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Guardians of Renal Health: Siddha Herbal Wisdom in the Modern Era: A Comprehensive Literature Review

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Abstract

Background: Chronic kidney disease (CKD) represents a significant health burden in South India, where traditional Siddha medicine has been employed for centuries as a primary therapeutic approach for renal disorders. Despite widespread use, limited systematic evaluation

exists regarding the efficacy, safety, and integration potential of Siddha herbal interventions within contemporary nephrology practice.

Objective: This comprehensive review synthesizes multidisciplinary evidence on Siddha herbal medicine's therapeutic role in CKD management, evaluating efficacy profiles, safety parameters, traditional treatment protocols, mechanistic foundations, and comparative effectiveness against conventional therapies within South Indian healthcare contexts.

Methods: A systematic synthesis of clinical trials, preclinical studies, molecular investigations, and ethnobotanical literature was conducted using qualitative synthesis and comparative analytical methodologies. Evidence sources encompassed peer-reviewed publications, classical Siddha texts, and contemporary ethnopharmacological studies to provide comprehensive evaluation of therapeutic potential and integration feasibility.

Results: Siddha herbal formulations demonstrate significant nephroprotective properties through multifaceted mechanistic pathways, predominantly involving antioxidant and anti-inflammatory activities that target oxidative stress and inflammatory cascades central to CKD pathogenesis. Clinical and preclinical investigations reveal measurable improvements in critical renal function biomarkers, including serum creatinine, blood urea nitrogen, and proteinuria, accompanied by symptomatic amelioration in diabetic nephropathy and urolithiasis.

Safety evaluations indicate generally acceptable profiles for standardized Siddha preparations administered under appropriate traditional protocols. However, substantial concerns persist regarding potential nephrotoxicity associated with inadequately processed herbomineral formulations, particularly those containing heavy metals. Literature evidence indicates that up to 35% of acute kidney injury cases in developing regions may be attributable to unregulated traditional medicine use, emphasizing critical importance of quality control and standardization measures.

Traditional Siddha therapeutic frameworks are comprehensively documented in classical texts and contemporary ethnobotanical studies, providing holistic CKD management approaches encompassing dietary interventions, lifestyle modifications, and graduated herbal protocols. Integration with modern nephrology requires substantial standardization efforts, including phytochemical profiling, biomarker validation, and harmonized treatment protocols.

Comparative analyses demonstrate promising potential for Siddha medicines as complementary interventions capable of delaying disease progression, reducing dialysis dependency, and enhancing quality of life parameters. Mechanistic studies reveal that key Siddha herbs modulate critical pathways involved in renal fibrosis, inflammation, and oxidative damage, providing scientific rationale for traditional applications.

Conclusion: Evidence synthesis positions Siddha medicine as a promising adjunctive approach for CKD management in South Indian populations, offering cultural acceptability, accessibility, and potential cost-effectiveness compared to conventional renal replacement therapies. However, successful integration into evidence-based nephrology practice requires substantial research investment in well-designed randomized controlled trials with appropriate sample sizes, standardized outcome measures, and comprehensive safety monitoring protocols. Critical knowledge gaps persist in optimal dosing strategies, drug-herb interactions, long-term safety profiles, and patient selection criteria, necessitating rigorous clinical validation studies and comprehensive toxicological assessments to support safe and effective integration within

contemporary healthcare systems.

Keywords: Siddha medicine, chronic kidney disease, nephroprotective, traditional medicine, South India, herbal therapy, diabetic nephropathy, urolithiasis, integrative medicine, safety assessment

Introduction

Research on chronic kidney disease (CKD) Siddha herbal medicine application has emerged as a critical area of inquiry due to the rising global prevalence of CKD and the limitations of conventional treatments. CKD affects approximately 10–14% of the global population, with significant morbidity and mortality, particularly in South India where traditional Siddha medicine is widely practiced (Kabilan et al., 2024; Castelino et al., 2019). Historically, Siddha medicine, developed by ancient Siddhars in Tamil Nadu, integrates herbal, mineral, and animal-based formulations, offering holistic approaches to renal ailments (Devi et al., 2019; Karunamoorthi et al., 2012). Over recent decades, there has been increasing scientific interest in validating Siddha treatments for CKD and diabetic nephropathy, reflecting a trajectory from traditional knowledge to modern clinical applications (Parvathy et al., 2023). The social and economic burden of CKD, especially in resource-limited settings, underscores the practical significance of exploring effective, affordable, and culturally acceptable therapies (Kapare et al., 2022; Raju, 2022).

The specific problem addressed is the efficacy and safety of Siddha herbal medicines in managing CKD and its complications, such as diabetic nephropathy, within South Indian populations (Parvathy et al., 2024; Parvathy et al., 2023). Despite numerous herbal formulations being traditionally used, there remains a paucity of rigorous clinical trials and standardized treatment protocols (Borkar et al., 2022; Gayathri et al., 2011; "Efficacy and Safety of CAM in Kidney Dis...", 2022). Moreover, controversies exist regarding the safety of herbomineral Siddha preparations due to potential heavy metal toxicity, necessitating balanced evaluation (Tharakan et al., 2010; Devi et al., 2019). While some studies report nephroprotective effects and improved renal parameters, others highlight risks and the need for detoxification methodologies (Dharshini et al., 2019; R & I, 2016). The knowledge gap lies in the lack of comprehensive comparative analyses integrating historical usage, treatment protocols, and modern scientific validation of Siddha herbal medicines for CKD (Borkar et al., 2022; Kumar et al., 2022; Kareem & Yoganandham, n.d.). This gap limits broader acceptance and integration of Siddha therapies into mainstream nephrology, potentially affecting patient outcomes and healthcare accessibility ("Efficacy and Safety of CAM in Kidney Dis...", 2022).

The conceptual framework for this review defines CKD as a progressive renal dysfunction often complicated by diabetic nephropathy, with Siddha herbal medicine encompassing monoherbal and polyherbal formulations, including herbomineral compounds traditionally used in South India (Parvathy et al., 2023; Devi et al., 2019; Borkar et al., 2022). The framework links the pharmacological properties of these formulations—such as antioxidant, anti-inflammatory, and nephroprotective effects—to their therapeutic potential in CKD management, grounded in both traditional knowledge and emerging scientific evidence (Lee et al., 2024; S & S, 2023; Gunasekaran & Chamundeeswari, 2024). This framework supports the purpose of systematically evaluating Siddha herbal medicine efficacy and safety within the context of CKD treatment.

The purpose of this systematic review is to critically assess the historical usage, treatment

protocols, efficacy, and safety of Siddha herbal medicines in managing chronic kidney disease, with a focus on South Indian traditional practices and their modern applications. This review aims to bridge the knowledge gap by synthesizing clinical, pharmacological, and toxicological evidence, thereby informing future research and clinical integration (Parvathy et al., 2024; Borkar et al., 2022; Gayathri et al., 2011). The value-added lies in providing a comprehensive comparative analysis that supports evidence-based utilization of Siddha medicine in CKD care, addressing both therapeutic benefits and safety concerns ("Efficacy and Safety of CAM in Kidney Dis...", 2022; Kapare et al., 2022).

This review employed a systematic literature search of peer-reviewed articles, case studies, and clinical trials focusing on Siddha herbal medicine applications in CKD. Inclusion criteria emphasized studies reporting efficacy, safety, and traditional treatment protocols, while excluding non-relevant or non-peer-reviewed sources. Analytical frameworks included comparative efficacy assessment, safety profiling, and historical contextualization. The findings are organized to reflect traditional practices, clinical evidence, safety evaluations, and modern integration approaches (Parvathy et al., 2024; Parvathy et al., 2023; Gayathri et al., 2011).

Purpose and Scope of the Review

Statement of Purpose

The objective of this report is to examine the existing research on "chronic kidney disease Siddha herbal medicine application efficacy safety historical usage treatment protocols traditional practices modern applications South India comparative analysis" to provide a comprehensive synthesis of the therapeutic potential and safety considerations of Siddha herbal medicines in managing chronic kidney disease (CKD). This review is important because CKD poses a significant health burden, particularly in South India where Siddha medicine has deep historical roots and contemporary relevance. By critically analyzing traditional practices alongside modern clinical applications and comparative studies, the report aims to elucidate the efficacy, safety profiles, and treatment protocols of Siddha formulations. This will facilitate informed integration of Siddha therapies into current CKD management frameworks and identify gaps for future research.

Specific Objectives:

The review encompasses several specific objectives aimed at comprehensively evaluating Siddha medicine's role in CKD management. First, to evaluate current knowledge on the efficacy and safety of Siddha herbal medicines in CKD treatment. Second, benchmarking of traditional Siddha treatment protocols against modern clinical applications in South India. Third, identification and synthesis of historical usage patterns and pharmacological mechanisms of Siddha formulations for CKD. Fourth, to compare clinical outcomes of Siddha herbal therapies with conventional treatments for chronic kidney disease. Finally, to deconstruct the integration challenges and opportunities of Siddha medicine within contemporary healthcare systems.

Results

Descriptive Summary of the Studies

This section maps the research landscape of the literature on chronic kidney disease Siddha herbal medicine application efficacy safety historical usage treatment protocols traditional practices modern applications South India comparative analysis, encompassing a diverse range

of studies including clinical trials, systematic reviews, molecular docking studies, and ethnobotanical surveys. The scope covers traditional Siddha formulations, herbomineral compounds, and integration with modern therapies, with a geographic focus primarily on South India and some comparative insights from other regions. Methodologies vary from in vivo animal models and in vitro analyses to clinical case series and meta-analyses, reflecting a multidisciplinary approach to evaluating efficacy, safety, and treatment protocols. This comparative analysis is relevant to understanding the therapeutic potential, safety considerations, and practical challenges of Siddha herbal medicines in CKD management, providing a foundation for integrating traditional and modern healthcare practices.

The comprehensive analysis of fifty key studies reveals significant patterns across multiple dimensions of Siddha medicine application in CKD treatment. In terms of efficacy outcomes, Parvathy et al. (2024) demonstrated improvement in GFR, reduced blood urea, and symptomatic relief in diabetic nephropathy cases, with mild transient creatinine increase but no severe adverse events reported. The treatment protocol involved monoherbal *Sirupeelai Kudineer* as oral decoction twice daily for one month, with traditional use for diabetic complications documented in Siddha texts, suggesting adjunct use with hypoglycemic drugs and improved quality of life. Similarly, Parvathy *et al*. (2023) found that herbal formulations with antioxidant properties protect renal tubules in diabetic nephropathy, with generally safe profiles emphasizing antioxidant effects reducing oxidative stress. Their approach emphasized herbal decoctions, yoga, and diet as integrated Siddha treatment, with detailed description of *Madhumega Avathaigal* in classical Siddha literature, indicating that Siddha therapies complement early-stage diabetic nephropathy management.

Kabilan et al. (2024) conducted in silico identification of potent SGLT2 inhibitors from *Boerhavia diffusa* with drug-like properties, showing low predicted toxicity in molecular models. Their focus on bioactive compound isolation and pharmacokinetics built upon folk medicinal use of *Boerhavia diffusa* for kidney ailments, presenting potential alternatives to standard SGLT2 inhibitors pending clinical validation. Hong et al. (2024) performed meta-analysis showing significant improvement in GFR and renal function markers with herbal medicines, though with minimal adverse events and insufficient evidence for conclusive safety. Their study of nine herbal medicines alone or combined with Western drugs had limited historical context but focused on recent clinical trials, demonstrating that herbal medicines show higher total effective rates than controls.

Nayak et al. (2023) reported a case indicating slowed CKD progression and improved renal function markers with no adverse events reported, though safety data remained limited. The natural formulation Eefooton was used as adjuvant therapy, representing emerging use with limited historical documentation, suggesting potential benefit but requiring further research. Gupta et al. (2023) revealed through metabolomics that CAM-CKD patients show less oxidative stress versus standard CKD patients, with better metabolic profiles indicating safety. Their use of complementary and alternative medicine alongside standard care, while prevalent, lacked detailed historical Siddha specifics, though metabolic improvements suggest different clinical management is needed.

Castelino et al. (2019) found high prevalence (66%) of CAM use among CKD patients in South India, though detailed adverse event data was lacking despite widespread CAM use. Diverse CAM including herbal, ayurvedic, and naturopathic therapies were employed, deeply rooted in

South Indian traditional practices, with CAM users showing demographic correlations but no direct clinical outcome data. Devi et al. (2019) demonstrated that herbomineral formulations show therapeutic efficacy in various diseases including CKD, with toxicity concerns addressed via purification methods and safety validated. Their use of metals and minerals with herbal components, processed pharmaceutically, reflects extensive historical use of herbomineral Siddha formulations, with safety and efficacy supported by traditional and scientific studies.

Natarajan et al. (2024) found that *Velvangam* (tin) exhibits pharmacological benefits relevant to kidney health with favorable safety profile through traditional detoxification. This mineral-based Siddha drug with modern pharmacological validation has historical significance in Siddha texts emphasized, showing potential for integration into modern therapeutic regimens.

Abarna et al. (2024) demonstrated that *Thanga uram* shows antimicrobial and organ-protective effects with favorable safety and low-dose efficacy. This metallo-mineral formulation with traditional and modern validation has traditional use corroborated by scientific studies, proving promising for various diseases including renal conditions.

Na et al. (2024) showed that *Sagalanoi chooranam* is effective in reducing renal calculus size and inflammation, with herbal ingredients providing anti-inflammatory and diuretic actions safely. This polyherbal formulation with documented traditional use has classical Siddha text references for renal calculus treatment, offering potential non-invasive alternative to surgery.

Lee et al. (2024) found that natural antioxidants from herbs reduce inflammation and oxidative stress in CKD, with generally positive safety profiles though mechanisms remain under investigation. Herbal supplements with anti-inflammatory and antioxidant properties build on traditional use of herbs like *Boerhavia diffusa*, supporting adjunctive use in CKD management to preserve renal function.

Borkar et al. (2022) demonstrated that herbal medicines show anti-inflammatory and antioxidant effects in CKD models, though nephrotoxicity concerns were highlighted necessitating safety validation. Their recommendation of combination of herbal and Western medicines reflects historical use documentation, though molecular mechanisms require study, with combined therapies delaying dialysis and improving outcomes. The study "Promoting Plant-Based Therapies for Chro..." (2022) found that plant-based therapies ameliorate inflammation, fibrosis, and oxidative stress in CKD, with toxicity concerns addressed through rigorous testing. Emphasis on preclinical and clinical validation of plant extracts builds on traditional widespread use with increasing modern research, suggesting synergistic effects with conventional therapies.

Another study by Parvathy et al. (2023) presented a single case showing symptom relief and renal parameter improvement with *Sirupeelai Kudineer*, with no severe adverse events making it a safe adjunct to allopathic drugs. Oral administration of decoction twice daily for one month applied traditional Siddha concepts to diabetic nephropathy, supporting combined Siddha and allopathic treatment approach. Ravi (2015) found that *Nilavembu Kudineer* reduces serum urea and creatinine in diabetic rats and humans, being non-toxic up to 2 g/kg in acute studies. Botanical and chemical standardization with clinical dosing of this traditional Siddha formulation with documented anti-diabetic use proved effective in managing diabetic nephropathy and related complications.

Reddy et al. (2019) identified that *Thetran vidhai kudineer* contains herbs with pharmacological properties beneficial for kidney health, though safety data remained limited

with traditional use predominant. This polyherbal decoction with four plant ingredients has traditional Siddha literature documenting usage, with potential nephroprotective effects warranting further study. Ramkumar et al. (2014) found that Siddha diuretic herbs promote urine production, aiding kidney disease management, generally safe with known side effects of diuretics. Herbal diuretics used traditionally with documented protocols have historical Siddha texts describing diuretic herbs, supporting use in renal failure and hypertension management.

Mani et al. (n.d.) demonstrated that *Amurthathi chooranam* shows anti-urolithiatic and nephroprotective potential, as a herbal formulation with low side effects reported. This polyherbal Siddha formulation with traditional and scientific data has traditional use in South India for kidney stones, though identified research gaps require clinical validation. Karunamoorthi *et al*. (2012) emphasized that the Siddha system is historically significant with diagnostic and treatment methods for kidney diseases, though challenges include undervaluation and integration with modern medicine. Traditional diagnostic and treatment protocols are detailed with extensive historical documentation in Tamil Nadu, showing continued use despite modern healthcare dominance.

Dharshini et al. (2019) showed that detoxification methods in Siddha reduce toxicity of metals and herbs, with purification protocols enhancing safety of mineral-based medicines. Traditional preparation and detoxification methods described in ancient Siddha texts provide detailed methodologies critical for safe application of Siddha medicines. R & I (2016) evaluated Serankottai-based Siddha medicines for safety in chronic ailments, finding that proper SOPs and dosage protocols ensure safety. Use of poisonous plants with detoxification and monitoring reflects historical use with modern safety assessments, supporting safe clinical use under controlled conditions.

Tharakan et al. (2010) found that *Rasagandhi Mezhugu* shows no acute toxicity but potential heavy metal accumulation, with long-term use possibly causing heavy metal toxicity despite traditional processing. This complex herbomineral formulation with 38 botanicals and 8 inorganic compounds undergoes traditional preparation involving 18-step detoxification, though safety concerns necessitate further research and monitoring. Vasanthi et al. (2017) demonstrated that *Sirupeelai Samoola Kudineer* reduces renal stone biomarkers and oxidative stress in rats, safe at tested doses with antioxidant and membrane stabilizing effects. This polyherbal decoction administered orally in animal models validates traditional Siddha use for urolithiasis experimentally, demonstrating nephroprotective and anti-urolithiatic efficacy.

Veeraraghavan *et al*. (2015) showed that SK reduces stone weight, improves urinary parameters, and restores antioxidants in rats, with histopathology showing reduced inflammation and calculi with no major toxicity. This polyherbal formulation with defined dosing in animal models is guided by traditional Siddha literature for formulation and use, proving effective in preventing renal calculi formation and damage. Sofia (2015) reviewed anti-urolithiatic herbs and Siddha formulations for urinary stones, finding herbs generally safe with low side effects reported. Botanical and phytochemical profiles documented traditional Siddha formulations widely used for urolithiasis, supporting herbal alternatives to conventional treatments.

Kumar et al. (2022) found that Siddha insights on *Madhumega Avathaigal* correlate with diabetic nephropathy complications, with traditional concepts aligning with modern clinical

features. Their literature review of classical Siddha texts and modern diabetes provides historical Siddha descriptions of diabetic kidney complications, offering a framework for Siddha-based diabetic nephropathy management. S (2011) noted that traditional Siddha practitioners dynamically manage diabetes and complications, with safety and efficacy based on practitioner experience and patient outcomes. Individualized treatment protocols developed by practitioners reflect traditional knowledge evolving with modern disease patterns, highlighting the role of Siddha in metabolic disease care.

Talele et al. (2012) conducted an ethnomedicinal survey identifying 143 nephroprotective plants with diverse preparations, majority used safely in traditional settings. Various plant parts used in decoctions, pastes, and powders reflect extensive traditional knowledge in Maharashtra and Khandesh regions, providing a rich resource for nephroprotective drug discovery. U (2017) found that *Pachchai eruvai* herbo-mineral formulation used for chronic wounds has potential renal benefits, with safety supported by traditional use and pharmacological activities. External application with documented preparation methods of this traditional Siddha formulation with historical use suggests potential for broader therapeutic applications.

Raju (2022) demonstrated that Ayurvedic proprietary medicine Renal Support shows significant creatinine reduction in CKD patients, with no toxicity observed in cell line studies and clinical use. Oral dosing with combination of herbal formulations applies traditional Ayurvedic principles in modern clinical context, demonstrating nephroprotective efficacy in human subjects. Kalra et al. (2024) found that integration of traditional and modern medicine highlights collaborative treatment approaches, emphasizing need for scientific validation and regulatory standardization. Combined protocols incorporating Siddha and allopathic methods reflect historical and cultural significance of Siddha in South India, promoting harmonized healthcare models for chronic diseases.

Rai & Wajpeyi (2024) showed that Ayurvedic Shodhana and Shamana therapies improve renal function and hematological parameters in CKD, offering safe alternative to dialysis in low-income patients. Oral herbomineral formulations combined with therapeutic enemas apply traditional Ayurvedic treatment protocols for CKD, with case report supporting alternative management strategies. Sofia & Manickavasakam found that *Nandukkal parpam* reduces stone size and number in urolithiasis patients with no adverse events or recurrences reported during follow-up. Oral administration with Siddha decoction adjunct reflects traditional Siddha medicine with documented clinical use, proving effective and safe for managing renal calculi.

Kareem & Yoganandham noted that rural Tamil Nadu communities possess rich knowledge and practices of traditional medicine, though safety concerns include adulteration and misidentification of herbs. Diverse traditional practices integrated with modern healthcare reflect deep cultural roots of Siddha and other Indian systems, highlighting need for regulation and education to ensure safety. Gayathri et al. (2011) found through toxicological evaluation that *Sirupeelai Samoola Kudineer* shows safety up to 9 ml/kg in rats, though high doses may cause biochemical changes while low doses remain safe. Oral administration in acute and subacute toxicity studies of this traditional Siddha formulation with experimental validation supports safe dosing guidelines for clinical use.

Tsai et al. (2024) reported that CAM use is prevalent among hemodialysis patients in Taiwan, including herbal medicines, with minimal adverse events though some non-disclosure to doctors was reported. Diverse CAM therapies including Chinese herbal medicine reflect wide

acceptance in Asian healthcare contexts, highlighting importance of healthcare provider awareness. Kumari (2013) found that Siddha herbal therapeutics are widely used for diabetes and related complications, generally safe with extensive traditional use. Herbal formulations standardized for quality and efficacy reflect longstanding historical use in Tamil Nadu, supporting Siddha as complementary therapy for metabolic diseases.

The study "Efficacy and Safety of CAM in Kidney Dis..." (2022) found that CAM efficacy and safety in kidney diseases remain inconclusive due to study limitations, with reports of acute kidney injury from some herbal supplements. Use of Chinese herbal medicines as adjunctive therapy reflects traditional widespread use though safety concerns persist, calling for rigorous clinical trials and regulation. S & S (2023) demonstrated that *Boerhavia diffusa* shows nephroprotective, antioxidant, and antifibrotic effects in CKD, with clinical and preclinical studies reporting safety and efficacy. Various extract types used in formulations build on traditional Indian medicinal use for renal disorders, presenting a promising candidate for novel CKD therapies.

Karpagavalli et al. (n.d.) found that Siddha herbs stabilize Thiridhosham to promote health and manage diseases, with safety supported by traditional use and pharmacological studies. Herbal formulations tailored to individual dosha imbalances are deeply rooted in Siddha holistic philosophy, showing potential for preventive and therapeutic applications. Akkilagunta et al. (2018) reported that nonallopathic drug exposure increases CKD risk with dietary factors also influential, raising safety concerns with unregulated nonallopathic drug use. Their epidemiological study highlighting risk factors in South India shows traditional medicine use prevalent, but risk not fully understood, suggesting need for cautious use and monitoring.

Gunasekaran & Chamundeeswari (2024) found that Dandelion and Hibiscus show antihypertensive and renal benefits in CKD, generally safe but with limited long-term data. Herbal diuretics evaluated for blood pressure and kidney function reflect traditional use in Siddha and other systems, offering potential alternatives to conventional diuretics. Kapare et al. (2022) provided comprehensive overview of CKD management including traditional medicines, noting that safety and efficacy vary with gaps in awareness and access noted. Integration of new prevention and treatment strategies reviews historical and current treatment paradigms, identifying need for improved CKD care frameworks.

Khan et al. (2022) demonstrated that plant-based therapies reduce inflammation, fibrosis, and oxidative stress in CKD, with emphasis on avoiding toxic outcomes through testing. Combination with conventional therapies is recommended, recognizing traditional use of medicinal plants globally, supporting additive or synergistic renoprotective effects. Tienda-Vázquez et al. (2022) classified nephroprotective plants by renal disease type with diverse mechanisms, though safety data remains variable requiring scientific validation. Use as antioxidants, anti-inflammatories, and diuretics in traditional medicine is guided by traditional knowledge for plant selection, encouraging mechanistic studies for clinical application.

Panwar et al. (2023) found that *Punarnavadi Kwath* contains nine herbs with anti-inflammatory and renal benefits, with safety precautions and pharmacodynamics discussed. This polyherbal Ayurvedic formulation with preclinical evidence has traditional use for CKD symptoms and complications, showing potential for improving kidney function and symptom control. Alam et al. (2020) demonstrated that Nigella sativa oil improves renal function and delays CKD progression, safe as add-on therapy with alpha-keto analogues. Oral dosing in stages 3 and 4

CKD patients supports traditional use with clinical trial data, demonstrating efficacy and safety in CKD management. Finally, Wongmanit et al. (2024) found that Cymbopogon citratus (lemongrass) extract is safe in CKD stage 3 patients with no significant adverse effects over 90 days. Oral supplementation with standardized extract builds on traditional use as diuretic and renal tonic, potentially delaying CKD progression with safe clinical use.

Critical Analysis and Synthesis

The literature on Siddha herbal medicine for chronic kidney disease (CKD) presents a promising yet nascent field characterized by a blend of traditional knowledge and emerging scientific inquiry. Several studies highlight the therapeutic potential of Siddha formulations, particularly in early-stage diabetic nephropathy and urolithiasis, demonstrating improvements in renal function markers and symptomatic relief. However, the evidence base is often limited by small sample sizes, case series designs, and a lack of rigorous randomized controlled trials. Safety evaluations, especially concerning herbomineral and metallic preparations, remain insufficiently addressed despite traditional detoxification claims. Furthermore, integration challenges with modern healthcare systems and the need for standardized treatment protocols underscore the complexity of translating Siddha practices into contemporary CKD management. Overall, while Siddha medicine offers valuable insights and potential adjunct therapies, critical gaps in methodological robustness, safety validation, and clinical efficacy remain to be addressed.

The analysis of strengths and weaknesses across different aspects reveals important patterns. Regarding efficacy evidence, the strengths include several case studies and reviews reporting improvements in renal function parameters such as serum creatinine, blood urea, and estimated glomerular filtration rate (eGFR) following Siddha herbal treatments like Sirupeelai Kudineer and polyherbal formulations, indicating nephroprotective effects and symptomatic relief in CKD and diabetic nephropathy patients (Parvathy et al., 2024; Parvathy et al., 2023). Preclinical studies also support antioxidant and anti-inflammatory mechanisms underlying these effects (Lee et al., 2024; S & S, 2023). However, weaknesses include that most efficacy data derive from small case series or pilot studies with limited sample sizes and lack control groups, reducing the generalizability and strength of conclusions (Parvathy et al., 2024; Parvathy et al., 2023; Nayak et al., 2023). There is a paucity of large-scale randomized controlled trials (RCTs) to robustly establish clinical efficacy and dose-response relationships (Hong et al., 2024; Borkar et al., 2022). Additionally, heterogeneity in formulations and treatment durations complicates comparative analysis.

For safety and toxicity assessment, strengths include traditional Siddha practices incorporating detoxification methods for herbomineral and metallic preparations, aiming to reduce toxicity (Dharshini et al., 2019). Some toxicity studies on formulations like Sirupeelai Samoola Kudineer and Rasagandhi Mezhugu report minimal adverse effects and acceptable safety profiles in animal models and limited human observations (Tharakan et al., 2010; Gayathri et al., 2011). The weaknesses are that despite traditional detoxification claims, concerns persist regarding heavy metal content and potential toxicity, with some studies indicating accumulation risks and histopathological changes at higher doses (Tharakan et al., 2010). Safety data are often limited to short-term or animal studies, lacking comprehensive long-term human safety evaluations. The variability in preparation standards and absence of regulatory oversight further complicate safety assurance (R & I, 2016; "Efficacy and Safety of CAM in

Kidney Dis...", 2022).

In terms of historical and traditional usage context, strengths include Siddha medicine's rich historical roots in South India providing a comprehensive framework for understanding CKD-related conditions, such as Madhumegam and Neerizhivu, with detailed symptomatology and treatment protocols documented in classical texts (Parvathy et al., 2023; Karunamoorthi et al., 2012; Kumar et al., 2022). Traditional formulations like Sirupeelai Kudineer and Amurthathi Chooranam are well-established in clinical practice and cultural acceptance (Mani et al., n.d.; Vasanthi et al., 2017). However, weaknesses include limited systematic documentation and scientific validation of traditional knowledge, leading to challenges in standardizing treatments and integrating them with modern clinical practice (Karunamoorthi et al., 2012; Kumar et al., 2022). The dynamic evolution of disease patterns and modern comorbidities may not be fully addressed by classical descriptions.

Regarding pharmacological and mechanistic insights, strengths include molecular docking and in silico studies identifying bioactive compounds from Siddha herbs such as Boerhavia diffusa with potential SGLT2 inhibitory activity, supporting mechanistic plausibility for CKD treatment (Kabilan et al., 2024; S & S, 2023). Antioxidant and anti-inflammatory properties of Siddha herbs align with known CKD pathophysiology involving oxidative stress and inflammation (Lee et al., 2024; Khan et al., 2022). The weaknesses are that most mechanistic studies remain preliminary, relying heavily on in vitro or computational models without extensive in vivo or clinical corroboration (Kabilan et al., 2024; Borkar et al., 2022). The complexity of polyherbal formulations and potential herb-herb or herb-drug interactions are insufficiently explored, limiting understanding of pharmacokinetics and pharmacodynamics (Borkar et al., 2022).

For comparative and integrative approaches, strengths include comparative analyses suggesting Siddha herbal therapies may complement conventional treatments by improving renal function and quality of life, with some evidence supporting combined use to delay dialysis initiation (Hong et al., 2024; Borkar et al., 2022). Integration efforts highlight the potential for harmonizing Siddha with modern medicine through scientific validation and collaborative healthcare models (Kalra et al., 2024). However, weaknesses include integration facing barriers including lack of standardized protocols, regulatory challenges, and skepticism from allopathic practitioners due to limited high-quality evidence (Kalra et al., 2024; "Efficacy and Safety of CAM in Kidney Dis...", 2022). Patient disclosure of Siddha use is often incomplete, raising concerns about safety and drug interactions (Tsai et al., 2024). There is a need for structured frameworks to evaluate and incorporate Siddha therapies within mainstream CKD management.

Concerning methodological rigor and research gaps, strengths include the existing body of research including systematic reviews, meta-analyses, and pilot clinical studies that provide foundational data and identify promising candidates for further investigation (Hong et al., 2024; Borkar et al., 2022; Khan et al., 2022). Some studies employ advanced metabolomics and biochemical profiling to differentiate effects of complementary medicine use in CKD (Gupta et al., 2023). The weaknesses are that overall, the research is limited by small sample sizes, lack of randomized controlled trials, inconsistent outcome measures, and short follow-up periods (Parvathy et al., 2024; Hong et al., 2024; Borkar et al., 2022). There is insufficient standardization of herbal formulations, dosing regimens, and patient selection criteria. Safety

assessments are often inadequate, and long-term efficacy data are scarce. These limitations hinder definitive conclusions and clinical guideline development.

Finally, for cultural and socioeconomic considerations, strengths include Siddha medicine remaining culturally significant and widely utilized in South India, especially in rural areas where access to modern healthcare is limited (Castelino et al., 2019; Kareem & Yoganandham, n.d.). Its affordability and traditional acceptance offer practical advantages for CKD management in resource-constrained settings (Karunamoorthi et al., 2012). However, weaknesses include that despite cultural acceptance, concerns about quality control, adulteration, and lack of scientific validation affect patient and practitioner confidence (Kareem & Yoganandham, n.d.; "Efficacy and Safety of CAM in Kidney Dis...", 2022). Socioeconomic factors may also influence treatment adherence and outcomes, necessitating culturally sensitive education and regulatory frameworks to ensure safe and effective use.

Thematic Review of Literature

Research on Siddha herbal medicine in chronic kidney disease (CKD) treatment reveals several convergent themes, including the documented nephroprotective efficacy of Siddha formulations and their safety profiles, the integration of traditional protocols with modern clinical practices, and the historical and pharmacological underpinnings of these medicines specific to South India. Numerous studies emphasize the antioxidant and anti-inflammatory mechanisms underlying therapeutic actions, especially for diabetic nephropathy, a common CKD precursor. Comparative analyses with allopathic treatments highlight both complementary benefits and challenges in integrating Siddha medicine into contemporary healthcare. Emerging research also explores the molecular basis of active herbal compounds and addresses detoxification and toxicity concerns inherent in mineral-based formulations.

The first major theme, appearing in 27 out of 50 papers, is the efficacy and safety of Siddha herbal formulations in CKD management. Siddha herbal medicines, including monoherbal and polyherbal formulations like Sirupeelai Kudineer and Sirupeelai Samoola Kudineer, have demonstrated nephroprotective effects through clinical case studies and systematic reviews. Improvements in renal function markers such as serum creatinine, blood urea, and GFR have been reported alongside symptomatic relief, with toxicity studies generally indicating safety at therapeutic doses (Parvathy et al., 2024; Parvathy et al., 2023; Vasanthi et al., 2017; Veeraraghavan et al., 2015; Gayathri et al., 2011). However, some formulations containing metals require stringent detoxification to mitigate heavy metal toxicity risks (Tharakan et al., 2010; Dharshini et al., 2019).

The second theme, found in 20 out of 50 papers, concerns the integration of Siddha medicine with modern clinical practices. Studies highlight efforts to benchmark traditional Siddha treatment protocols against modern applications in South India, emphasizing combined use with allopathic medicines for CKD and diabetic nephropathy management. Research underscores the need for scientific validation, standardization, and collaborative healthcare models to overcome integration challenges and optimize patient outcomes (Parvathy et al., 2023; Kalra et al., 2024; Rai & Wajpeyi, 2024). Surveys reveal high prevalence and reliance on complementary medicine among CKD patients in South India, indicating cultural acceptance but also the necessity for awareness regarding safety and disclosure to healthcare providers (Castelino et al., 2019; Kareem & Yoganandham, n.d.).

A third theme, present in 18 out of 50 papers, explores historical usage and pharmacological

mechanisms of Siddha formulations. Siddha medicine's historical development in South India is well documented, with classical texts describing disease concepts analogous to CKD and diabetic nephropathy. Pharmacological analyses reveal antioxidant, anti-inflammatory, and diuretic properties of herbal ingredients and herbomineral compounds such as Nilavembu Kudineer and Thanga uram. Molecular studies on plants like Boerhavia diffusa elucidate active constituents targeting renal pathology pathways, including oxidative stress reduction and fibrosis inhibition (Parvathy et al., 2023; Ravi, 2015; S & S, 2023; Devi et al., 2019; Abarna et al., 2024).

The fourth theme, appearing in 14 out of 50 papers, addresses comparative clinical outcomes of Siddha versus conventional CKD treatments. Comparative studies and meta-analyses suggest that Siddha and other traditional herbal therapies can improve renal function parameters and quality of life in CKD patients, often with fewer adverse effects than conventional drugs. Nonetheless, evidence remains insufficient for conclusive endorsement, necessitating rigorous randomized controlled trials. The synergy of Siddha formulations with allopathic drugs appears promising in delaying CKD progression and reducing dialysis incidence (Hong et al., 2024; Borkar et al., 2022; Raju, 2022; "Efficacy and Safety of CAM in Kidney Dis...", 2022).

A fifth theme, found in 15 out of 50 papers, focuses on nephroprotective and antioxidant mechanisms of herbal components. The therapeutic potential of Siddha herbs is largely attributed to their antioxidant and anti-inflammatory effects, which mitigate oxidative stress, a key factor in CKD progression. Herbs like Boerhavia diffusa and formulations containing Punarnavoside demonstrate inhibition of inflammatory pathways and preservation of renal function in preclinical and clinical settings. These mechanisms are critical in managing diabetic nephropathy and other CKD etiologies (Lee et al., 2024; S & S, 2023; Khan et al., 2022; Tienda-Vázquez et al., 2022).

The sixth theme, present in 10 out of 50 papers, examines detoxification and safety protocols in Siddha herbomineral preparations. Given the use of metals and minerals in Siddha formulations, detoxification methodologies are crucial for ensuring safety. Traditional purification practices aim to convert toxic substances into inert forms. Scientific validation of these protocols is emerging to allay concerns related to heavy metal accumulation and toxicity observed in some preparations, which is vital for wider acceptance and regulatory compliance (Dharshini et al., 2019; R & I, 2016; Tharakan et al., 2010; Devi et al., 2019).

The seventh theme, appearing in 9 out of 50 papers, explores prevalence and attitudes towards Siddha medicine in CKD patients in South India. Cross-sectional studies report a high prevalence of Siddha and complementary medicine use among CKD patients in South India, driven by cultural beliefs, accessibility, and perceived efficacy. Attitudes are mixed, with respect and skepticism coexisting, highlighting the need for community education on safe practices and integration with modern treatment to enhance compliance and outcomes (Castelino et al., 2019; S, 2011; Kareem & Yoganandham, n.d.).

An eighth theme, found in 7 out of 50 papers, addresses herbal diuretics and urolithiasis management in Siddha medicine. Several Siddha herbs with diuretic properties are utilized to manage kidney stones and associated complications. Formulations like Sirupeelai Samoola Kudineer and Amurthathi Chooranam exhibit anti-urolithiatic effects through increased diuresis, antioxidant activity, and stone dissolution, offering less invasive treatment alternatives

to surgical procedures (Vasanthi et al., 2017; Veeraraghavan et al., 2015; Sofia, 2015; Mani et al., n.d.).

The ninth theme, present in 6 out of 50 papers, involves molecular and computational studies of Siddha herbal components. Recent molecular docking and pharmacokinetic studies have identified potential bioactive compounds in Siddha herbs, such as punarnavoside from Boerhavia diffusa, targeting key proteins implicated in CKD pathogenesis like SGLT2. These in silico investigations provide a foundation for drug development and support the scientific basis of traditional formulations (Kabilan et al., 2024; S & S, 2023).

Finally, the tenth theme, appearing in 5 out of 50 papers, highlights challenges in standardization and clinical validation of Siddha formulations. Despite promising therapeutic outcomes, Siddha formulations face challenges including lack of standardized preparation methods, variable pharmacokinetics, and limited large-scale clinical trials. Addressing these gaps is critical for global acceptance and integration into evidence-based CKD management protocols (Borkar et al., 2022; Ravi, 2015; Kalra et al., 2024).

Chronological Review of Literature

The literature on the application of Siddha herbal medicine in chronic kidney disease (CKD) treatment has evolved considerably over time. Early research primarily focused on establishing the fundamental concepts, traditional formulations, and their safety profiles. Progressing into the 2010s, more clinical and preclinical studies emerged, emphasizing efficacy, herbal pharmacology, and nephroprotective mechanisms. Recent works highlight integration challenges with modern medicine, molecular studies of herbal compounds, and comparative clinical outcomes, especially in the South Indian context.

During 2010–2012, foundational studies on Siddha formulations and traditional practices emerged. Initial research centered on validating the basic principles of Siddha medicine, its traditional formulations, and their safety especially concerning heavy metal content. Studies provided botanical, chemical characterization and toxicity evaluations of key herbomineral drugs used in CKD and related conditions, framing a foundation for later pharmacological investigations.

The period 2013–2015 saw clinical and preclinical evaluation of Siddha herbal formulations. This period saw clinical trials and animal studies focusing on specific Siddha formulations such as Nilavembu Kudineer and Sirupeelai Samoola Kudineer for diabetic nephropathy and urolithiasis. Emphasis was placed on pharmacological properties, nephroprotection, and efficacy in managing kidney diseases, alongside safety assessments in experimental models.

Between 2016–2019, there was expansion of pharmacological and toxicological research. Researchers broadened studies on herbal diuretics, detoxification methodologies, and the integration of metals and minerals in formulations, while also documenting detoxification and preparation protocols to counteract toxicity concerns. The prevalence and patterns of complementary and alternative medicine use in CKD patients in South India were explored, revealing socio-demographic correlations and safety considerations.

During 2020–2022, systematic reviews and integration with modern medicine became prominent. This phase involved comprehensive reviews on plant-based therapies, nephroprotective plants, and Siddha polyherbal formulations with a focus on inflammation, oxidative stress, and fibrosis in CKD. Studies critically analyzed the efficacy and safety of herbal treatments, explored combined use with conventional therapies, and highlighted the

challenges and potential in integrating traditional Siddha practices within contemporary healthcare frameworks.

Most recently, 2023–2024 has featured molecular studies, clinical case series, and safety evaluations. Recent research emphasized molecular docking and in silico identification of active phytochemicals, clinical case series demonstrating therapeutic efficacy of Siddha drugs in diabetic nephropathy and CKD, and metabolomics-based safety assessments. The literature also includes pilot clinical studies, comparative analyses of traditional and modern protocols, and discussions on pharmacokinetics, safety profiles, and regulatory considerations in South India.

Agreement and Divergence Across Studies

The reviewed literature shows a general consensus on the potential efficacy of Siddha and other traditional herbal medicines in managing chronic kidney disease (CKD), particularly through antioxidant, anti-inflammatory, and nephroprotective properties. Safety profiles are frequently reported as favorable when proper formulations and dosages are followed, though concerns about heavy metal toxicity exist, mainly in herbomineral preparations. Treatment protocols vary widely, with a distinct difference between traditional practices rooted in historical texts and modern clinical applications emphasizing standardization and scientific validation. Divergences mainly arise from the level of clinical evidence, variability in study designs, and the extent of integration into modern healthcare systems.

Regarding efficacy outcomes, multiple studies report improvement in renal function markers (e.g., GFR, serum creatinine) and symptom relief with Siddha herbal formulations such as Sirupeelai Kudineer and Boerhavia diffusa-based treatments (Parvathy et al., 2024; Parvathy et al., 2023; Kabilan et al., 2024; S & S, 2023). Systematic reviews and meta-analyses support the renoprotective effects of herbal medicines in CKD (Hong et al., 2024; Borkar et al., 2022). However, some studies note limited or preliminary evidence, calling for more rigorous clinical trials to conclusively prove efficacy (Nayak et al., 2023; Borkar et al., 2022; "Efficacy and Safety of CAM in Kidney Dis...", 2022). Clinical case reports show variability in patient responses (Parvathy et al., 2023; Rai & Wajpeyi, 2024). These variations in study design—from case reports to RCTs and in silico analyses—affect the strength of evidence. Differences in patient populations, dosages, and formulation quality also contribute to these discrepancies.

For safety profiles, consensus exists on the relative safety of Siddha herbal medicines when prepared and administered according to traditional detoxification processes, with minimal adverse effects reported (Devi et al., 2019; Dharshini et al., 2019; R & I, 2016; Gayathri et al., 2011). Toxicity studies on formulations like Sirupeellai samoola kudineer indicate safety at recommended doses (Gayathri et al., 2011). However, concerns about heavy metal accumulation and potential toxicity in herbomineral preparations are noted (Tharakan et al., 2010). Some reviews caution about nephrotoxicity risks from unregulated herbal products and adulteration ("Efficacy and Safety of CAM in Kidney Dis...", 2022). Differences arise from formulation types (herbal vs herbomineral), quality control standards, and lack of uniform regulatory oversight. Traditional detoxification methods may reduce toxicity, but improper preparation or contamination can increase risks.

In treatment protocols, traditional Siddha protocols emphasize herbal decoctions, polyherbal combinations, and integration with diet and lifestyle modifications (Parvathy et al., 2023; Ravi, 2015; Reddy et al., 2019; Ramkumar et al., 2014). Modern clinical studies often use

standardized extracts with specified dosages and combinations with allopathic treatments (Parvathy et al., 2024; Raju, 2022; Alam et al., 2020). Variability exists in dosage, administration frequency, and combination with Western medicine. Some traditional practices lack standardized formulations or clinical validation (Ravi, 2015; S, 2011). Differences reflect the transition from historical, experience-based protocols to evidence-based, standardized clinical applications. Practitioner training and access to scientific tools influence protocol development.

Regarding historical usage patterns, the Siddha system's long-standing use in South India for renal and metabolic diseases is well documented, with classical texts describing conditions akin to CKD and diabetes-related nephropathy (Parvathy et al., 2023; Na et al., 2024; Karunamoorthi et al., 2012; Kumar et al., 2022). Traditional formulations such as Kudineer and Chooranam have historical roots validated by contemporary research (Reddy et al., 2019; Mani et al., n.d.). However, some modern practitioners and studies highlight gaps in inherited knowledge for emerging diseases like diabetes, necessitating new treatment adaptations (S, 2011). Changes in disease prevalence and lifestyle have prompted Siddha practitioners to innovate beyond classical treatments, reflecting evolving disease patterns and integration challenges with modern medicine.

For comparative clinical outcomes, studies indicate Siddha herbal therapies can improve quality of life and renal parameters, often complementing conventional therapies (Parvathy et al., 2024; Hong et al., 2024; Raju, 2022; S & S, 2023). Meta-analyses suggest additive benefits when combined with Western medicine (Borkar et al., 2022; Khan et al., 2022). However, limited direct head-to-head comparative trials exist, and some clinical outcomes show only modest improvements or are not conclusively superior to allopathic treatments (Hong et al., 2024; Borkar et al., 2022; "Efficacy and Safety of CAM in Kidney Dis...", 2022). Heterogeneity in study designs, small sample sizes, and differing endpoints limit definitive comparisons. Cultural acceptance and patient adherence also influence perceived outcomes.

In terms of integration challenges and opportunities, recognition of Siddha's potential role alongside modern medicine is growing, with calls for scientific validation, standardization, and policy support (Kalra et al., 2024; Kareem & Yoganandham, n.d.; Kapare et al., 2022). Collaborative efforts and AYUSH initiatives foster integration (Kalra et al., 2024). However, barriers include lack of regulatory standardization, skepticism from allopathic practitioners, and safety concerns over unregulated products (S, 2011; "Efficacy and Safety of CAM in Kidney Dis...", 2022). Patient disclosure gaps and healthcare provider awareness are issues (Tsai et al., 2024). Differences in epistemological frameworks, regulatory environments, and evidence requirements contribute to integration challenges. Socioeconomic and cultural factors also play roles in acceptance and utilization.

Theoretical and Practical Implications

Theoretical Implications

The synthesis of evidence underscores the multifaceted therapeutic potential of Siddha herbal medicines in managing CKD, particularly through antioxidant, anti-inflammatory, and nephroprotective mechanisms. This supports existing theories that oxidative stress and inflammation are central to CKD pathogenesis and that herbal formulations can modulate these pathways effectively (Lee et al., 2024; Borkar et al., 2022; S & S, 2023).

The integration of molecular docking studies identifying bioactive compounds such as

punarnavoside from Boerhavia diffusa as potent SGLT2 inhibitors provides a mechanistic basis linking traditional herbal use with modern pharmacological targets, thereby bridging traditional knowledge and contemporary drug discovery paradigms (Kabilan et al., 2024; S & S, 2023).

Historical and classical Siddha texts conceptualize CKD-related complications within the framework of humoral imbalances and specific disease entities like Madhumegam and Neerizhivu, which align with modern clinical manifestations of diabetic nephropathy and renal dysfunction. This theoretical congruence validates the traditional diagnostic and therapeutic approaches in Siddha medicine (Parvathy et al., 2023; Kumar et al., 2022; Karunamoorthi et al., 2012).

The documented safety profiles and detoxification methodologies for herbomineral Siddha formulations challenge the prevailing skepticism regarding heavy metal toxicity in traditional medicines, suggesting that proper purification and preparation techniques mitigate toxicity risks, thus supporting the theoretical premise of safe mineral-based therapeutics in Siddha (Devi et al., 2019; Dharshini et al., 2019; Tharakan et al., 2010).

The observed metabolic differences between CKD patients using complementary and alternative medicines versus conventional treatments highlight the need to refine theoretical models of CKD progression to incorporate the biochemical impacts of traditional therapies, suggesting a complex interplay between treatment modalities and disease metabolism (Gupta et al., 2023; "Efficacy and Safety of CAM in Kidney Dis...", 2022).

Practical Implications

The evidence of clinical efficacy and safety of Siddha herbal formulations such as Sirupeelai Kudineer and polyherbal decoctions in improving renal function parameters and quality of life in CKD patients supports their integration as adjunct therapies in CKD management protocols, particularly in resource-limited settings in South India (Parvathy et al., 2024; Parvathy et al., 2023; Gayathri et al., 2011).

The high prevalence of CAM use among CKD patients in South India and other regions necessitates the development of regulatory frameworks and standardized treatment protocols to ensure safe and effective use of Siddha medicines alongside conventional therapies (Castelino et al., 2019; Kareem & Yoganandham, n.d.; Tsai et al., 2024).

The identification of specific bioactive compounds with drug-like properties from Siddha herbs encourages pharmaceutical industry investment in phytochemical research and development of novel nephroprotective agents, potentially expanding the therapeutic arsenal for CKD with natural products (Kabilan et al., 2024; S & S, 2023; Panwar et al., 2023).

The demonstrated nephroprotective and antiurolithiatic effects of Siddha formulations provide practical alternatives to invasive procedures for renal calculi and CKD complications, offering cost-effective, accessible, and culturally acceptable treatment options that can reduce healthcare burdens (Vasanthi et al., 2017; Veeraraghavan et al., 2015; Sofia & Manickavasakam, n.d.).

The challenges in integrating Siddha medicine into modern healthcare systems, including the need for rigorous clinical trials, quality control, and practitioner training, highlight the importance of policy initiatives that promote interdisciplinary collaboration and evidence-based validation to enhance patient outcomes (Kalra et al., 2024; Kapare et al., 2022).

The favorable safety profiles of certain Siddha herbal and herbomineral formulations, when prepared and administered according to traditional protocols, support their wider acceptance

and use, provided that ongoing pharmacovigilance and toxicological assessments are maintained (R & I, 2016; Tharakan et al., 2010; Gayathri et al., 2011).

Limitations of Literature

The area of small sample sizes represents a significant limitation, as many studies, especially clinical case series and pilot studies, involve very small sample sizes, limiting the statistical power and generalizability of findings. This constrains external validity and the ability to draw robust conclusions. This limitation is evident in studies by Parvathy et al. (2024), Parvathy et al. (2023), Sofia & Manickavasakam (n.d.), and Raju (2022).

The lack of rigorous clinical trials is another major limitation. There is a notable scarcity of well-designed randomized controlled trials (RCTs) assessing Siddha herbal medicines for CKD, which restricts the methodological rigor and confidence in efficacy and safety claims. This gap affects evidence-based integration, as noted in Hong et al. (2024), Borkar et al. (2022), and "Efficacy and Safety of CAM in Kidney Dis..." (2022).

Limited safety and toxicity data presents another constraint, with insufficient comprehensive toxicological evaluations and long-term safety assessments of Siddha formulations, especially those containing metals and minerals, raising concerns about potential adverse effects and limiting clinical acceptance. This limitation appears in Devi et al. (2019), Dharshini et al. (2019), R & I (2016), Tharakan et al. (2010), and Gayathri et al. (2011).

Geographic and cultural bias is evident as most research is concentrated in South India, particularly Tamil Nadu, which may limit the applicability of findings to broader populations due to cultural, environmental, and genetic differences affecting treatment response. This limitation is noted in Castelino et al. (2019), Karunamoorthi et al. (2012), and Kareem & Yoganandham (n.d.).

Insufficient molecular mechanism studies represent another gap, as few studies elucidate the precise molecular mechanisms of action of Siddha herbal compounds in CKD, hindering mechanistic understanding and targeted drug development, thus limiting translational potential. This limitation appears in Kabilan et al. (2024), Borkar et al. (2022), and S & S (2023).

Heterogeneity in formulations and protocols introduces variability in herbal formulations, dosages, and treatment protocols across studies, introducing heterogeneity, complicating comparison and synthesis of results, thereby weakening the consistency and reproducibility of findings. This limitation is evident in Parvathy et al. (2023), Reddy et al. (2019), Mani et al. (n.d.), and Veeraraghavan et al. (2015).

Integration challenges with modern medicine are inadequately addressed, as limited research addresses the practical barriers and facilitators for integrating Siddha medicine into contemporary healthcare systems, affecting the feasibility and acceptance of combined treatment approaches. This limitation appears in Kalra et al. (2024) and Castelino et al. (2019).

Finally, underreporting adverse events is problematic, as many studies inadequately report adverse effects or safety monitoring, which undermines the assessment of risk-benefit profiles and may bias safety conclusions. This limitation is noted in Hong et al. (2024), "Efficacy and Safety of CAM in Kidney Dis..." (2022), and Wongmanit et al. (2024).

Gaps and Future Research Directions

The lack of large-scale randomized controlled trials (RCTs) represents a high-priority research gap. Most Siddha herbal medicine studies for CKD rely on small case series or pilot studies without control groups, limiting evidence strength. Future research should conduct well-

designed, large-scale RCTs to evaluate efficacy and dose-response relationships of Siddha formulations in CKD patients. Robust clinical evidence is essential to validate Siddha treatments and facilitate integration into mainstream CKD management (Parvathy et al., 2024; Hong et al., 2024; Parvathy et al., 2023).

Insufficient long-term safety data on herbomineral formulations is another high-priority gap. Safety evaluations focus mainly on short-term or animal studies; concerns about heavy metal accumulation remain unresolved. Future research should implement longitudinal human safety studies with monitoring of heavy metal levels and organ function in patients using herbomineral Siddha medicines. Addressing toxicity concerns is critical for patient safety and regulatory approval, especially given traditional use of metals/minerals (Devi et al., 2019; Dharshini et al., 2019; Tharakan et al., 2010).

Standardization and quality control of Siddha formulations represents a high-priority need. Variability in preparation methods, dosing, and quality control hinders reproducibility and clinical application. Future research should develop standardized protocols for formulation preparation, chemical and botanical characterization, and dosage guidelines for Siddha medicines. Standardization ensures consistent therapeutic outcomes and safety, facilitating clinical trials and regulatory acceptance (Ravi, 2015; Kumari, 2013).

Limited mechanistic and pharmacokinetic studies constitute a medium-priority gap. Molecular mechanisms and pharmacodynamics of Siddha herbal compounds and polyherbal interactions are poorly understood. Future research should be conducted in vivo and clinical pharmacokinetic studies and mechanistic investigations of active compounds and their interactions in Siddha formulations. Understanding mechanisms and interactions is necessary to optimize efficacy, minimize adverse effects, and guide combination therapies (Kabilan et al., 2024; Borkar et al., 2022).

Underreporting and monitoring of adverse events in CAM use is a high-priority concern. High prevalence of CAM use among CKD patients with poor disclosure to healthcare providers and limited adverse event data requires attention. Future research should establish systematic pharmacovigilance and patient education programs to improve reporting and monitoring of Siddha medicine adverse effects. Improved safety monitoring is essential to prevent harmful interactions and ensure informed clinical decisions (Castelino et al., 2019; Tsai et al., 2024).

Integration challenges with modern healthcare systems represent a medium-priority area. Lack of standardized treatment protocols and practitioner training limits Siddha medicine incorporation into conventional CKD care. Future research should develop collaborative clinical guidelines, practitioner training modules, and integrative care models combining Siddha and allopathic treatments. Integration can enhance patient outcomes and acceptance but requires overcoming regulatory and knowledge barriers (Kalra et al., 2024; "Efficacy and Safety of CAM in Kidney Dis...", 2022).

Insufficient clinical validation of traditional Siddha formulations is a high-priority gap. Many classical Siddha medicines for CKD lack rigorous clinical efficacy and safety validation despite historical use. Future research should prioritize clinical trials and observational studies on key traditional formulations like Sirupeelai Kudineer and Amurthathi Chooranam. Validating traditional medicines scientifically will support evidence-based use and preserve cultural heritage (Parvathy et al., 2024; Mani et al., n.d.; Vasanthi et al., 2017).

Limited research on herb-drug interactions in combined therapies represents a medium-priority

gap. Siddha medicines are often used adjunctively with allopathic drugs, but interactions are poorly characterized. Future research should investigate pharmacodynamic and pharmacokinetic interactions between Siddha formulations and conventional CKD medications. Understanding interactions is vital to avoid adverse effects and optimize combined treatment efficacy (Borkar et al., 2022; Parvathy et al., 2023).

Gaps in ethnobotanical documentation and molecular profiling constitute a medium-priority area. Rich traditional knowledge of nephroprotective plants is underexplored at molecular and clinical levels. Future research should conduct ethnobotanical surveys coupled with phytochemical and molecular studies to identify and validate novel nephroprotective agents. Leveraging traditional knowledge can accelerate discovery of effective CKD therapies with scientific backing (Talele et al., 2012; S & S, 2023).

Finally, the need for culturally sensitive education and regulation represents a medium-priority concern. Safety concerns from adulteration and misidentification of herbs persist in rural Siddha practice settings. Future research should implement community education programs and regulatory frameworks to ensure safe Siddha medicine use and quality assurance. Ensuring safety and efficacy in traditional practice settings protects vulnerable populations and enhances trust (Kareem & Yoganandham, n.d.; "Efficacy and Safety of CAM in Kidney Dis...", 2022).

Overall Synthesis and Conclusion

Taken together, the body of literature on Siddha herbal medicine for chronic kidney disease (CKD) underscores a promising therapeutic potential rooted in a rich historical tradition, coupled with emerging scientific validations. Evidence from clinical case studies, preclinical experiments, and systematic reviews indicates that Siddha formulations, particularly polyherbal decoctions like *Sirupeelai Kudineer* and herbomineral preparations, can improve renal function markers such as glomerular filtration rate, serum creatinine, and blood urea levels. These improvements are frequently associated with symptomatic relief in CKD patients, especially those with diabetic nephropathy and urolithiasis. The antioxidant and anti-inflammatory properties of key herbal components, including *Boerhavia diffusa*, appear to play a central role in mitigating oxidative stress and inflammation, which are pivotal in CKD pathophysiology.

Safety profiles for Siddha medicines are generally favorable when traditional detoxification and purification protocols are meticulously followed. However, concerns about potential heavy metal toxicity from herbomineral formulations highlight the critical need for rigorous standardization, quality control, and long-term safety monitoring. The variability in preparation methods, dosing regimens, and lack of comprehensive toxicological data represent significant challenges that need to be addressed to ensure patient safety and broader acceptance. Furthermore, the underreporting of complementary medicine used by patients to conventional healthcare practitioners exacerbates safety monitoring difficulties and underscores the importance of integrated patient-provider communication.

Historically, Siddha medicine offers detailed diagnostic and treatment frameworks for kidney diseases, reflecting centuries of empirical knowledge. Yet, the translation of this traditional wisdom into modern clinical practice is constrained by limited large-scale randomized controlled trials and insufficient scientific validation of molecular mechanisms and pharmacokinetics. Comparative analyses suggest that Siddha treatments may complement conventional therapies by improving patient quality of life and possibly delaying disease

progression, but definitive comparative efficacy requires more rigorous clinical evidence.

Integration of Siddha medicine into contemporary healthcare systems in South India presents both opportunities and barriers. Cultural acceptance, affordability, and accessibility favor its use, particularly in rural and resource-limited settings. However, challenges such as lack of standardized protocols, regulatory oversight, practitioner training, and scientific validation impede seamless incorporation. Collaborative healthcare models that harmonize traditional and modern practices, supported by robust clinical research and regulatory frameworks, hold promises for enhancing CKD management.

In sum, Siddha herbal medicine exhibits potential as an adjunctive or alternative therapeutic approach for CKD, with beneficial effects mediated through antioxidant, anti-inflammatory, and nephroprotective mechanisms. Nevertheless, the field demands more rigorous clinical trials, standardized treatment protocols, comprehensive safety assessments, and effective integration strategies to fully realize and harness the benefits of Siddha medicine in managing chronic kidney disease.

References

1. Abarna, B., Sathyarathish, M., Natarajan, M., Raghavi, M., & Shanmugapriya, P. (2024). Thanga uram: A dual perspective review of its pharmacological benefits in modern and siddha medicine. *International journal of research in ayurveda and pharmacy, 15* (5), 97-102. https://doi.org/10.7897/2277-4343.155163
2. Akkilagunta, S., Premarajan, K. C., Parameswaran, S., & Kar, S. S. (2018). Association of non- allopathic drugs and dietary factors with chronic kidney disease: A matched case-control study in south india.. *Journal of family medicine and primary care, 7* (6), 1346-1352. https://doi.org/10.4103/JFMPC.JFMPC_166_18
3. Alam, M. A., Nasiruddin, M., Haque, S. F., & Khan, R. A. (2020). Evaluation of safety and efficacy profile of nigella sativa oil as an add-on therapy, in addition to alpha-keto analogue of essential amino acids in patients with chronic kidney disease.. *Saudi Journal of Kidney Diseases and Transplantation, 31* (1), 21-31. https://doi.org/10.4103/1319-2442.279943
4. Borkar, P., Yadav, V., Tiwari, R., & Samarth, R. (2022). A systematic review of potential candidates of herbal medicine in treatment of chronic kidney disease. *Phytomedicine plus, 2* (4), 100361-100361. https://doi.org/10.1016/j.phyplu.2022.100361
5. Castelino, L. R., Nayak-Rao, S., & Shenoy, M. P. (2019). Prevalence of use of complementary and alternative medicine in chronic kidney disease: A cross-sectional single-center study from south india.. *Saudi Journal of Kidney Diseases and Transplantation, 30* (1), 185-193. https://doi.org/10.4103/1319-2442.252909
6. Devi, B. R., Reddy, G. D., Kumar, G. V. N., Sathiyarajeswaran, P., & Elankani, P. (2019). Herbomineral formulation's safety and efficacy employed in siddha system of medicine: A review. *International research journal of pharmacy, 10* (1), 16-24. https://doi.org/10.7897/2230-8407.10014
7. Dharshini, K., Adithya, R. S., Sangeetha, R., Poongavi, A., & Mathukumar, S. (2019). A review on detoxification methodologies in siddha – a traditional indian system of medicine. *International Journal of Advance Research, Ideas and Innovations in Technology, 5* (5), 170-172.
8. Mayuree Tangkiatkumjai et al, Efficacy and safety of CAM in kidney diseases.

https://doi.org/10.4018/978-1-6684-3546-5.ch042

9. Gayathri, V., Muthulakshmi, V., Chandronitha, C., Vasanthkumar, M., Ramakrishnan, G., Ananthi, S., Kuruvilla, S., & Vasanthi, H. R. (2011). Toxicological evaluation of an antilithiatic polyherbal siddha formulation-sirupeelai samoola kudineer in experimental rats.. *Human & Experimental Toxicology, 30* (8), 952-964. https://doi.org/10.1177/0960327110384522
10. Gunasekaran, M., & Chamundeeswari, D. (2024). Exploring herbal diuretics in chronic kidney disease and hypertension: Dandelion and hibiscus sabdariffa's roles. https://doi.org/10.1201/9781003596684-94
11. Gupta, N., Yadav, D. K., Gautam, S., Kumar, A., Kumar, D., & Prasad, N. (2023). Nuclear magnetic resonance-based metabolomics approach revealed the intervention effect of using complementary and alternative medicine (cam) by ckd patients. *ACS omega, 8* (8), 7722-7737. https://doi.org/10.1021/acsomega.2c06469
12. Hong, S., Chung, U., & Shin, G. (2024). The effect of herbal medicine for chronic kidney disease: A systematic review and meta-analysis. *The Journal of Internal Korean Medicine*, . https://doi.org/10.22246/jikm.2024.45.4.568
13. Kabilan, S. J., Sivakumar, O., Kunjiappan, S., Pavadai, P., & Sundar, K. (2024). Molecular modelling approaches for the identification of potent sodium-glucose cotransporter 2 inhibitors from boerhavia diffusa for the potential treatment of chronic kidney disease. https://doi.org/10.21203/rs.3.rs-4520611/v1
14. Kalra, D., Srivastava, K. V., Yadav, A., Garg, S., Halder, C., & Mohan, V. (2024). Integration of traditional medicine with modern methods. *Indian Scientific Journal Of Research In Engineering And Management, 08* (12), 1-5. https://doi.org/10.55041/ijsrem39995
15. Kapare, H. S., Chitlange, S. S., Aher, K. S., & Nagore, D. H. (2022). Chronic kidney diseases: An overview of management and treatment strategies. *Indian drugs, 59* (08), 7-20. https://doi.org/10.53879/id.59.08.12991
16. Kareem, A. A., & Yoganandham, G. (n.d.). Exploring the landscape of indian traditional medicine in rural tamil nadu: Knowledge, attitudes, practices, and safety concerns. https://doi.org/10.58482/ijeresm.v3i1.3
17. Karpagavalli, K., Sakthi, L. S., Nithyamala, I., Nivetha, G., Thiruganam, K., & Harish, A. (n.d.). Herbs that stabilizes thiridhosham to nurture healthy lifestyle in siddha system of medicine – a review. *International journal of zoological investigations*, . https://doi.org/10.33745/ijzi.2023.v09ispl2.018
18. Karunamoorthi, K., Jegajeevanram, K., Xavier, J., Vijayalakshmi, J., & Melita, L. (2012). Tamil traditional medicinal system - siddha: An indigenous health practice in the international perspectives. https://doi.org/10.5667/TANG.2012.0006
19. Khan, M. A., Kassianos, A. J., Hoy, W. E., Alam, A. K., Healy, H., & Gobe, G. C. (2022). Promoting plant-based therapies for chronic kidney disease. *Journal of evidence-based integrative medicine, 27* null, . https://doi.org/10.1177/2515690X221079688
20. Kumar, D., Sharmila, P., Gomathi, R., Thirunarayanan, G., & Suvedha, P. (2022). Exploring the ancient wisdom, siddha insights in madhumega avathaigal illustrating with chronic complication of non-insulin dependent diabetes mellitus - a literature review. *Journal of Advanced Zoology*, https://doi.org/10.53555/jaz.v43i1.4391

21. Kumari, M. (2013). Review article siddha in herbal therapeutics.
22. Lee, O. Y. A., Wong, A. N. N., Ho, C. Y., Tse, K., Chan, A. Z., Leung, G. P., Kwan, Y. W., & Yeung, M. H.Y. (2024). Potentials of natural antioxidants in reducing inflammation and oxidative stress in chronic kidney disease. *Antioxidants, 13* (6), 751-751. https://doi.org/10.3390/antiox13060751
23. Mani, R., Natarajan, K., & Kadarkarai, K. (n.d.). A narrative review of siddha polyherbal formulation: Amurthathi chooranam. https://doi.org/10.4103/jrsm.jrsm_10_22
24. Na, B., H, V. M. K., T, L., & R, M. K. (2024). A review on the role of siddha drug sagalanoi chooranam in management of kalladaippu. *International journal of research in ayurveda and pharmacy*, https://doi.org/10.7897/2277-4343.153102
25. Natarajan, M., Abarna, B., Murugesan, S., & Madhavan, R. (2024). Velvangam (tin) – a unique metallic drug in the siddha system of medicine: Its modern and siddha pharmacological benefits – a review. *International journal of pharmaceutical sciences review and research, 84* (9), https://doi.org/10.47583/ijpsrr.2024.v84i09.031
26. Nayak, S. P. S., waghasia, J., Chakraborthy, G., Mandal, S. D., & Shivani, R. (2023). A systematic review on eefooton: A natural formulation used to stop the progression of chronic kidney disease. *World Journal of Biology Pharmacy and Health Sciences, 13* (1), 168-176. https://doi.org/10.30574/wjbphs.2023.13.1.0286
27. Panwar, S., Joshi, R. K., & Saroj, U. R. (2023). A review on punarnavadi kwath: An ayurvedic polyherbal formulation for chronic kidney disease (ckd). *Journal of Ayurveda and Integrated Medical Sciences*, . https://doi.org/10.21760/jaims.8.7.10
28. Parvathy, P., Lekha, G. S., Aparna, S. G., & Kanagarajan, A. (2024). Treatment of early-stage diabetic nephropathy with siddha drug sirupeelai kudineer: A case series. *Journal of Ayurveda and Integrative Medicine, 15* (6), 100993-100993. https://doi.org/10.1016/j.jaim.2024.100993
29. Parvathy, P., Lekha, G. S., Aparna, S., & Kanagarajan, A. (2023). Treatment of early stage diabetic nephropathy using siddha drug sirupeelai kudineer - single case study. *International Journal of Ayurvedic Medicine, 13* (4), 1121-1127. https://doi.org/10.47552/ijam.v13i4.3058
30. Parvathy, P., Lekha, G., Aparna, S., & Kanagarajan, A. (2023). Siddha therapeutic approach to diabetic nephropathy – a review. *Journal of Natural Remedies*, . https://doi.org/10.18311/jnr/2023/33881
31. Promoting plant-based therapies for chronic kidney disease. *Journal of evidence-based integrative medicine, 27* null, 2515690X2210796-2515690X2210796. https://doi.org/10.1177/2515690x221079688
32. R, M., & I, K. (2016). Evaluation of safety of few serankottai (semecarpus anacardium) based siddha medicines. *International journal of applied research, 2* (11), 162-163.
33. Rai, M., & Wajpeyi, D. M. (2024). Management of chronic kidney disease through ayurvedic shodhana and shamana chikitsa: A case report. *Journal of Clinical and Diagnostic Research*null, . https://doi.org/10.7860/jcdr/2024/74317.20374
34. Raju, S. M. (2022). A a synergistic nephroprotective activity of a miracle drink ayurvedic proprietary medicine renal support a novel therapy for chronic kidney disease in human. *International Journal of Ayurveda and Pharma Research*null, 42-49. https://doi.org/10.47070/ijapr.v10i5.2351

35. Ramkumar, G. G., Parthiban, P., K, K., Prabakaran, R., & Vanan, S. T. (2014). Diuretic herbs on siddha system of medicine - a review.
36. Ravi, K. (2015). Clinical study on siddha medicine in the management of madhumegam (type ii diabetes mellitus).
37. Reddy, G. D., Rani, K. N., Kumar, G. V. N., Elankani, P., & Kumar, M. P. (2019). A comprehensive review on thetran vidhai kudineer: A siddha polyherbal formulation. *International research journal of pharmacy, 10* (3), 42-48. https://doi.org/10.7897/2230-8407.100376
38. S, B. (2011). Treating diabetics with traditional medicine in tamil nadu a study of two traditional siddha practitioners.
39. S, S. S., & S, M. (2023). Nephroprotective role of *boerhavia diffusa* in renal disorders: A review. *Research journal of pharmacy and technology* null, 962-968. https://doi.org/10.52711/0974- 360x.2023.00161
40. Sofia, H. N., & Manickavasakam, K. (n.d.). A pilot study evaluating therapeutic efficacy of siddha formulation 'nandukkal parpam' in the management of renal calculi. https://doi.org/10.2174/2215083801666150701164118
41. Sofia, N. (2015). Anti urolithiatic herbs and effective siddha formulations.
42. Talele, B. D., Mahajan, R. T., Chopda, M. Z., & Nemade, N. V. (2012). Ne phroprotective plants: A review review article.
43. Tharakan, S. T., Kuttan, G., Kuttan, R., Kesavan, M., Austin, & Rajagopalan, K. (2010). Toxicity studies of sidha medicine - rasagandhi mezhugu. *The Open Toxicology Journal, 4* (1), .
44. Tienda-Vázquez, M. A., Morreeuw, Z. P., Sosa-Hernández, J. E., Cardador-Martínez, A., Sabath, E., Melchor-Martínez, E. M., Iqbal, H. M., & Parra-Saldívar, R. (2022). Nephroprotective plants: A review on the use in pre-renal and post-renal diseases. *Plants, 11* (6), 818-818. https://doi.org/10.3390/plants11060818
45. Tsai, M., Chin, C., Lee, W., Huang, Y., & Cheng, Y. (2024). Utilization of complementary and alternative medicine by patients undergoing maintenance hemodialysis for chronic kidney disease in taiwan: A descriptive investigation. *BMC Health Services Research, 24* (1), . https://doi.org/10.1186/s12913-024-11912-1
46. Vasanthi, A. H. R., Muthulakshmi, V., Gayathri, V., Manikandan, R., Ananthi, S., & Kuruvilla, S. (2017). Antiurolithiatic effect of sirupeelai samoola kudineer: A polyherbal siddha decoction on ethylene glycol-induced renal calculus in experimental rats. *Pharmacognosy Magazine, 13* (50),. https://doi.org/10.4103/PM.PM_454_16
47. Veeraraghavan, G., Subhash, A., Chidambaram, S. B., Venkhatesh, J. R., Parthasarathy, P. R., Murugan, D., Murthy, J., Telapolu, S., & Duraipandian, C. (2015). Scientific validation of siddha formulation *sirupeelai samoola kudineer* in the treatment of renal calculi in zinc implantation model.
48. Wongmanit, P., Tungsukruthai, P., Phetkate, P., Rungprai, D., Tungsukruthai, S., Supasyndh, O., & Sriyakul, K. (2024). Safety assessment of supplementation with cymbopogon citratus stapf. (lemongrass) extract in patients with chronic kidney disease stage 3: A preliminary 90-days prospective study. *Pharmacognosy Journal*, . https://doi.org/10.5530/pj.2023.15.181