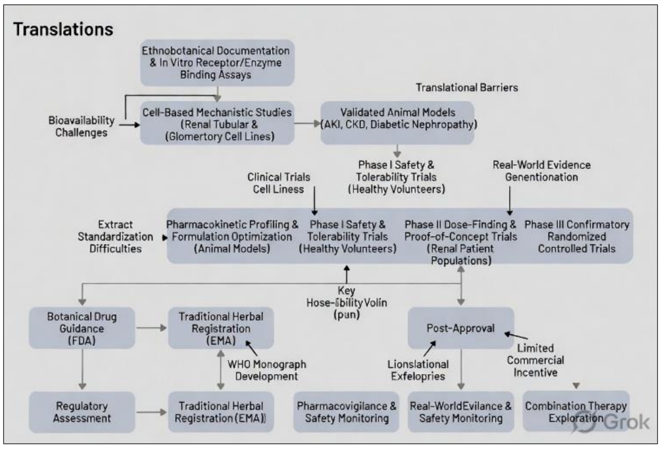

Fig 3: Translational pathway from medicinal plant discovery to clinical application in kidney disease treatment.

Tables

Table 1: Medicinal Plants, Active Constituents, and Mechanisms of Action in Kidney Disorders

Plant (Family)	Active Constituent(s)	Pharmacological Class	Primary Mechanism in Renal Protection
Phyllanthus niruri (Phyllanthaceae)	Phyllanthin, geraniin	Flavonoid, lignan	Inhibits calcium oxalate crystallization; antioxidant via NF-κB suppression
Orthosiphon stamineus (Lamiaceae)	Rosmarinic acid, sinensetin	Flavonoid, phenolic acid	Diuresis promotion; inhibition of renal inflammation via COX-2 downregulation
Tribulus terrestris (Zygophyllaceae)	Protodioscin, tribulosin	Saponin, flavonoid	Nephroprotection against cisplatin-induced oxidative damage; diuretic effect
Boerhavia diffusa (Nyctaginaceae)	Boeravinone, punarnavine	Alkaloid, flavonoid	Anti-fibrotic via TGF-β1 suppression; renal hemodynamic improvement
Astragalus membranaceus (Fabaceae)	Astragaloside IV, cycloastragenol	Triterpene saponin	Activates telomerase; podocyte protection in diabetic nephropathy
Curcuma longa (Zingiberaceae)	Curcumin, bisdemethoxycurcumin	Polyphenol	Inhibits NF-κB, Nrf2 activation, anti-fibrotic, anti-inflammatory in AKI and CKD
Nigella sativa (Ranunculaceae)	Thymoquinone	Quinone terpenoid	Scavenges reactive oxygen species; reduces renal tubular apoptosis
Punica granatum (Lythraceae)	Punicalagin, ellagic acid	Ellagitannin, polyphenol	Reduces proteinuria; anti-inflammatory via TNF-α and IL-6 suppression

Table 2: Clinical Applications and Efficacy of Plant-Based Therapies for Renal Conditions

Medicinal Plant	Renal Condition	Study Type	Key Outcome	Evidence Level
Phyllanthus niruri	Nephrolithiasis	RCT, systematic review	Reduced stone passage time; decreased urinary calcium	Level I-II
Orthosiphon stamineus	UTI, early CKD	Pilot RCT, cohort study	Improved creatinine clearance; diuretic efficacy confirmed	Level II-III
Astragalus membranaceus	Diabetic nephropathy	Meta-analysis (RCTs)	Reduced proteinuria and serum creatinine; glomerular protection	Level I
Curcumin (Curcuma longa)	CKD, diabetic nephropathy	RCT, open-label trial	Decreased urinary TGF-β1; reduced inflammation markers	Level II
Nigella sativa	Hypertensive nephropathy	RCT	Reduced blood pressure and serum creatinine; kidney function preservation	Level II
Punica granatum	CKD on dialysis	Randomized pilot study	Reduced oxidative stress markers; improved lipid profile	Level II-III

Table 3: Advantages, Limitations, and Pharmacokinetic Considerations of Medicinal Plant Compounds

Plant Compound	Advantages	Limitations	Pharmacokinetic Considerations
Curcumin	Pleiotropic activity; well-characterized; widely available	Poor oral bioavailability (<1%); rapid metabolism	Undergoes extensive first-pass; enhanced by piperine or nanoformulation
Thymoquinone	Potent ROS scavenger; low cost; anti-apoptotic	Instability at physiological pH; dose-dependent hepatotoxicity	Lipophilic; improved by lipid-based carriers; Tmax 1-2 hours
Astragaloside IV	Podocyte-protective; activates telomerase; anti-fibrotic	High molecular weight; poor membrane permeability	Low oral absorption; improved by self-emulsifying formulations
Geraniin (Phyllanthus)	Calcium oxalate inhibitor; antioxidant; anti-lithiasis	Limited clinical data; variable plant extract composition	Hydrolysed in gut; ellagic acid as active metabolite; renal excretion
Rosmarinic acid	Anti-inflammatory; renal COX-2 inhibitor; diuretic	Short plasma half-life; susceptibility to oxidative degradation	Moderate oral bioavailability; conjugated in liver; urinary excretion

Table 4: Current Research Status and Development Stages of Plant-Based Renal Therapies

Compound / Plant	Target Condition	Current Stage	Key Development Challenge	Regulatory Pathway
Astragaloside IV	CKD, diabetic nephropathy	Phase II/III trials	Standardization of extract; bioavailability optimization	New Drug Application (NDA) pending
Curcumin formulations	CKD, AKI	Phase I/II (nanoformulations)	Achieving therapeutic plasma levels; stability in formulation	Botanical Drug Guidance (FDA)
Phyllanthus niruri extract	Nephrolithiasis	Phase III (select regions)	Standardization of active phytochemical content	Traditional Use Registration (EMA)
Thymoquinone (Nigella sativa)	Hypertensive nephropathy	Phase II	Dose optimization; toxicity threshold in renal patients	Investigational New Drug (IND)
Boerhavia diffusa extract	Renal fibrosis, CKD	Preclinical / Phase I	Mechanistic elucidation; human pharmacokinetics needed	Ethnomedical regulatory framework

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