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Chronic Kidney Disease, Molecular Insight and Its Herbal Modulation

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Abstract

The human body is equipped with a natural system for internal cleansing and maintenance, with the kidneys serving as the primary organs responsible for filtering waste and maintaining fluid balance. However, modern lifestyle choices including poor diet, excessive intake of harmful beverages, and substance abuse can compromise kidney function. Two major types of kidney diseases are recognized: acute kidney injury (AKI) and chronic kidney disease (CKD). AKI, or acute renal failure, involves a sudden decline in kidney function and is often reversible. In contrast, CKD, also known as chronic renal failure, progresses slowly over at least three months and may lead to irreversible damage if remains untreated. Additional renal conditions include Glomerulonephritis, Polycystic Kidney Disease, Kidney Stones, UTIs, Lupus Nephritis, and nephropathies linked to diabetes and hypertension. While allopathic medications are widely prescribed, their side effects often limit long-term use, especially in elderly or immunocompromised individuals. Herbal formulations are gaining attention as supportive therapies due to their multi-targeted action and lower toxicity. This study considers multiple risk factors diet, lifestyle, alcohol and tobacco use, age, gender, ethnicity, and comorbidities when evaluating herbal interventions. Different kidney disorders may require tailored herbal combinations, warranting systematic research to validate efficacy and safety. Identifying and characterizing bioactive compounds through modern pharmacological techniques can strengthen the clinical credibility of these formulations. This paper aims to present a conceptual framework that bridges traditional herbal medicine with scientific validation, encouraging further exploration of plant-based therapies as complementary, or alternative approaches in kidney disease management.

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INTRODUCTION

Chronic kidney disease (CKD) is no longer an uncommon disorder; it is a looming global health challenge. It already ranks among the top ten causes of death and is projected to reach fifth place by 2040, creating major clinical and economic.[1,2] The pathophysiology of CKD is complex and multifactorial, common features include scarring of the glomeruli (glomerulosclerosis), shrinking of kidney tubules (tubular atrophy), tissue fibrosis and chronic inflammation.[3] At the molecular level, several signalling pathways such as NF-κB, TGF-β/Smad, MAPK, PI3K/Akt, and Nrf2 drive oxidative stress, inflammation, cell death, and fibrosis. Other contributing factors include overactivation of the renin–angiotensin–aldosterone system (RAAS), mitochondrial damage, and metabolic imbalances.[4] Recent research points to the gut–kidney axis as a key player in systemic inflammation and toxin clearance.[5] Beyond environmental and metabolic factors, genetics plays a crucial role in CKD susceptibility and progression. Genome-wide association studies (GWAS), and candidate gene analyses have revealed multiple genetic loci associated with renal function and eGFR,[6] with more than 600 genes implicated in kidney physiology and pathology.[7] Some forms of CKD are caused by single-gene (monogenic) defects, such as Alport syndrome (mutations in *COL4A3, COL4A4, COL4A5*), autosomal dominant polycystic kidney disease (*PKD1, PKD2*), and autosomal

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recessive polycystic kidney disease (*PKHD1*), which affect structural proteins or ciliary signalling. More commonly, CKD is influenced by multiple genes (polygenic). Variants in genes like *UMOD, APOL1, SHROOM3,* and *SLC7A9* increase susceptibility.[8] Notably; *APOL1* alleles (G1, G2) confer markedly higher risk for focal segmental glomerulosclerosis (FSGS) and hypertensive nephropathy in individuals of African ancestry. Likewise, variations in RAAS genes (*ACE, AGT, AGTR1*) and oxidative stress regulators can worsen CKD in individuals with diabetes or hypertension.[9] Epigenetic mechanisms such as DNA methylation, histone modifications, and noncoding RNAs further modulate disease pathways, adding another regulatory layer.[10] Current therapeutic strategies focus on slowing disease progression and managing complications through agents like ACE inhibitors, angiotensin receptor blockers (ARBs), and SGLT2 inhibitors.[11] While, these drugs reduce proteinuria and delay progression, they cannot reverse structural damage and often cause adverse effects such as hyperkalaemia and hypotension. In advanced stages, dialysis or kidney transplantation remains the only option, both associated with high costs, and significant psychosocial burdens.[12] This underscores the urgent need for safe, cost-effective, multi-targeted therapeutic alternatives. Herbal medicine, rooted in traditional systems such as Ayurveda and Traditional Chinese Medicine (TCM), offers potential solutions. Many plants traditionally used for kidney disorders are now validated by modern research, showing antioxidant, anti-inflammatory, antifibrotic, and immunomodulatory activities.[13] Molecular studies reveal that several botanicals can modulate signalling pathways implicated in CKD. For example, curcumin from *Curcuma longa* activates Nrf2, enhancing antioxidant gene expression (*HO-1, GCLC, GCLM, NQO1, GST*) and reducing oxidative stress, inflammation, and fibrosis, in experimental models.[14] *Astragalus membranaceus,* and its active compound astragaloside IV inhibit TGF-β/Smad signalling, downregulating fibrosis-related genes (*COL1A1, FN1, α-SMA*) and restoring *CDH1*, thereby preventing epithelial-to-mesenchymal transition (EMT) and renal scarring.[15] Other botanicals, including *Salvia miltiorrhiza* and berberine, though less studied at the gene-specific level, exhibit significant nephroprotective effects. They suppress TGF-β/Smad and NF-κB signalling while activating AMPK, thereby reducing inflammation and fibrosis.[16] These multi-targeted actions position herbal medicines as promising adjunct therapies. However, challenges remain, including variability in phytochemical content, lack of standardization, herb–drug interactions, and scarcity of large-scale randomized clinical trials. Emerging omics technologies genomics, transcriptomics, proteomics, and metabolomics combined with network pharmacology and bioinformatics, offer new opportunities to map herb–gene interactions and optimize therapeutic strategies.[17] Identifying key molecular targets, pathways, and gene expression profiles modulated by phytochemicals will not only validate traditional practices but also accelerate discovery of novel nephroprotective agents. In conclusion, herbal therapeutics hold significant potential in CKD management by attenuating oxidative stress, inflammation, and fibrosis through modulation of critical signalling networks. Bridging the gap between traditional practices and molecular evidence through robust clinical trials and advanced mechanistic research is critical for integrating herbal medicine into evidence-based nephrology.

MONOGENIC KIDNEY DISEASES

Cystic Kidney Diseases

Autosomal Dominant Polycystic Kidney Disease (ADPKD)

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is one of the most common inherited kidney disorders, characterized by the progressive development of renal cysts (Figure 1), leading to enlarged kidneys and eventual renal failure.[18] The molecular foundation of ADPKD lies in mutations affecting two critical genes: *PKD1* (85–90% of cases) and *PKD2* (10–15% of cases), which encode polycystin-1 (*PC1*) and polycystin-2 (*PC2*) proteins, respectively.[18] These polycystins form a functional complex primarily located in the primary cilia of renal epithelial cells, where they serve as mechanosensors responding to fluid flow and mediate crucial calcium signalling pathways.[19] Loss-of-function mutations in *PKD1* or *PKD2* impair calcium signalling, leading to altered expression of calcium-regulated genes, including those controlling proliferation (*CCND1, cyclin D1*), apoptosis (*BCL2, CASP3*), and fluid transport (*CFTR*).[20] This genetic disruption creates a cascade of transcriptional changes that promote cyst initiation and expansion. Hyperactivation of cAMP-dependent pathways in ADPKD results from increased expression of genes encoding adenylyl cyclase isoforms (ADCY6) and reduced expression of phosphodiesterase genes (*PDE1*), elevating intracellular cAMP levels.[21] This upregulates PKA-regulated transcription factors such as CREB, which enhance expression of proliferative genes (*MYC, FOS, EGR1*), chloride transporters (*CFTR*), and secretory machinery genes, accelerating cyst growth. Similarly, aberrant activation of the mTOR pathway reflects dysregulation of *TSC2* (tuberin), normally stabilized by *PC1*. Loss of *PC1* function decreases *TSC2* activity, increasing expression of genes involved in protein synthesis (*RPS6KB1*, *S6 kinase*) and cell growth regulators (*EIF4EBP1*), further driving cystic expansion.[22]

Autosomal Recessive Polycystic Kidney Disease (ARPKD)

Autosomal recessive polycystic kidney disease (ARPKD) is a severe hereditary disorder typically presenting in infancy or childhood characterized by cystic dilation of the collecting ducts and congenital hepatic fibrosis.[23] The molecular

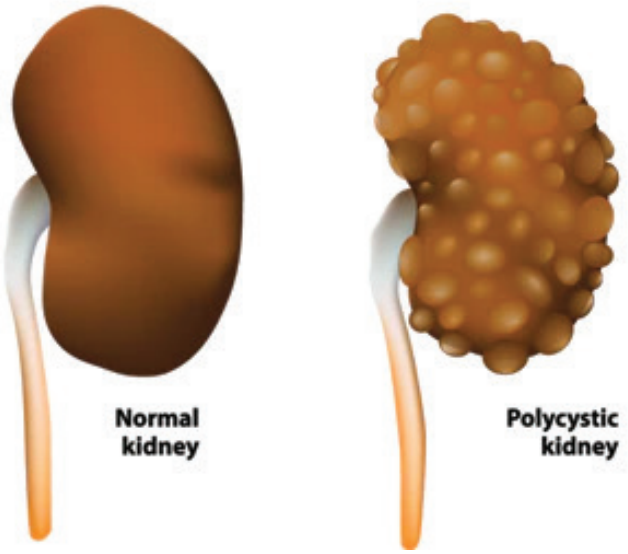

Figure 1: Morphologies of normal and polycystic kidney.

foundations and cellular mechanisms of ARPKD centre on defects in primary cilia and associated signalling pathways in renal tubular epithelial cells. Most ARPKD cases result from mutations in the *PKHD1* gene, which encodes fibrocystin/polyductin (*FPC*), a large transmembrane protein.[24] *FPC* is predominantly located in the primary apical cilia and basal bodies of kidney epithelial cells, as well as cholangiocytes in the liver. Primary cilia are non-motile, microtubule-based organelles that sense mechanical and chemical stimuli in the renal tubule lumen and regulate crucial signalling pathways involved in cell proliferation and differentiation.[25] Loss of function in *FPC* disrupts the structural integrity and signalling functions of the primary cilium. This leads to impaired regulation of cell growth, differentiation, and tubulogenesis, resulting in abnormal and uncontrolled dilatation of the collecting ducts. *FPC* interacts indirectly with other PKD proteins (*PC1* and *PC2*, involved in ADPKD), and there is evidence that PKD proteins form a functional ciliary complex, sharing downstream effectors such as the mTOR, MAPK/ERK, cAMP/PKA, and calcium signalling pathways.[26] Ciliary dysfunction alters calcium influx, disrupting calcium-dependent signalling and affecting pathways governing cell proliferation and fluid secretion. Abnormal regulation of adenylate cyclase and phosphodiesterase lead to elevated cAMP levels, which, via PKA activation, promotes cystic cell proliferation and fluid secretion into cysts. Defects in sodium and chloride channels (*ENaC, CFTR*) and aquaporins (*AQP2*) contribute to disturbed fluid movement and cyst expansion.[27] TGF-β, EGFR, and VEGF signalling are implicated in fibrosis and abnormal tissue transformation in ARPKD.[28]

Nephronophthisis

Nephronophthisis (NPHP) is an autosomal recessive ciliopathy and the leading genetic cause of end-stage renal disease in children and young adults. It is characterized by chronic tubulointerstitial fibrosis, and progressive cyst formation that culminates in kidney failure within the first three decades of life. The disease arises from mutations in more than 26 genes (*NPHP1–26*), most of which encode proteins critical for primary cilium function, with *NPHP1* mutations accounting for 21–25% of cases, while other individual genes contribute less than 3% each. Approximately, 70% of cases remain genetically unresolved, highlighting the likelihood of additional unidentified genes.[29] The protein products of *NPHP* genes, termed nephrocystins, are primarily localized to the transition zone or inversion compartment of primary cilia, centrosomes, or components of intraflagellar transport complexes. They operate in modules such as *NPHP14–8, NPHP2–3–9–16, NPHP5–6*, and the MKS module. Disruption of these ciliary structures leads to multiple signalling defects, including abnormal Hedgehog (Hh) signalling marked by increased Gli3 repressor protein levels, which can be partially rescued by the Hh agonist purmorphamine. Additionally, defective inversin skews the Wnt pathway toward canonical signalling at the expense of non-canonical planar cell polarity (PCP) signalling, thereby impairing epithelial polarity. *NPHP* pathogenesis involves dysregulated cAMP/PKA signalling, where impaired ciliary control reduces basal cAMP levels essential for Gli regulation and cellular homeostasis. Emerging evidence also implicates defective DNA damage response mechanisms, leading to genomic instability and cell cycle abnormalities, suggesting that *NPHP* is not a solely ciliary disease but also involves broader cellular pathway.[30,31]

Medullary Cystic Kidney Disease (MCKD)

Medullary Cystic Kidney Disease (MCKD) is an autosomal dominant inherited disorder. It is characterized by progressive tubulointerstitial fibrosis and the formation of cysts in the renal medulla. This leads to adult-onset chronic kidney disease and eventually progresses to end-stage renal failure. MCKD is closely related to nephronophthisis (NPH) and together, they are sometimes referred to as the nephronophthisis–medullary cystic kidney disease complex due to overlapping clinical and genetic features.[32] MCKD is primarily caused by mutations in two genes: *MUC1* (*MCKD1*, chromosome1), and *UMOD* (MCDK2, chromosome 16p12). The *UMOD* gene encodes uromodulin (Tamm-Horsfall protein), which is the most abundant protein in normal urine and is expressed by the thick ascending limb cells of the loop of Henle in the kidney. Mutations in *UMOD* lead to the accumulation of misfolded uromodulin in the endoplasmic reticulum (ER) of renal tubular epithelial cells, triggering ER stress, apoptosis, and progressive tubular damage and fibrosis. This process also results in decreased urinary excretion of uromodulin, consistent with MCKD›s clinical findings. Specific exons of *UMOD* (notably exons 4 and 5) are important for its calcium-binding and folding properties. Mutations disrupt protein structure and trafficking, exacerbating ER stress

and damage. Chronic accumulation of mutant uromodulin in the ER induces apoptosis and a scarring process, leading to tubulointerstitial injury and renal fibrosis. The disease process is not linked to ciliary dysfunction, unlike many other cystic kidney diseases, since *UMOD* is not expressed in the cilia of tubular epithelial cells. Inflammation and immune mechanisms may also be implicated, as protein aggregates can stimulate antibody formation and cellular infiltration, enhancing the risk of progressive renal insufficiency and scarring. Unlike polycystic kidney diseases (PKD), MCKD cysts are usually fewer, smaller, limited to the corticomedullary junction, and are secondary to underlying tubular atrophy and interstitial fibrosis rather than primary cyst formation.[33]

GLOMERULAR DISEASES

1. Alport Syndrome

Alport syndrome is a hereditary kidney disorder caused by mutations in *COL4A3*, *COL4A4*, and *COL4A5*, which encode the α3, α4, and α5 chains of type IV collagen, essential for the structural integrity of the glomerular basement membrane (GBM).[34] These mutations disrupt the assembly of the α3α4α5(IV) collagen heterotrimer. This leads to thinning of the glomerular basement membrane (GBM), splitting of the lamina densa and a characteristic basket-weave appearance. As a result, affected individuals develop progressive glomerulosclerosis, kidney failure, sensorineural hearing loss, and ocular abnormalities.[35] Abnormal collagen assembly also alters extracellular matrix remodelling, causing aberrant laminin deposition and persistence of immature isoforms, which correlate with podocyte injury. Furthermore, changes in integrin signalling, particularly overexpression of αvβ6, activate profibrotic pathways such as TGF-β and increase matrix metalloproteinase activity (*MMP2, MMP9, MMP14*), promoting mesangial migration and fibrosis. Proteomic studies also reveal mitochondrial dysfunction and impaired energy metabolism through *PPARα* pathway downregulation, indicating metabolic dysregulation as a potential therapeutic target.[36]

2. Fabry Disease

Fabry disease is a rare X-linked lysosomal storage disorder caused by mutations in the *GLA* gene, which encodes the enzyme α-galactosidase A (*α-GalA*). Enzyme deficiency leads to progressive accumulation of glycosphingolipids, primarily globotriaosylceramide (Gb3) and its derivative lyso-Gb3, within lysosomes. This buildup occurs across multiple tissues, disrupting normal cellular function and initiating complex pathogenic cascades. Gb3 accumulation results in lysosomal dysfunction and impaired autophagy, contributing to defective organelle turnover and mitochondrial injury.[37] These changes exacerbate oxidative stress and mitochondrial dysfunction, promoting reactive oxygen species (ROS) production and oxidative damage, partly through RIPK3-dependent mechanisms. Furthermore, inflammatory pathways are activated, with macrophage polarization, elevated cytokine expression, and activation of the NF-κB pathway, leading to chronic tissue injury and fibrosis.[38] Additionally, Gb3-driven energy depletion alters metabolic signalling, activating AMP-activated protein kinase (AMPK) and inhibiting mTORC1, impairing autophagy and shifting cellular metabolism from fatty acid oxidation to glycolysis.[39] Collectively, these molecular events lipid storage, oxidative stress, immune activation, and metabolic dysregulation drive the multisystemic manifestations of Fabry disease.

3. Pierson Syndrome

Pierson syndrome is a rare autosomal recessive disorder caused primarily by mutations in the *LAMB2* gene, which encodes the laminin β2 subunit, an essential component of basement membranes, particularly the glomerular basement membrane (GBM) in the kidney and ocular structures.[40] Laminin β2 normally forms part of the α5β2γ1 heterotrimer, crucial for GBM stability and podocyte adhesion. Loss or dysfunction of laminin β2 disrupts extracellular matrix organization, integrin signalling, and slit diaphragm integrity, resulting in congenital nephrotic syndrome, ocular abnormalities, and, in some cases, neuromuscular defects. Functionally connected genes, including *NPHS1, NPHS2, COL4A3, COL4A5, PLCE1*, and *AGRN*, contribute to glomerular development and podocyte function, explaining overlapping clinical features with other congenital nephrotic syndromes.[40] The severity of Pierson syndrome correlates with *LAMB2* mutation type: truncating variants typically cause complete loss of protein, whereas missense or compound heterozygous mutations lead to partial function and variable phenotypes. Overall, the disorder reflects a fundamental defect in basement membrane assembly, affecting GBM integrity, neuromuscular junctions, and ocular structure maintenance.[41]

4. Congenital Nephrotic Syndrome (Finnish Type) (CNF)

It is a severe autosomal recessive kidney disorder characterized by massive proteinuria and edema, typically manifesting in utero or shortly after birth. The condition results primarily from mutations in the *NPHS1* gene, which encodes nephrin, a transmembrane protein crucial for the structure and function of the glomerular slit diaphragm (SD), the main size-selective filtration barrier in the kidney. Nephrin belongs to the immunoglobulin superfamily and forms a zipper-like structure between podocyte foot processes. Its absence or dysfunction disrupts SD integrity, causing increased glomerular permeability and massive proteinuria. Ultrastructural changes include podocyte foot process effacement and disappearance of slit diaphragms. In Finland, CNF is associated with two founder *NPHS1* mutations Fin-major and Fin-minor which account for most cases. While *NPHS1* mutations define CNF, other podocyte-related genes (e.g., *NPHS2, ACTN4*) can cause similar but distinct congenital

nephrotic syndromes. Overall, *NPHS1* mutations and nephrin deficiency are the molecular hallmark of CNF, leading to disruption of the glomerular filtration barrier and severe proteinuric nephropathy.[42]

5. Denys-Drash syndrome (DDS) and Frasier syndrome (FS)

These are rare disorders caused by mutations in the *WT1* gene on chromosome 11p13, which encodes a zinc-finger transcription factor essential for kidney and gonadal development. *WT1* regulates genes critical for nephron differentiation, podocyte function, and gonadal morphogenesis. DDS is most commonly associated with missense mutations in exons 8 and 9 within the DNA-binding zinc finger domains, particularly the p.Arg394Trp variant, leading to dominant-negative disruption of *WT1*'s transcriptional regulation and resulting in diffuse mesangial sclerosis, gonadal dysgenesis, and a high risk of Wilms tumour. Conversely, FS typically arises from splice site mutations in exon 9 that alter the ratio of WT1 isoforms containing or lacking the KTS sequence, shifting the normal 2:1 (+KTS/−KTS) balance to approximately 1:2.[43] This isoform imbalance affects podocyte gene expression and gonadal development, causing progressive nephropathy (commonly focal segmental glomerulosclerosis), gonadal dysgenesis, and an increased risk of gonadoblastoma but rarely Wilms tumour. Both syndromes disrupt pathways involved in slit diaphragm integrity, mesenchymal-epithelial transition, and glomerular development, intersecting with genes such as *NPHS1, NPHS2*, *PAX2*, and *CD2AP*.[44]

6. Thin Basement Membrane Nephropathy (TBMN)

TBMN is primarily associated with heterozygous mutations in *COL4A3* and *COL4A4*, which encode the α3 and α4 chains of type IV collagen essential components of the mature glomerular basement membrane (GBM).[45] Normally, the GBM undergoes a developmental transition from an α1: α2 collagen IV network to an α3: α4: α5 network, providing structural integrity and selective permeability. In TBMN, pathogenic variants most often single-nucleotide substitutions unique to families disrupt assembly of the α3α4α5 collagen IV network, causing diffuse GBM thinning and persistent microscopic hematuria.[46] Beyond the core *COL4A3/COL4A4* mutations, modifying variants in genes regulating podocyte cytoskeleton and basement membrane interactions (e.g., *MYO1E, LAMA5, NPHS2, ITGB4*) have been reported to influence disease severity and progression to chronic kidney disease.[47] Disruption of collagen IV architecture also alters GBM interactions with laminins and nidogens, impacting extracellular matrix signalling and podocyte adhesion.[45] Overall, TBMN reflects a primary defect in collagen IV network assembly, with secondary involvement of podocyte and extracellular matrix pathways modulating phenotypic variability.

TUBULAR AND ELECTROLYTE DISORDERS

1. Bartter Syndrome

Bartter syndrome comprises a group of rare inherited renal tubulopathies characterized by defective salt reabsorption in the thick ascending limb (TAL) of the loop of Henle, leading to hypokalaemia, metabolic alkalosis, and secondary hyperreninemia.[48] The disorder is genetically heterogeneous, involving mutations in genes encoding key transporters and channels in the TAL. Type 1 results from mutations in *SLC12A1*, encoding the Na-K-2Cl cotransporter (*NKCC2*), essential for sodium chloride reabsorption. Type 2 involves *KCNJ1* mutations affecting potassium channels, disrupting potassium recycling required for *NKCC2* function. Type 3 is caused by *CLCNKB* mutations impairing basolateral chloride exit, while Type 4a results from *BSND* mutations encoding barttin, an accessory subunit for ClC-Ka/Kb channels, and is associated with sensorineural deafness. Combined *CLCNKA* and *CLCNKB* mutations produce a similar phenotype (Type 4b). Type 5 involves *MAGED2* mutations (X-linked), affecting *NKCC2* trafficking, causing transient antenatal Bartter syndrome.[49] A CaSR gain-of-function variant mimicking Bartter syndrome further illustrates the regulatory role of calcium signalling in TAL function. Disruption of these pathways causes salt wasting, chronic prostaglandin E2 activation, and polyuria, highlighting how diverse genetic defects converge on impaired TAL salt handling.

2. Gitelman Syndrome (GS)

Gitelman syndrome is an autosomal recessive salt-wasting tubulopathy caused by impaired sodium-chloride reabsorption in the distal convoluted tubule (DCT), clinically characterized by hypokalaemia, hypomagnesemia, metabolic alkalosis, and hypocalciuria.[50] The primary genetic defect occurs in *SLC12A3*, which encodes the thiazide-sensitive Na-Cl co-transporter (NCC), essential for sodium and chloride reabsorption; its dysfunction leads to salt wasting and the hallmark electrolyte abnormalities.[51] Mutations in *CLCNKB*, encoding the ClC-Kb chloride channel, or in genes indirectly modulating NCC function such as *KCNJ10, KCNJ16, FXYD2, ATP1A1,* and *HNF1B* can produce Gitelman-like phenotypes. Additionally, maternally inherited variants in mitochondrial tRNA genes (*MT-TI*, *MT-TF*) have been implicated in rare Gitelman-like syndromes, likely due to impaired ATP generation required for NCC phosphorylation and transport. These findings underscore that while NCC dysfunction remains the central defect, GS reflects a broader disruption of pathways governing sodium, chloride, potassium, and magnesium handling in the DCT, often involving complex regulatory and metabolic networks.[52]

3. Cystinuria

Cystinuria is an inherited renal tubular disorder characterized by defective reabsorption of cystine and dibasic amino acids (ornithine, lysine, arginine) in the proximal tubule and small

intestine, leading to excessive urinary cystine excretion and recurrent nephrolithiasis.[53] The condition primarily results from mutations in *SLC3A1* and *SLC7A9*, which encode the heavy and light subunits of the heterodimeric amino acid transporter localized on the apical membrane of proximal tubular epithelial cells.[54] These subunits are essential for renal amino acid reabsorption; pathogenic variants disrupt transporter assembly or function, resulting in cystinuria types A, B, or AB depending on whether *SLC3A1*, *SLC7A9*, or both are mutated.[55] Since cystine is poorly soluble in urine, elevated levels promote crystal precipitation and stone formation. In rare cases, larger chromosomal deletions involving *SLC3A1* and neighbouring genes such as *PREPL* can lead to syndromic forms with neuromuscular symptoms. Overall, cystinuria exemplifies a disorder of amino acid transport with high clinical relevance for stone disease and potential genetic counselling implications.[55]

POLYGENIC KIDNEY DISEASES

1. Chronic Kidney Disease (CKD)

CKD involves a complex interplay of inflammatory, metabolic, and fibrotic pathways, influenced by many genetic factors. Inflammation is a key driver, with genes such as *ICAM1*, *CXCL8*, and *CCL2* mediating leukocyte infiltration and cytokine-driven injury. Oxidative stress further exacerbates kidney damage, where *NRF2* functions as a central regulator of antioxidant responses and metabolic homeostasis.[56] Additionally, activation of signalling pathways such as PI3K-Akt and dysregulation of cell cycle and extracellular matrix genes (*CDKN1C*, *COL4A2*, *SERPINE2*) contribute to fibrosis and progressive nephron loss, while downregulation of podocyte-specific genes like *NPHS1* compromises the filtration barrier.[57] These findings underscore the polygenic nature of CKD, with over 600 implicated genes converging on common molecular networks that drive chronic inflammation, oxidative injury, and fibrogenesis.[58]

2. Diabetic Nephropathy (DN)

Diabetic nephropathy is a progressive microvascular complication of diabetes driven by interlinked pathways involving inflammation, oxidative stress, and fibrosis. Key molecular mechanisms include immune and inflammatory pathways such as complement activation, chemokine signalling, and antigen-antibody interactions, which underline the strong immune-mediated nature of DN.[59] Hyperglycaemia induces activation of PI3K-Akt and Rap1 signalling pathways, contributing to altered cell survival, proliferation, and metabolism. NFκB and MAPK signalling cascades, activated by oxidative stress and advanced glycation end-products (AGEs), further amplify inflammatory and apoptotic responses in podocytes and tubular epithelial cells. Among profibrotic mechanisms, the TGF-β1 pathway plays a central role in driving extracellular matrix (ECM) accumulation and fibrosis, often enhanced by angiotensin-II and protein kinase C (PKC) signalling. Additionally, epigenetic modifications such as DNA methylation at the *TXNIP* locus mediate metabolic memory; sustaining disease progression even after glycaemic control improves. JAK/STAT signalling, particularly through *STAT3*, also regulates inflammatory cytokines and Notch1-dependent profibrotic gene expression.[60] Several key genes have been identified as central regulators of DN pathology, including *TYROBP, ITGB2, CD53, IL10RA, LAPTM5, CD48, C1QA*, and *IRF8*. Additional transcription factors like *SPI1, HIF1A, STAT1, KLF5, RUNX1*, and *WT1* contribute to podocyte injury, endothelial dysfunction, and progression of renal fibrosis.[61]

3. Hypertensive Nephropathy (HN)

It is a progressive kidney disorder driven by sustained high blood pressure, leading to structural and functional damage through a complex network of molecular pathways and genetic regulators. Key mechanisms include proteasome-mediated protein degradation, which alters turnover of regulatory proteins, and dysregulation of Rho GTPase signalling and cytoskeletal organization, impairing podocyte and tubular integrity. Inflammatory signalling pathways such as NF-κB, IFN-γ, IL-12, and Wnt are upregulated, promoting immune cell infiltration and chronic inflammation, while metabolic derangements involving the tricarboxylic acid (TCA) cycle and amino acid/purine metabolism highlight the role of HN as a metabolic disorder.[62] Additionally, renal tissue hypoxia and oxidative stress exacerbate injury, triggering redox imbalance and reactive oxygen species accumulation. Principal genes implicated in these pathways include *SORD, CUBN,* and albumin, associated with energy metabolism, and *POLR2I, POLR2L,* and *POLR2G,* subunits of RNA polymerase II involved in transcriptional regulation and oxidative stress responses. *TRIM31*, an E3 ubiquitin ligase, promotes proteasomal degradation of *MAP3K7,* thereby modulating inflammation. Other significant genes include *NR4A1, TNFSF10, CX3CR1, CXCR4, CCL5*, and *ATF3,* which regulate cytokine signalling and immune activation. Epigenetic and non-coding RNA regulation also play critical roles, with microRNAs such as hsa-miR-1248, hsa-miR-200b-5p, and hsa-miR-23b-5p fine-tuning gene expression.[63] Functionally, these interactions affect pathways such as proteasome-mediated degradation (*TRIM31, MAP3K7*), TCA cycle and metabolic processes, transcriptional regulation and oxidative stress (*POLR2I, POLR2L, POLR2G*), inflammatory signalling (*NR4A1, TNFSF10, NF-κB, CCL5*), and cytoskeletal integrity (actin-associated proteins). Collectively, these molecular alterations converge to cause progressive renal fibrosis, glomerular sclerosis, and loss of kidney function in HN.[63]

4. Lupus Nephritis

Lupus nephritis (LN) is driven by a complex interplay of genetic and molecular factors that promote immune complex deposition, inflammation, and kidney tissue damage. Recent studies have identified key genes and pathways central

to LN pathogenesis. Driver genes such as *CD53*, *TGFBI*, *MS4A6A*, and *HERC6* are implicated in immune activation, macrophage activity, and inflammation, correlating with disease severity and proteinuria. Other upregulated genes, including *C1QA, C1QB, IFI44L*, *TYROBP*, and *MS4A4A*, participate in complement activation, interferon signalling, and macrophage differentiation, underscoring their role in immune cell infiltration. Polymorphisms in *IRF5, IRF7, TNFAIP3, TNIP1*, and *UBE2L3* regulate type I interferon, NF-κB, and MAPK pathways, enhancing autoantibody production and inflammatory signaling.[64] Additionally, epigenetic changes, including DNA methylation affecting genes such as *ITGAL, TNFSF7*, and *CD40LG*, further contribute to immune dysregulation. Critical pathways such as complement activation, toll-like receptor (TLR)/MyD88 signalling, and type I interferon responses play dominant roles, while HLA-DRB1 strongly associates with LN susceptibility[65].

5. IgA Nephropathy (Berger's Disease)

IgA nephropathy (IgAN), or Berger's disease, is characterized by the deposition of IgA antibodies in the glomeruli, leading to inflammation and progressive kidney damage. The disease arises from a complex interplay of immune dysregulation, genetic susceptibility, and abnormal IgA1 glycosylation. Aberrantly glycosylated IgA1 (galactose-deficient IgA1, Gd-IgA1) forms immune complexes with glycan-specific autoantibodies, triggering mesangial deposition and renal injury. Several signalling pathways, including NF-κB, JAK-STAT, TGF-β, MAPK, and PI3K-Akt, regulate inflammation, immune responses, fibrosis, and cell survival in IgAN. Long noncoding RNAs (lncRNAs) modulate these processes via PI3K/AKT/mTOR, PTEN, Notch, and JNK pathways, influencing immune activation and kidney damage. LncRNAs such as NQO1-DT, RP5-1057120.6, and G21551 have emerged as potential biomarkers and therapeutic targets. Genetically, GWAS studies have revealed multiple susceptibility loci associated with immune regulation (e.g., *TNFSF4, TNFSF18, REL, CD28, LY86, LYN, ETS1, IRF8, TNFRSF13B, FCAR*) and IgA production or clearance (*IGH, FCGR3B*). Genes controlling glycosyltransferases are particularly important in mediating the IgA1 glycosylation defect, which has an estimated heritability of 50–70%. Hub genes such as *FOS, JUN, EGFR, SIRT1, IGF1, HIF1A, SOCS3, ACTR2*, and *CTNNB1* are implicated in inflammatory responses, cell proliferation, and apoptosis, highlighting key molecular drivers of disease progression.[66]

6. Kidney Stone Disease (Nephrolithiasis)

A multifactorial condition influenced by genetic, metabolic, and environmental factors, with recent studies emphasizing the involvement of specific molecular pathways and genes. Among key genes, *KLK1* (Kallikrein 1) and *MMP10* (Matrix Metalloproteinase-10) have emerged as significant diagnostic markers, showing upregulation in stone-bearing kidneys where they contribute to metabolic regulation, inflammation, immune responses, and extracellular matrix remodelling, thereby promoting stone formation.[67] Other genes, including *LCN2, IL11, PTGS1, GPX3*, and *MMD*, are upregulated in Randall's plaque, the nidus for stone anchoring, while genes such as *SLC12A1* and *NALCN* are downregulated, implicating changes in ion transport and tubular function. Variations in *ATP1A1*, which encodes the Na^+/K^+-ATPase α1-subunit, reduce its expression and may promote renal crystal deposition by altering sodium and calcium homeostasis. Broader genetic studies also highlight both monogenic forms, such as mutations causing familial hypomagnesemia with hypercalciuria and nephrocalcinosis, and polygenic risk, suggesting that multiple low-effect alleles modulate susceptibility.[68] At the molecular level, pathways regulating ion transport, metabolic homeostasis, and oxalate/calcium balance are central to stone pathogenesis. Inflammatory and immune responses, mediated by cytokines and immune cell recruitment, contribute to renal tissue injury and crystal retention, while oxidative stress from reactive oxygen species promotes tubular damage and alters gene expression linked to stone growth. Moreover, signalling cascades such as MAPK, PI3K/Akt, and those associated with type I diabetes are enriched in stone-forming tissues, reflecting their role in stress response, apoptosis, and metabolic dysregulation. Dysregulation of sodium and calcium reabsorption through channels and pumps, including Na^+/K^+-ATPase and related transporters, further increases urinary supersaturation, reinforcing the risk of stone formation.[69]

KIDNEY CANCER

Kidney Cancer, also known as renal cancer, is a malignancy that originates in the kidney tissue, with renal cell carcinoma (RCC) being the most common subtype, accounting for nearly 90% of cases. This cancer typically develops in the renal tubules and is often detected incidentally through imaging studies, although advanced stages present with symptoms such as haematuria, flank pain, and unexplained weight loss. RCC pathogenesis involves complex molecular and genetic alterations that promote uncontrolled cell growth, angiogenesis, and immune evasion. A hallmark of RCC is inactivation of the *VHL* (Von Hippel–Lindau) tumour suppressor gene, leading to stabilization of hypoxia-inducible factors (*HIF-1α* and *HIF-2α*) under normoxic conditions. This upregulates target genes such as *VEGF* and *PDGF*, driving angiogenesis and tumour growth.[70] Another critical signalling network in RCC is the PI3K/AKT/mTOR pathway, frequently activated through mutations in mTOR, TSC1, and TSC2, promoting uncontrolled cell proliferation and inhibiting autophagy.[71] Dysregulated angiogenic signalling through VEGF is a major feature of RCC and forms the therapeutic basis for VEGF-targeted tyrosine kinase inhibitors. In addition, *MET* proto-oncogene alterations, often seen in papillary RCC, activate downstream RAS/RAF/MAPK signalling, enhancing tumour progression.[70] Epigenetic dysregulation is also common, with frequent mutations in chromatin remodelling genes such as *PBRM1, BAP1,* and *SETD2*, which affect transcription, DNA repair, and

immune microenvironment; notably, BAP1 loss is associated with aggressive disease, while *PBRM1* mutations influence immunotherapy response.[72] Furthermore, immune evasion mechanisms, particularly overexpression of *PD-1/PD-L1*, contribute to RCC progression and justify the use of immune checkpoint inhibitors in treatment.[73] Collectively, these molecular events illustrate that RCC is driven by an interplay of pathways involving hypoxia signalling, growth factor receptor activation, chromatin remodelling, and immune modulation, which has paved the way for targeted therapies and immunotherapies that have significantly improved patient outcomes.

COMPLEX GENE INTERACTIONS

A comprehensive search in the Online Mendelian Inheritance in Man (OMIM), revealed 18,683 gene entries mapped across the human genome, distributed across all autosomes and sex chromosomes, including 56 genes on the Y chromosome.[74] Notably, several transcripts such as members of the TTTY family were present in this dataset. Chromosome-specific evaluation indicated that nearly every chromosome contains genes potentially associated with CKD (Table.1.). While these findings do not imply that all 18,000+ genes directly contribute to CKD, they highlight the extensive genetic complexity of the disease. This broad association likely reflects the involvement of numerous biological pathways that regulate renal development, glomerular filtration, tubular transport, immune modulation, and fibrosis. Many of these pathways operate in a stage-specific and context-dependent manner to maintain kidney function. The large gene count may also arise from pleiotropic effects, wherein variants in genes implicated in metabolic, inflammatory, or vascular processes exert indirect effects on CKD susceptibility. Although the exact number of genes actively driving CKD remains uncertain, current genomic and transcriptomic studies estimate approximately 600–625 genes as significantly associated with CKD onset and progression.[75,76] The representative signalling network is shown in Figure 2. This summarizes major genetic regulators and interconnected pathways implicated in CKD pathogenesis. While this schematic is not exhaustive, it provides insight into the molecular interplay between inflammation, oxidative stress, fibrotic remodelling, and metabolic dysregulation underlying CKD.

Table 1: Chromosome specific entries of genes with their total number and association with CKD.[74]

Chromosome Number	Total Genes on the Chromosomes	Number of Genes Associated with CKD	Names of the Noted CKD Associated Genes
1	2,050	21	FAM78B, MYH9, APOL1
2	1,301	47	APOL1
3	1,079	18	FAM78B
4	753	25	SHROOM3
5	884	19	COL4A3, COL4A4
6	1,045	60	UMOD, HLA-DRB1
7	992	26	PKD1, PKD2
8	1,021	16	TSC2
9	778	8	FRMD3
10	731	14	COL4A5
11	1,316	33	WT1
12	1,036	26	TTR
13	321	7	VHL
14	821	1	COL11A1
15	616	33	CASR
16	862	29	BBS1
17	1,188	24	UBE2Z
18	269	13	SLC12A3
19	1,474	9	SLC7A9
20	543	9	MMP9
21	232	2	HNF1A
22	492	8	TSC2
X	846	4	AVPR2, PAX2
Y	63	52	26 genes

REACTOME PATHWAY

This network diagram illustrates key gene-pathway associations involved in chronic kidney disease (CKD). Although over 600 genes are linked to CKD, the figure highlights representative genes and their roles in critical processes such as podocyte function, RAAS regulation, creatine metabolism, immune response, and cytoskeletal organization. Blue nodes represent genes, while green nodes represent biological functions, with edges indicating gene involvement. The diagram reveals a modular structure, where distinct yet interconnected pathways collectively maintain kidney function. Disruption in these pathways through mutations or gene dysregulation can impair renal processes, leading to CKD. This highlights the multifactorial nature of CKD and the need for a systems-level understanding to uncover therapeutic targets.[77]

HERBAL REMEDIES TARGETING KIDNEY DISEASES AND THEIR PATHWAYS

Herbal therapeutics have shown promising potential in managing various kidney disorders by modulating molecular pathways involved in fibrosis, oxidative stress, inflammation, and electrolyte imbalance. These plant-based interventions act through bioactive compounds such as curcumin, astragalosides, catechins, and salvianolic acids, which influence signalling mechanisms like mTOR, TGF-β, NF-κB, and

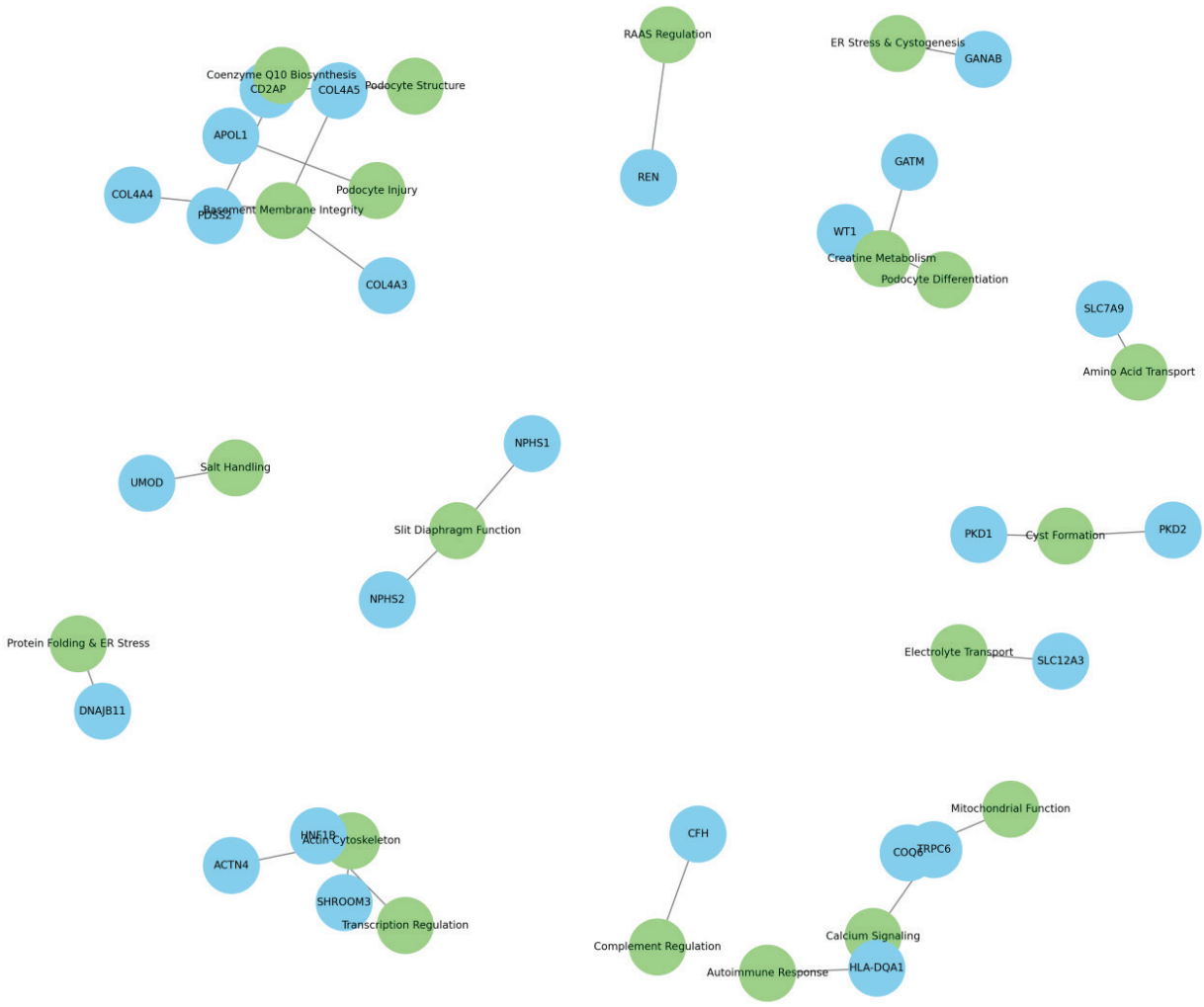

Figure 2: Schematic illustration showing the interplay between key pathways of the genes involved in CKD.

RAAS, thereby slowing disease progression and improving renal function. The following table summarizes kidney conditions, their pathological features, potential herbal remedies, active compounds, and targeted mechanisms.[78]

Herbal Supplements as Sources of Potassium and Phosphorus: Critical Considerations in CKD Management

Potassium and phosphorus play essential roles in cellular function, neuromuscular activity, and energy metabolism; however, their regulation becomes critically important in chronic kidney disease (CKD) management. Impaired renal excretion predisposes CKD patients to hyperkalaemia and hyperphosphatemia, which can cause life-threatening arrhythmias, vascular calcification, bone-mineral disorders, and accelerated cardiovascular risk. Herbal supplements, often perceived as safe, may act as hidden sources of potassium and phosphorus, complicating dietary control strategies that are fundamental in CKD care. Potassium directly influences RAAS signalling, WNK-SPAK/OSR1 pathways, and genes such as *SLC12A1*, *KCNJ1*, and *WNK1*, which regulate sodium–potassium transport and blood pressure critical targets in CKD. Similarly, phosphorus homeostasis involves the FGF23–Klotho axis, PTH signaling, and Na^+/Pi cotransporters (*SLC34 family*), linked to genes like *FGF23*, *KL*, and *PTH*, all central to mineral-bone metabolism and cardiovascular protection in CKD patients. Understanding the mineral content of herbal formulations, and their bioactive compounds is essential for safe therapeutic use, preventing electrolyte imbalance while harnessing potential nephroprotective and anti-inflammatory benefits in CKD management.[99]

CKD and Future Prospects

Despite major advancements in understanding CKD pathophysiology, current treatments remain largely supportive, rather than curative. Integrating multi-omics data can deepen insights into monogenic and polygenic

Table 2: Summary of various CKD conditions with their pathological features, herbal interventions, active compounds, and key molecular targets.

S. No.	CKD Condition	Evidence From Studies	Potential Herbal Drugs	Active Compounds	Targeted Mechanisms
1.	Autosomal Dominant Polycystic Kidney Disease (ADPKD)	Reduces Cyst growth, lowers proliferative indices, induce fibrosis	Curcuma longa, Salvia miltiorrhiza, Resveratrol (Polygonum cuspidatum) Cordyceps sinensis	Curcumin, Salvianolic acids, Resveratrol, Cordycepin	↓mTOR pathway, ↓TGF-β, anti-inflammatory, antioxidant.[79-81]
2.	Autosomal Recessive Polycystic Kidney Disease (ARPKD)	Reduces Hepatorenal cysts, fibrosis, enhances antioxidant activity	Curcuma longa, Astragalus membranaceus, Cordyceps sinensis	Curcumin, Astragaloside IV, Cordycepin	↓Fibrosis (TGF-β inhibition), antioxidant, mitochondrial support.[82,83]
3.	Nephronophthisis (NPHP)	Reduces renal & tubulointerstitial, fibrosis, oxidative stress	Astragalus membranaceus, Curcuma longa, Salvia miltiorrhiza, Rheum officinale	Astragaloside IV, Curcumin, Salvianolic acids, Anthraquinones	↓TGF-β/Smad signaling, ↓NF-κB, antioxidant.[84,85]
4.	Medullary Cystic Kidney Disease (MCKD)	Tubulointerstitial nephritis, hyperuricemia, improved renal function, reduce inflammation	Astragalus membranaceus, Salvia miltiorrhiza, Punica granatum	Astragaloside IV, Salvianolic acids, Polyphenols	↓Fibrosis, ↓inflammation, improves renal perfusion.[86-88]
5.	Alport Syndrome	Glomerulosclerosis, enhances antioxidant property	Astragalus membranaceus, Curcuma longa, Green Tea, Cordyceps sinensis	Astragaloside IV, Curcumin, Catechins, Cordycepin	↓Fibrosis, antioxidant, podocyte protection.[84,89]
6.	Fabry Disease	reduced oxidative stress markers	Green Tea, Curcuma longa, Salvia miltiorrhiza	Catechins, Curcumin,	Antioxidant, anti-inflammatory.[82,90]
7.	Pierson Syndrome	GBM defect, proteinuria	Astragalus membranaceus, Curcuma longa	Astragaloside IV, Curcumin	Podocyte protection, ↓oxidative stress[83]
8.	Congenital Nephrotic Syndrome	attenuated renal injury, Massive proteinuria	Astragalus membranaceus, Curcuma longa	Astragaloside IV, Curcumin	↓Inflammation, enhances glomerular function.[82,87]
9.	Denys-Drash & Frasier Syndromes	Podocyte dysfunction, progressive CKD	Astragalus membranaceus, Salvia miltiorrhiza	Astragaloside IV, Salvianolic acids	Podocyte stabilization, ↓fibrosis.[87,91]
10.	Thin Basement Membrane Nephropathy	Mild hematuria	Green Tea, Curcuma longa	Catechins, Curcumin	Antioxidant, GBM protection.[92]
11.	Bartter Syndrome	Salt wasting, hypokalemia	Astragalus membranaceus	Astragaloside IV	Electrolyte balance, anti-inflammatory.[89]
13.	Cystinuria	↓ urinary oxalate and uric acid	Phyllanthus niruri, Camellia sinensis	Lignans, Catechins	↓Stone formation, antioxidant.[93]
14.	Primary Hyperoxaluria	alleviate CaOx crystal deposition in the mouse kidney	Phyllanthus niruri, Curcuma longa	Lignans, Curcumin	↓Oxalate synthesis, antioxidant.[93,94]
17.	Renal Cysts and Diabetes (RCAD)	Cysts	Astragalus membranaceus, Curcuma longa	Astragaloside IV, Curcumin	↓Fibrosis, antioxidant.[95,]
20.	Hypertensive Nephropathy	Reduced BP, fibrosis	Curcuma longa, Green Tea	Curcumin, Catechins	↓BP (RAAS), antioxidant, anti-fibrotic.[96,97]
23.	Focal Segmental Glomerulosclerosis (FSGS)	Podocyte loss, sclerosis	Astragalus membranaceus, Salvia miltiorrhiza	Astragaloside IV, Salvianolic acids	Podocyte protection, ↓TGF-β.[84,89,98]
24.	Kidney Stone Disease (Nephrolithiasis)	Calcium/uric acid stones	Camellia sinensis, Curcuma longa	Catechins, Curcumin	↓Crystal aggregation, antioxidant.[94]

Table 3: Herbal supplements serving as sources of potassium and phosphorus, including their common forms, bioactive compounds and consideration for CKD management.[99,100,101,102,103]

S. No.	Herb	Common Form	Scientific Name	No. of Bioactive Compounds	P/K Content	CKD Considerations
1	Alfalfa	Leaf, Sprout	*Medicago sativa*	11	High K	Risk of hyperkalemia in CKD
2	Bitter Melon	Fruit, Leaf	*Momordica charantia*	>60	Moderate P & K	Hypoglycemia risk
4	Coriander	Leaf, Seed	*Coriandrum sativum*	44–53	Moderate P & K	Allergy possible
5	Evening Primrose	Oil, Capsule	*Oenothera biennis*	2	Moderate P	Interaction with anticoagulants
7	Sugar Kelp	Whole Plant	*Saccharina latissima*	Several	High K	Avoid in severe CKD
9	Purslane	Leaf	*Portulaca oleracea*	184	High K	Hyperkalemia risk
10	Scullcap	Root, Leaf	*Scutellaria baicalensis*	>300	Moderate K	Monitor K in CKD
11	Turmeric	Rhizome, Powder	*Curcuma longa*	~235	Moderate P	Drug interactions
12	American Ginseng	Root, Extract	*Panax quinquefolius*	>100	Moderate P	May alter BP and glucose
13	Black Mustard	Leaf	*Brassica nigra*	26	Moderate K	Thyroid caution
14	Chicory	Leaf, Root	*Cichorium intybus*	15	Moderate K	GI discomfort possible
15	Dandelion	Root, Leaf	*Taraxacum officinale*	>300	High K	Hyperkalemia risk
16	Feverfew	Leaf	*Tanacetum parthenium*	39	Moderate P	Avoid with anticoagulants
17	Gotu Kola	Leaf	*Centella asiatica*	Several	Moderate K	Mild diuretic effect; monitor K
18	Kudzu	Root, Shoot	*Pueraria tuberosa*	23	Moderate K	Phytoestrogen activity caution
19	Noni	Fruit, Leaf	*Morinda citrifolia*	200	Moderate K	Limited CKD safety evidence
21	Shepherd's Purse	Whole Plant	*Capsella bursa-pastoris*	50	Moderate P & K	May lower BP; monitor electrolyte balance
22	Water Lotus	Whole Plant	*Nymphaea lotus*	50	Moderate P	Limited data; avoid overdose
23	Bai Zhi	Root	*Angelica dahurica*	>300	Moderate K	Possible herbal-drug interactions
26	Dulse	Seaweed	*Palmaria palmata*	50	High K	Avoid in advanced CKD
27	Garlic	Leaf, Bulb	*Allium sativum*	50	Moderate P	Anticoagulant effect; BP lowering
28	Japanese Honeysuckle	Flower	*Lonicera japonica*	140	Moderate K	Limited CKD data
29	Lemongrass	Leaf	*Cymbopogon citratus*	70	Moderate K	Monitor K in CKD
30	Papaya	Leaf, Fruit	*Carica papaya*	40	Moderate K	May affect glucose regulation
32	Stinging Nettle	Leaf	*Urtica dioica*	40	Moderate P & K	Diuretic effect; monitor electrolytes
33	Borage	Leaf, Capsule	*Borago officinalis*	20–25	Moderate P	Possible anticoagulant interactions
35	Flaxseed	Seed, Oil	*Linum usitatissimum*	40+	Moderate P	High fiber; digestive discomfort possible
38	Milk Thistle	Seed, Extract	*Silybum marianum*	~200	Moderate P	Nephroprotective; drug interactions possible
39	Onion	Leaf	*Allium cepa*	40+	Moderate P	Anticoagulant interaction; allergy risk
42	Sunflower	Seed, Oil	*Helianthus annuus*	~30	Moderate P	High calories; avoid in obese CKD
43	Yellow Dock	Root, Capsule	*Rumex crispus*	20+	Moderate P	GI irritation possible; avoid excess intake

forms, while precision medicine, CRISPR gene editing, and AI-driven approaches hold promise for targeted interventions and early risk prediction. In parallel, the exploration of herbal therapeutics offers a promising alternative to conventional treatment regimens. However, meticulous translational studies are needed to validate the molecular mechanisms, pharmacokinetics, and safety profiles of plant-derived compounds, as well as to standardize their formulations.

CONCLUSION

In the search for reliable and safe herbal formulations to manage CKD, we explored key genes involved in renal function, their chromosomal localization, and their regulatory roles. Under normal physiological conditions, these genes contribute to maintaining kidney homeostasis. However, in pathological states, their dysregulation leads to cellular dysfunction and progression of CKD. While several genetic and environmental contributors have been identified, many remain undiscovered. This review highlights existing and investigational drug molecules that have shown therapeutic potential in CKD, with some already validated through multiple clinical trials. Herbal formulations, due to their multifaceted bioactivity and historical usage, offer a promising complementary approach to current treatments. If properly characterized and standardized, these formulations may progress toward regulatory approval and clinical use. However, the safety profile of herbal medicines must be carefully assessed. Herbal therapies hold great promise, rigorous identification, validation, and standardization are essential. Alternatively, these formulations could be developed as dietary supplements to support renal health. We hope this report will encourage further research and evoke clinical interest in evidence-based herbal therapeutics for CKD, promoting safer, accessible, and culturally relevant treatment strategies.

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