Int. J. Sci. R. Tech., 2025 2(10)
A Multidisciplinary peer-reviewed Journal
www.ijsrtjournal.com [ISSN: 2394-7063]

Original Article

Comprehensive Review of Polycystic Kidney Disease and Herbal Ingredients for its Management

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ABSTRACT

Polycystic kidney disease (PKD) is a common hereditary nephropathy characterized by the progressive development of numerous fluid-filled cysts in the kidneys, often leading to end-stage renal disease (ESRD). It primarily exists in two forms: autosomal dominant PKD (ADPKD), the most prevalent, and the rarer autosomal recessive PKD (ARPKD). Despite advancements in understanding the genetic and molecular mechanisms underlying PKD, current pharmacological treatments remain limited in efficacy and are often accompanied by adverse effects. In recent years, growing attention has been directed toward herbal and plant-derived compounds for their potential nephroprotective, anti-inflammatory, and anti-fibrotic properties. This review provides a comprehensive overview of the pathophysiology, genetic basis, and clinical manifestations of PKD, followed by an in-depth evaluation of herbal ingredients and phytochemicals that have shown promise in experimental or clinical settings for PKD management. Key herbs such as Astragalus membranaceus, Salvia miltiorrhiza, Cordyceps sinensis, and curcumin are examined for their mechanisms of action in modulating cyst growth, oxidative stress, and renal fibrosis. Additionally, this review highlights the need for standardized formulations, dose optimization, and clinical trials to validate the efficacy and safety of these natural therapies in PKD patients.

Keywords: Polycystic kidney disease (PKD), Herbal medicine, Phytochemicals, Nephroprotection, Oxidative stress

INTRODUCTION

Polycystic kidney disease (PKD) is a genetically inherited disorder characterized by the progressive formation of multiple cysts in the renal parenchyma, leading to enlarged kidneys, impaired renal function, and, eventually, end-stage renal disease (ESRD). PKD is a significant contributor to chronic kidney disease (CKD) worldwide, affecting approximately 1 in 500 to 1,000 individuals, with autosomal dominant PKD (ADPKD) accounting for the vast majority of cases, and autosomal recessive PKD (ARPKD) occurring less frequently but with more severe early-onset symptoms. [1] The pathogenesis of PKD is complex and multifactorial, involving genetic mutations (notably in *PKD1* and *PKD2* genes), disrupted calcium signaling, increased cell proliferation, abnormal fluid secretion, and chronic inflammation. As cysts grow, they compress surrounding nephrons, gradually reducing kidney function and contributing to complications such as hypertension, hematuria, urinary tract infections, and kidney stones. Although pharmacological interventions such as vasopressin V2 receptor antagonists (e.g., tolvaptan)—have shown some success in slowing cyst progression, their efficacy is limited and they are often associated with adverse effects and high costs. As a result, there is growing interest in alternative and complementary therapies, particularly herbal and plant-based compounds, which have demonstrated promising anti-inflammatory, antioxidant, and anti-fibrotic properties in preclinical models. [3] Herbal medicine, an integral component of traditional medical systems such as Ayurveda, Traditional Chinese Medicine (TCM), and Unani, offers a wide array of bioactive compounds that may modulate the molecular pathways involved in PKD progression. Notably, phytochemicals such as curcumin, resveratrol, cordycepin, and salvianolic acid B have been investigated for their potential to reduce cyst growth, oxidative damage, and renal fibrosis. This review aims to provide a comprehensive examination of the current understanding of PKD, including its molecular mechanisms, clinical manifestations, and conventional treatments, while exploring the

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

therapeutic potential of herbal ingredients for its management. By synthesizing evidence from experimental and clinical studies, we aim to highlight promising natural compounds and identify gaps in research that warrant further investigation. [2]

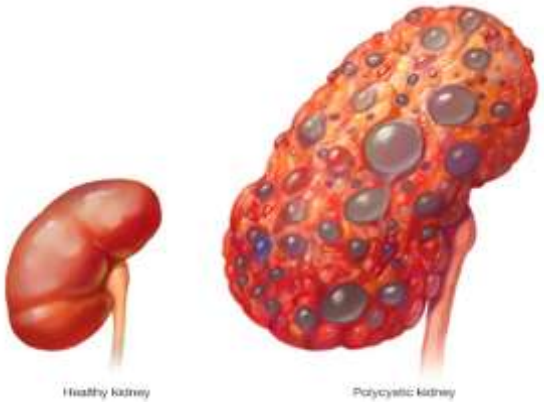


Figure 1: Polycystic kidney

Overview of Polycystic Kidney Disease (PKD)

Polycystic Kidney Disease (PKD) is a genetic disorder characterized by the development and progressive enlargement of multiple fluid-filled cysts within the kidneys. These cysts arise from various segments of the renal tubules and eventually disrupt normal renal architecture and function, often leading to chronic kidney disease (CKD) and ultimately end-stage renal disease (ESRD). PKD is one of the **most common inherited kidney disorders**, and it exists in two primary forms:

1. Autosomal Dominant Polycystic Kidney Disease (ADPKD) [5]

- **Prevalence**: Affects ~1 in 400 to 1,000 live births.
- **Inheritance**: Autosomal dominant (only one mutated allele is required for disease manifestation).
- **Genetics**:
  - Caused primarily by mutations in the **PKD1 gene** (chromosome 16) encoding **polycystin-1**, and less commonly in **PKD2** (chromosome 4) encoding **polycystin-2**.
  - PKD1 mutations tend to result in **more severe disease progression**.
- **Clinical Onset**: Typically presents in **adulthood**, but cysts begin forming much earlier. [7]
- **Common Symptoms**:
  - Hypertension
  - Flank pain
  - Hematuria
  - Recurrent urinary tract infections (UTIs)
  - Progressive renal enlargement
- **Extra-renal Manifestations**:
  - Hepatic cysts
  - Intracranial aneurysms
  - Cardiac valve abnormalities (e.g., mitral valve prolapse)
  - Colonic diverticulosis [11]

2. Autosomal Recessive Polycystic Kidney Disease (ARPKD)

- **Prevalence**: Much rarer (~1 in 20,000 live births).
- **Inheritance**: Autosomal recessive (both alleles must be mutated).
- **Genetics**: Caused by mutations in the **PKHD1 gene**, which encodes **fibrocystin/polyductin**.
- **Clinical Onset**: Presents in **infancy or early childhood**.
- **Features**:
  - Enlarged echogenic kidneys detected prenatally
  - Pulmonary hypoplasia due to oligohydramnios

- Portal hypertension from hepatic fibrosis
- High perinatal mortality [13]

Pathophysiology of PKD

PKD involves dysregulation of tubular epithelial cell proliferation, fluid secretion, apoptosis, and extracellular matrix remodeling. Mutations in polycystin or fibrocystin disrupt calcium signaling, ciliary function, and mTOR pathways, which are critical in maintaining the structural integrity and polarity of renal tubular cells. These disruptions lead to abnormal cyst formation and progressive kidney enlargement. [15]

Disease Progression and Complications

- In **ADPKD**, renal function typically remains stable until the **4th or 5th decade**, after which there is a rapid decline toward ESRD.
- Complications include:
  - Renal insufficiency
  - Kidney stones
  - Cyst rupture and hemorrhage
  - Cardiovascular complications (due to hypertension)
  - Increased risk of infections (especially cyst infections)

Current Management Strategies

While no cure exists, disease-modifying strategies aim to delay progression and manage complications: [17]

- **Tolvaptan**, a vasopressin V2 receptor antagonist, is the only FDA- and EMA-approved drug to slow cyst growth in ADPKD.
- **Supportive therapy** includes:
  - Blood pressure control (ACE inhibitors or ARBs)
  - Pain management
  - Infection control
  - Dietary modifications
  - Dialysis or renal transplantation in ESRD

Herbal and Natural Approaches in PKD Management

The management of Polycystic Kidney Disease (PKD) has traditionally focused on supportive care and, more recently, disease-modifying agents like tolvaptan. However, limitations such as side effects, cost, and incomplete efficacy have spurred interest in herbal and natural therapies. Medicinal plants and their bioactive compounds offer a promising adjunctive approach due to their anti-inflammatory, antioxidant, anti-fibrotic, and cytostatic properties, which may target several pathophysiological mechanisms of cyst growth and renal damage.[12]

1. Mechanistic Rationale for Herbal Use in PKD

Herbal therapies can influence PKD progression through:

- Inhibition of cyst epithelial proliferation
- Suppression of oxidative stress
- Modulation of inflammatory pathways
- Regulation of fibrogenesis
- Inhibition of mTOR and cAMP signaling, both implicated in cyst growth

Many plant-derived compounds have been shown to interact with these pathways in preclinical models of PKD.

2. Key Herbal Ingredients and Their Therapeutic Potential [14]

a. Curcumin (*Curcuma longa*)

- **Actions**: Antioxidant, anti-inflammatory and anti-fibrotic
- **Mechanisms**:
  - Inhibits **NF-κB** and **TGF-β** signaling
  - Reduces cyst formation in animal models of PKD
- **Evidence**:
  - Curcumin treatment in murine models of ADPKD has shown reduced cystic burden and improved renal function.



Figure 2: ***Curcumin***

b. Resveratrol

- **Source**: Found in grapes, berries, and peanuts
- **Actions**: Sirtuin activation, antioxidant, anti-inflammatory
- **Mechanisms**:
  - Activates SIRT1, suppressing mTOR signaling
  - Reduces oxidative stress in kidney tissues [18].
- **Evidence**:
  - Shown to decrease renal fibrosis and delay cyst progression in rodent studies.

c. Astragalus membranaceus

- **Used in**: Traditional Chinese Medicine (TCM)
- **Actions**: Immunomodulatory, diuretic, anti-inflammatory
- **Mechanisms**:
  - Reduces serum creatinine and BUN levels
  - Inhibits renal interstitial fibrosis
- **Evidence**:
  - Used in Chinese herbal prescriptions for CKD and PKD, often in combination with other herbs. [13]



Figure 3: ***Astragalus Membranaceus***

d. Cordyceps sinensis

- **Actions**: Antioxidant, immunomodulatory, anti-fibrotic
- **Mechanisms**:
  - Modulates **AMPK** and **TGF-β1** signaling



Figure 4: ***Cordyceps sinensis***

- **Evidence**:
    - Clinical studies in CKD show improved renal function markers and decreased proteinuria. Figure (4).

e. Salvia miltiorrhiza (Danshen)

- **Actions**: Anti-fibrotic, vasodilatory, anti-inflammatory
- **Mechanisms**:



Figure 5: ***Salvia Miltiorrhiza*** **(Danshen)**

    - Inhibits **TGF-β1/Smad** pathway
    - Improves renal microcirculation
- **Evidence**:
    - Demonstrated renal protective effects in diabetic nephropathy and PKD-related studies. **Fig (5)**

f. Tripterygium wilfordii (Thunder God Vine)

- **Actions**: Immunosuppressive, anti-inflammatory
- **Mechanisms**:
    - Inhibits **pro-inflammatory cytokines** and immune cell activation
- **Cautions**:
    - Potent but potentially **toxic**; use requires careful dosing and monitoring. [14]



Figure 6: *Tripterygium wilfordii* (*Thunder God Vine*)

3. Dietary and Nutraceutical Compounds

Some natural dietary compounds and plant extracts have also shown promise in PKD models: **Table 1: Dietary and Nutraceutical Compounds**

Compound	Effect	Sources
Quercetin	Antioxidant, inhibits cyst growth	Onions, apples, tea
Green tea polyphenols	Anti-inflammatory, mTOR modulation	Green tea
Berberine	Anti-fibrotic, regulates AMPK	*Berberis* spp.
Naringin	Antioxidant, anti-proliferative	Citrus fruits

4. Challenges and Considerations

While herbal remedies show potential, several challenges must be addressed:

- Lack of standardized dosages and formulations
- Insufficient clinical trials specifically for PKD
- Potential for herb–drug interactions, especially in patients on immunosuppressants or diuretics
- Toxicity and quality control concerns with poorly regulated herbal products
- Variability in bioavailability and pharmacokinetics of plant compounds. [21]

5. Integrative Potential and Future Directions

- Combination therapies involving herbal extracts and conventional agents (e.g., tolvaptan + curcumin) may offer synergistic effects.
- Nano-formulations and encapsulation techniques are being explored to improve bioavailability.
- Clinical trials are needed to translate promising preclinical data into validated, evidence-based therapies. [23]

Preclinical and Clinical Evidence

The exploration of herbal and natural compounds for the treatment of Polycystic Kidney Disease (PKD) has expanded in recent years, driven by the need for safer, more accessible therapies with fewer side effects than current pharmacologic options. A growing body of preclinical studies supports the efficacy of various herbal agents in modulating key pathways involved in PKD pathogenesis, such as mTOR signaling, oxidative stress, inflammation, and fibrosis. However, clinical evidence remains limited, highlighting the need for well-designed trials. [13]

1. Preclinical (*In-Vitro and In-Vivo)* Evidence

Numerous animal models (e.g., Pkd1 or Pkd2 knockout mice, Han: SPRD rats) and renal epithelial cell lines have been used to evaluate herbal compounds mentioned below Table (2).

Table 2: Preclinical (*In-Vitro and In-Vivo)* Evidence

Herbal Agent	Model	Observed Effects	Mechanisms	Reference (Year)
Curcumin	Pkd1 mouse model	↓ Cyst volume, ↓ inflammation, improved renal morphology	NF-κB inhibition, antioxidant effects	Trudel et al., 2009
Resveratrol	Han:SPRD rats, cell cultures	↓ Cyst cell proliferation, ↓ oxidative stress	Activates SIRT1, modulates AMPK/mTOR pathways	Salvi et al., 2016
Cordyceps sinensis	Adenine-induced CKD rats	↓ Renal fibrosis, ↑ renal function markers	TGF-β1 inhibition, immunomodulation	Chen et al., 2015
Astragalus membranaceus	5/6 nephrectomy rats	↓ Serum creatinine, ↓ interstitial fibrosis	Antioxidant and anti-inflammatory activity	Zhang et al., 2013
Salvianolic acid B	PKD cell lines	↓ Cyst expansion in vitro	Inhibition of ERK1/2 pathway	Wang et al., 2018
Berberine	Pkd1-deficient cells	↓ Cell proliferation, ↓ inflammation	AMPK activation, suppression of mTOR	Liu et al., 2019

2. Clinical Evidence

Despite robust preclinical data, clinical trials evaluating herbal interventions specifically for PKD are limited. Most available studies assess herbal formulations in general chronic kidney disease (CKD) populations or as part of Traditional Chinese Medicine (TCM) therapies.

Notable Clinical Studies and Observations:

1. **Cordyceps sinensis in CKD patients**:
   - Several trials in China reported improvements in serum creatinine, albuminuria, and hemoglobin levels.
   - Some studies included PKD patients, but lacked subgroup analysis.
   - Generally well tolerated, though long-term safety remains under investigation.

2. **Astragalus membranaceus**:
   - Used in TCM formulations for CKD and PKD.
   - A randomized trial (Zhou et al., 2014) in CKD patients showed reduced proteinuria and improved renal function with Astragalus-based therapy. [16]

3. **Curcumin in renal disease**:
   - Small-scale studies in diabetic nephropathy showed reduced inflammation and oxidative markers.
   - No PKD-specific clinical trials yet, but evidence supports its safety and renal benefits.

4. **TCM compound formulas**:
   - Multi-herbal decoctions like Shen Qi Wan, Huangkui capsules, and Liuwei Dihuang Wan are used in China for PKD treatment.
   - Some observational studies report slowed cyst growth and improved quality of life, but high-quality RCTs are lacking. [14]

5. **Safety Profile**:
   - Most herbal agents are well-tolerated at recommended doses.
   - Concerns include:
     - Hepatotoxicity (e.g., from Tripterygium wilfordii)
     - Interaction with conventional drugs
     - Variability in product quality and standardization.

Limitations of Current Evidence

- Few herbal interventions have undergone phase II/III clinical trials for PKD.
- Many studies have:
  - Small sample sizes

  - Poor blinding or randomization
  - Use of multi-herb formulations, making it difficult to attribute effects to a single ingredient
- Lack of standardized herbal extracts and bioavailability data
- Endpoints often vary (e.g., cyst size vs. renal function vs. patient-reported outcomes)

Future Research Directions

To translate preclinical promise into clinical utility:

- Well-designed RCTs are needed with clearly defined inclusion criteria (e.g., confirmed ADPKD diagnosis).
- Biomarker-based endpoints (e.g., TKV, eGFR) should be included.
- Herbal pharmacokinetics and metabolism in CKD patients must be better understood.
- Combination therapy studies (herbal + conventional) could evaluate synergistic effects. [15]

Safety, Toxicity and Interactions

While herbal and natural compounds offer promising therapeutic potential in the management of Polycystic Kidney Disease (PKD), their use must be carefully evaluated for safety, potential toxicity, and interactions with conventional medications. Unlike regulated pharmaceuticals, many herbal products vary in composition, dosage, and purity, posing unique risks, especially in individuals with impaired renal function. [16]

1. General Safety Concerns in PKD Patients

Patients with PKD, particularly those in the later stages of chronic kidney disease (CKD), are more vulnerable to toxic effects due to:

- Impaired drug clearance, increasing the risk of accumulation and toxicity
- Altered metabolism of herbal compounds due to compromised renal or hepatic function
- Polypharmacy, heightening the potential for drug-herb interactions [17]

2. Toxicity of Commonly Used Herbal Ingredients:

Table 3: Herbal Ingredients

Herbal Agent	Toxicity Concerns	Risk Level	Notes
Curcumin (*Curcuma longa*)	Generally, well tolerated at therapeutic doses	Low	High doses may cause gastrointestinal discomfort or interact with anticoagulants
Resveratrol	Mild GI upset at high doses	Low	Safe in most studies, but limited renal-specific toxicity data
Cordyceps sinensis	Contamination with heavy metals in low-quality products	Moderate	Ensure sourcing from reputable suppliers
Astragalus membranaceus	Potential immune stimulation; not recommended in transplant patients	Moderate	Can lower blood pressure or cause diuresis
Tripterygium wilfordii	Reproductive toxicity, hepatotoxicity, immunosuppression	High	Use only under medical supervision; narrow therapeutic window
Salvia miltiorrhiza	Can potentiate anticoagulant effects	Moderate	Avoid in patients on warfarin or aspirin

3. Herb–Drug Interactions

Many herbal compounds can alter the pharmacokinetics or pharmacodynamics of prescription drugs through:

Cytochrome P450 enzyme modulation

- Some herbs (e.g., St. John's Wort, ginseng) induce or inhibit CYP enzymes, potentially altering metabolism of drugs like:
  - Tolvaptan (used in ADPKD)
  - ACE inhibitors/ARBs (used for hypertension)
  - Immunosuppressants (in post-transplant patients)

Pharmacodynamic interactions

- Herbs that lower blood pressure, blood sugar, or act as diuretics may amplify effects of prescribed medications, risking hypotension, hypoglycemia, or dehydration. [18]

Examples of Known Interactions

Table 4: Examples of Known Interactions

Herbal Ingredient	Interacting Drugs	Potential Effect
Curcumin	Warfarin, NSAIDs	↑ Bleeding risk
Astragalus	Immunosuppressants (e.g., cyclosporine)	↓ Drug efficacy via immune stimulation
Danshen (Salvia)	Anticoagulants	↑ Risk of bleeding
Licorice root	Diuretics, corticosteroids	↑ Potassium loss, hypertension

4. Contamination and Adulteration Risks

- Heavy metals (lead, arsenic, mercury) have been found in unregulated herbal products, especially from poorly monitored suppliers.
- Adulteration with pharmaceuticals (e.g., steroids, diuretics) is a known issue in some traditional medicine markets.
- Mislabeled products can contain incorrect herbs or incorrect dosages, posing additional safety concerns.

5. Recommendations for Safe Use

- Use standardized extracts from reputable, GMP-certified manufacturers.
- Consult a nephrologist or clinical pharmacologist before starting herbal therapies.
- Avoid herbal products during acute kidney injury or in patients on multiple medications with narrow therapeutic indices.
- Monitor renal function, electrolytes, and blood pressure regularly if herbs are used long-term.
- Encourage pharmacovigilance reporting for adverse reactions related to herbal products. [19]

Challenges and Research Gaps

Despite the growing interest in herbal and natural therapies for managing Polycystic Kidney Disease (PKD), their clinical application remains limited. While preclinical studies have shown promising results, significant challenges hinder the widespread adoption and regulatory acceptance of these therapies. Understanding these barriers is critical to designing effective future research and clinical strategies.

1. Lack of High-Quality Clinical Evidence

One of the most pressing gaps is the absence of robust clinical trials:

- Most available data are preclinical or observational, with few randomized controlled trials (RCTs) specific to PKD.
- Existing clinical studies are often:
  - Small in sample size
  - Lacking control or placebo groups [20]
  - Poorly standardized in terms of dose and preparation

Gap: Need for large-scale, multicenter RCTs focused on validated endpoints like total kidney volume (TKV), glomerular filtration rate (eGFR), and cyst burden.

2. Standardization of Herbal Products

Herbal compounds vary widely in:

- Chemical composition
- Purity and potency
- Extraction methods
- Plant part used (root, leaf, bark, etc.)

This variability makes it difficult to compare study results or replicate findings.

Gap: Development of standardized extracts and Good Manufacturing Practices (GMP)-certified products is urgently needed. [21]

3. Safety and Herb–Drug Interactions

- Many PKD patients are on multiple medications, increasing the risk of herb–drug interactions.

- Some herbs have nephrotoxic potential or may interfere with critical drugs like tolvaptan, antihypertensives, or immunosuppressants.
- Long-term safety data is lacking for most herbal compounds in renal populations.

Gap: Comprehensive toxicology and interaction studies are required, especially in renal-impaired and transplant patients.

4. Limited Mechanistic Understanding

While some herbs show efficacy in animal models, the exact molecular mechanisms by which they affect cystogenesis, fibrosis, and inflammation remain unclear.

Gap:

- Need for omics-based studies (genomics, proteomics, metabolomics) to identify pathways modulated by herbal compounds.
- Exploration of synergistic effects in multi-compound herbal formulations.

5. Inadequate Long-Term Follow-Up

- Most studies only assess short-term outcomes.
- The progressive nature of PKD, with changes occurring over years, necessitates longitudinal studies.

Gap: Absence of long-term data on whether herbal treatments can delay ESRD, reduce need for dialysis, or improve quality of life. [22,23]

6. Regulatory and Ethical Challenges

- Herbal products often fall into a regulatory grey area, classified as supplements rather than drugs.
- Lack of regulation leads to:
  - Poor quality control
  - Inconsistent labeling
  - Variable dosing

- Ethical concerns also exist regarding the unproven use of alternative therapies in vulnerable populations.

Gap: Need for clearer regulatory frameworks and ethical guidelines governing the use of herbal medicine in chronic diseases like PKD.

7. Limited Funding and Research Infrastructure

- Research into herbal therapies often receives less funding than pharmaceutical drug development. [24]
- Collaboration between nephrologists, herbal pharmacologists, and clinical researchers remains limited.

Gap: Lack of interdisciplinary research and institutional support hampers innovation in this field.

FUTURE PERSPECTIVES

The growing interest in herbal and natural therapies for Polycystic Kidney Disease (PKD) reflects a global shift toward integrative and personalized medicine. Although current treatment options are limited to supportive measures and a few pharmacological agents, advances in herbal pharmacology and biomedical research are paving the way for safer and more effective therapeutic alternatives. The future of herbal medicine in PKD lies in scientific validation, technological innovation, and interdisciplinary collaboration. Integration of herbal medicine into evidence-based practice will require rigorous clinical evaluation of promising compounds such as curcumin, resveratrol, and cordycepin through well-designed phase I/II trials targeting total kidney volume (TKV) reduction, slower decline in eGFR, and improved quality of life, supported by regulatory frameworks ensuring safety, efficacy, and standardized production. [25] Molecular and systems biology approaches utilizing omics technologies such as; transcriptomics, metabolomics, and proteomics will elucidate the influence of herbal agents on key PKD pathways like mTOR, cAMP signalling, oxidative stress, mitochondrial dysfunction, fibrogenesis, and epithelial-mesenchymal transition (EMT), thereby identifying new molecular targets and refining compound selection. Formulation and drug delivery innovations, including nano-formulations, liposomal carriers, co-encapsulation of synergistic phytochemicals, and ligand-receptor-based targeted renal delivery, can enhance bioavailability and therapeutic indices of herbal compounds. Future success also depends on collaborative and cross-disciplinary research bridging traditional medicine, nephrology, pharmaceutical sciences, and regulatory agencies through international consortia that promote

protocol standardization, data sharing, and regulatory harmonization, alongside collaboration with Ayurveda, Traditional Chinese Medicine (TCM), and Kampo medicine experts to identify new candidates. Personalized and precision herbal medicine, leveraging genetic testing and biomarker profiling, could tailor treatments to PKD1 or PKD2 genotypes, individual metabolic patterns, and patient-specific drug tolerance, improving outcomes and minimizing side effects. Furthermore, sustainable and ethical sourcing of herbs will be crucial, emphasizing biotechnological production methods such as plant cell culture and synthetic biology to ensure biodiversity conservation and develop optimized phytochemical derivatives. Finally, patient education and digital tools, including mobile applications, AI-based herb-drug interaction systems, and teleconsultations with herbal specialists, will empower patients with knowledge, enable real-time treatment monitoring, and integrate herbal medicine into future PKD care models. [28-30]

CONCLUSION

Polycystic Kidney Disease (PKD) is a complex, genetically driven disorder with significant clinical and societal burden. Current conventional therapies, including the use of vasopressin receptor antagonists and supportive measures, can slow disease progression but are limited by side effects, cost, and partial efficacy. These limitations have spurred increasing interest in herbal and natural therapies, many of which demonstrate promising antioxidant, anti-inflammatory, and anti-fibrotic properties in preclinical models. A variety of medicinal plants and phytochemicals, such as curcumin, resveratrol, cordycepin, Astragalus membranaceus, and Salvia miltiorrhiza, have shown the ability to modulate key molecular pathways involved in cystogenesis and renal fibrosis. However, despite encouraging laboratory results, the clinical translation of these findings remains limited due to several challenges, including lack of standardized formulations, insufficient clinical trials, safety concerns, and regulatory ambiguity.

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HOW TO CITE: Poonam Yadav*, Sushil Patil, Granthali Shape, Comprehensive Review of Polycystic Kidney Disease and Herbal Ingredients for its Management, Int. J. Sci. R. Tech., 2025, 2 (10), 364-375. https://doi.org/10.5281/zenodo.17374127