

The Role of Natural Products in Kidney Protection: A Review of Recent Pharmacological Findings

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Abstract—Natural products have emerged as promising agents for kidney protection, offering diverse therapeutic benefits through their unique biological activities and chemical structures. This review explores the role of natural products in promoting renal health, focusing on recent pharmacological findings. The growing interest in natural products for kidney health is driven by factors such as the limitations of current pharmaceutical treatments, the potential for fewer side effects, and the increasing global prevalence of kidney disease. Various natural products, including herbal extracts, phytochemicals, marine-derived compounds, mushroom extracts, and essential oils, have demonstrated nephroprotective effects through multiple mechanisms of action. These mechanisms include antioxidant properties, anti-inflammatory effects, blood pressure regulation, glucose metabolism modulation, fibrosis inhibition, and oxidative stress reduction. Specific natural products, such as Anacyclus pyrethrum, phytovesicularnanoconstructs, and bioactive compounds with diuretic effects, have shown promising results in preclinical studies.

Clinical investigations have also yielded encouraging outcomes regarding the efficacy and safety of natural substances for renal protection in human studies. However, challenges and limitations, such as the need for standardized dosing, long-term safety assessments, and a comprehensive understanding of interactions and mechanisms, must be addressed to ensure the effective integration of natural products into kidney disease management. Future research directions include the development of innovative drug delivery systems, regenerative therapies, and advanced disease modeling techniques, as well as integrating natural products into conventional kidney treatments to improve therapeutic outcomes. This review serves as a foundation for further research and the application of natural products in promoting renal health and managing kidney diseases.

Index Terms—Natural products, Kidney protection, Nephroprotective effects, Herbal extracts, Phytochemicals, Antioxidant properties

I. INTRODUCTION

Natural products are chemical entities produced by plants, animals, fungi, and microorganisms, and are distinguished by their unique biological activities and chemical structures. These include a diverse array of compounds, such as alkaloids, flavonoids, terpenoids, glycosides, and phenolic compounds. Historically, natural products have been foundational to numerous medicinal systems and continue to play a crucial role in modern drug discovery and the healthcare industry [1]. Their importance in medicine is multifaceted and complex. Many contemporary pharmaceuticals, including antibiotics such as penicillin, anticancer agents such as paclitaxel, and neuroprotective drugs such as galantamine, are derived directly or indirectly from natural products. These compounds provide a wide range of therapeutic benefits, including anti-inflammatory, antioxidant, antimicrobial, anticancer, neuroprotective, and immunomodulatory effects, making them indispensable for treating various diseases [2]. Furthermore, natural products are extensively employed in traditional medicine systems, such as Traditional Chinese Medicine and Ayurveda, where they promote health and address conditions that may be inadequately managed by synthetic drugs owing to their limitations or side effects. They also serve as lead compounds or structural templates in drug development, offering chemical diversity that is often challenging to replicate through synthetic chemistry alone [3], [4].

Kidney diseases are prevalent and have a substantial global impact, contributing to elevated morbidity and mortality rates and increased healthcare costs. The incidence of kidney diseases, particularly chronic kidney disease (CKD), has been increasing worldwide, driven by the rising incidence of hypertension, diabetes, obesity, and metabolic syndrome, and an aging population. The prevalence of CKD is expected to continue to rise, posing a significant public health challenge beyond the costs associated with renal replacement therapy. It markedly increases the risk of premature mortality, particularly from cardiovascular conditions. Among individuals with diabetes, the prevalence of CKD can reach approximately 26.5%, with factors such as hypertension, prolonged duration of diabetes, and family history elevating this risk.

The overall prevalence of kidney diseases, including glomerulonephritis, pyelonephritis, and congenital conditions, is approximately 15.7% of the population, with an estimated 8.6% exhibiting kidney dysfunction based on indicators such as eGFR and urinary albumin-to-creatinine ratio, although awareness of the disease remains very low at approximately 5% [5]. Infectious and immune-related kidney diseases, such as those observed in individuals with HIV, are exhibiting changing trends, with a decrease in certain types, such as HIV-associated nephropathy, but an increase in tubulointerstitial diseases and diabetic kidney disease. Kidney cancer also represents a significant and growing concern, with incidence and prevalence rates increasing globally, particularly in some populations, such as in China. Kidney diseases often result in the deterioration of renal function and can lead to renal failure. Despite these advancements, current treatments primarily slow disease progression without reversing the damage, underscoring the need for improved diagnostic tools and novel therapeutic strategies [6].

This review examines the nephroprotective effects of natural substances, with particular emphasis on botanicals and medicinal herbs recognized for their antioxidative and anti-inflammatory properties. This review explores the roles of natural compounds, such as flavonoids, polysaccharides, and micronutrients, in the prevention and treatment of kidney diseases through their specific mechanisms of action. This

analysis serves as a foundation for further research and the application of natural products in promoting renal health and managing kidney disease.

II. OVERVIEW OF KIDNEY:

The kidneys are essential organs that perform several critical functions to maintain homeostasis in the body. Their primary function is to purify the blood by removing waste products, excess substances, and fluids, which are subsequently excreted as urine. This filtration process is vital for regulating the electrolyte levels, blood pressure, and acid-base balance. Furthermore, the kidneys play a role in hormone production, including erythropoietin, which stimulates red blood cell production, and renin, which assists in blood pressure regulation.[7], [8] Various kidney disorders can significantly impact the structure and function of the kidneys. Chronic kidney disease (CKD) is a prevalent condition characterized by a gradual decline in kidney function, potentially leading to kidney failure if untreated. CKD can result from diabetes mellitus, hypertension, and glomerular inflammation. Acute kidney injury (AKI) is another condition characterized by a sudden reduction in kidney function, often precipitated by factors such as dehydration, infection, or toxins.[9], [10] Other significant kidney conditions include nephrotic syndrome, which involves excessive protein loss in urine due to glomerular damage; polycystic kidney disease, a genetic disorder that results in cyst formation and kidney enlargement; and kidney stones, which are solid deposits that can obstruct urinary flow and cause discomfort. Early detection and treatment are crucial to prevent the progression of kidney disorders and preserve kidney function.[11], [12]

III. LIMITATIONS OF CURRENT PHARMACEUTICAL TREATMENTS

Current pharmaceutical therapies are limited across various disease domains, primarily due to their constrained efficacy and potential adverse effects. For instance, antipsychotic medications targeting dopamine D2 receptors can effectively mitigate psychotic symptoms but are associated with numerous adverse effects, including weight gain, cardiovascular complications and extrapyramidal

symptoms. Moreover, a substantial proportion of patients exhibit inadequate responses to these treatments, particularly with respect to the negative and cognitive symptoms of schizophrenia. Additionally, many newly developed antipsychotic drugs, although marketed as non-dopaminergic, frequently affect dopaminergic neurotransmission, resulting in only marginal improvements in their efficacy or side-effect profiles [13]. In the context of pain management, traditional pharmaceutical treatments face challenges, such as limited effectiveness, short duration of action, and undesirable side effects, which impede their ability to enhance patients' quality of life and daily activities. These challenges highlight the urgent need for innovative drug delivery methods to improve therapeutic outcomes [14].

Medications for Parkinson's disease illustrate similar limitations; traditional treatments demonstrate limited effectiveness and do not halt the disease progression. Drug administration to the brain is particularly problematic because of the blood-brain barrier, which reduces bioavailability at target sites and exacerbates adverse effects. Nanotechnology-based delivery systems are being explored as potential solutions to these challenges, although their clinical translation remains incomplete [15]. The treatment of infectious diseases also faces several pharmaceutical constraints, including inadequate accessibility of drugs and vaccines, poor bioavailability, high costs, and low patient compliance. These factors contribute to the persistently high mortality rates. Controlled-release injectable formulations may alleviate some of these issues by enabling sustained drug release, reducing dosing frequency, and potentially improving clinical outcomes [16].

Topical pharmaceutical treatments for skin conditions are often hindered by the skin's protective barrier, which limits drug penetration and efficacy. New approaches, such as laser-assisted drug delivery, show promise but present challenges, including limited penetration depth, potential tissue damage, cost, and complexity in optimizing the laser parameters and drug formulations [17]. Conventional chemotherapy for lung cancer and analogous diseases encounters significant challenges, including inadequate water solubility, limited bioavailability at specific tumor sites, off-target adverse effects, and drug resistance. Nanocarrier-based delivery systems

offer the potential for targeted and controlled drug release with improved solubility and stability. However, issues pertaining to nanoparticle toxicity and delivery efficiency must be resolved to facilitate their broader clinical applications [18].

Although drug repurposing is a cost-effective strategy, it faces obstacles such as clinical trial challenges, variable evidence bases, and risks such as antimicrobial resistance, which complicate the assessment of efficacy and safety profiles [19]. Furthermore, the drug development process is often characterized by high costs, extended timelines and substantial failure rates. Although artificial intelligence holds promise for enhancing drug discovery and clinical trials, its current application is constrained by issues related to data quality, methodological challenges, and integration complexity [20].

IV. NATURAL PRODUCTS FOR KIDNEY HEALTH:

The growing emphasis on natural products for kidney health is driven by factors rooted in traditional practices and contemporary scientific research. Kidney diseases often lack specific treatments and can lead to irreversible loss of function, underscoring the significance of prevention and supportive care in this field. Natural products, particularly medicinal herbs, offer a promising complementary approach owing to their rich content of bioactive micronutrients with antioxidant and anti-inflammatory properties, which are essential for preserving kidney function. Traditional medical systems, such as those in China and India, have long employed certain botanicals recognized for their dual role as food and medicine ("medicine-food homology") to promote renal health. Botanicals such as *Astragalus membranaceus* and *Angelica sinensis* are rich in flavonoids, polysaccharides, and other compounds that protect renal tissues by reducing oxidative stress, inflammation, and related pathological processes [21], [22]. The kidney's role in eliminating endogenous and exogenous substances is closely linked to dietary inputs, rendering medicinal herbal foods particularly effective for kidney protection.

Natural products exhibit significant potential for modulating the complex pathways implicated in

kidney diseases, including those regulating apoptosis, oxidative stress response, and immune modulation. These properties confer nephroprotective benefits that may not be fully provided by synthetic drugs. For instance, BushenHuashi decoction, a formulation of traditional Chinese medicine, has been shown to reduce kidney stone formation and enhance renal function by influencing signaling pathways associated with oxidative stress and apoptosis [23]. Interest in natural products is further driven by the limitations and adverse effects of current synthetic drugs for metabolic disorders closely linked to kidney diseases, such as hypertension and diabetes. Natural products are being explored for their potential to manage metabolic syndromes while reducing reliance on synthetic medications that may have detrimental effects [24].

Recent research underscores the critical importance of safety in assessing nephrotoxicity risks associated with herbal medicines. Empirical evidence indicates that certain herbal formulations, when administered appropriately, do not adversely affect key renal function indicators, such as blood urea nitrogen or estimated glomerular filtration rate, thereby supporting their safe incorporation into treatment regimens [25]. Furthermore, databases dedicated to natural health products for individuals with chronic kidney disease or renal transplants aim to provide evidence-based safety insights by identifying beneficial products and potential nephrotoxins. The growing interest in natural products for kidney health is driven by their traditional use, promising nephroprotective properties, potential for fewer side effects, and increasing global prevalence of kidney diseases. This trend is further supported by accumulating experimental, clinical, and safety data advocating the integration of these compounds into dietary and therapeutic strategies for renal protection and disease management.

V. CATEGORIES OF NATURAL PRODUCTS

Herbal extracts:-

Herbal extracts have garnered significant attention for their potential renal protective effects, attributed to their antioxidant, anti-inflammatory, immunomodulatory, and cytoprotective properties. Numerous plants commonly used in traditional medicine have been investigated for their

nephroprotective effects, underlying mechanisms, and safety profiles. Astragalus membranaceus and Angelica sinensis are herbs frequently employed in traditional practices that highlight the intersection of their medicinal and nutritional benefits. These herbs are rich in flavonoids, polysaccharides, and various micronutrients, and exhibit antioxidative and anti-inflammatory properties that contribute to the protection of kidney function. Furthermore, these compounds may influence the gut-kidney axis, potentially affecting renal health through dietary intake.

Eucommiae cortex: Extracts from Eucommiae cortex have shown efficacy in reducing renal fibrosis in chronic kidney disease (CKD) models by modulating the TGF- β 1/Smad signaling pathway. This herb has been observed to decrease creatinine and urea nitrogen levels in CKD mice and impede the progression of renal fibrosis, underscoring its potential for renal protection [26]. Lespedeza species, specifically Lespedeza bicolor and Lespedeza capitata, are notable for their high flavonoid, procyanidin, and hydroxycinnamic acid content, including significant glycosides such as quercetin and luteolin. Extracts from these plants have demonstrated hypoazotemic properties, offering renal protection and exhibiting antioxidant, anti-inflammatory, and diuretic effects. They enhance renal filtration, reduce azotemia, and show promise in the management of chronic kidney failure and nephritis [27]. Regarding herbal formulations with antioxidant activity, multi-plant herbal products have demonstrated protective effects against nephrotoxicity induced by agents such as cisplatin in animal models. These formulations have been shown to decrease oxidative stress markers and increase antioxidant enzyme levels in renal tissues, suggesting their potential for preventing renal damage [28].

Safety Considerations: While patients with kidney disease frequently utilize herbal medicines, there are concerns regarding their potential nephrotoxicity. Empirical studies, including randomized controlled trials, have demonstrated no significant differences in renal function indicators, such as glomerular filtration rate (GFR) and creatinine levels, between herbal remedies and placebo, suggesting safety within controlled environments. However, the variability in formulations and the absence of standardized dosing present challenges. Evidence-based safety databases

have been established to guide the clinical application of natural health products in patients with chronic kidney disease (CKD) and those who have undergone transplantation [29].

Herbal remedies are commonly employed by patients with end-stage renal disease undergoing hemodialysis, with a significant proportion opting for botanical treatments. This highlights the necessity of a more comprehensive understanding of the interactions and mechanisms to improve patient communication and ensure safety [30]. Numerous herbal extracts, including *Astragalus membranaceus*, *Angelica sinensis*, *Eucommia cortex*, and *Lespedeza* species, demonstrate nephroprotective effects primarily through antioxidant, anti-inflammatory, and signaling modulation pathways. These botanicals show promise in slowing kidney disease progression, protecting against nephrotoxicity, and improving renal function parameters. Comprehensive safety evaluations and further research are crucial for the effective and safe integration of herbal substances into kidney disease management.

Phytochemicals (e.g., flavonoids, polyphenols, terpenoids)

Phytochemicals, including flavonoids, polyphenols, and terpenoids, have shown significant potential in promoting kidney health due to their diverse biological activities. Flavonoids, a comprehensive class of polyphenolic compounds, exhibit antioxidant, anti-inflammatory, and antifibrotic properties essential for preserving renal health. These compounds can modulate oxidative stress and inflammation, which are critical contributors to kidney damage and chronic kidney disease (CKD). Flavonoids affect cellular signaling pathways associated with renal fibrosis and apoptosis, thereby assisting in the prevention of the progressive decline in kidney function, which is characteristic of CKD and other renal disorders. Their ability to mitigate oxidative stress and regulate inflammatory mediators is pivotal in reducing renal fibrosis, a pathological hallmark of many chronic kidney diseases [31].

Polyphenols, including flavonoids, also confer renal protection by neutralizing reactive oxygen species (ROS) and reducing oxidative stress, thereby reducing tissue damage in the kidneys. These compounds also exhibit anti-inflammatory effects, which help prevent chronic inflammation that contributes to renal deterioration. Terpenoids, another

diverse group of plant-derived compounds, play a crucial role in renal protection. Research suggests that terpenoids can inhibit deleterious pathways, such as oxidative stress, inflammation, and fibrosis, which are key drivers of CKD progression. Their therapeutic advantages include the reduction of glomerulosclerosis, tubular atrophy, and interstitial fibrosis, which are common features of chronic kidney injury (CKI). Terpenoids have shown potential in enhancing renal function by modulating the multiple pathological processes that lead to kidney dysfunction [32].

The synergistic effects of these phytochemicals are crucial for preserving mitochondrial health in kidney cells, especially considering the impact of mitochondrial dysfunction on renal disease. By mitigating oxidative stress, encouraging mitochondrial biogenesis, and controlling apoptosis, flavonoids and terpenoids enhance cellular energy metabolism and survival in kidney tissues, thereby aiding renal protection [33]. Flavonoids, polyphenols, and terpenoids exert antioxidant, anti-inflammatory, and antifibrotic effects to protect the kidney structure and function. Their broad-spectrum activity presents promising therapeutic options for the management and prevention of kidney diseases, particularly chronic kidney disease (CKD) and renal fibrosis, which are significant global health problems.

VI. MARINE-DERIVED COMPOUNDS

Marine-derived compounds have considerable potential for promoting renal health through various biological activities, particularly their anti-inflammatory, antioxidant, and cytoprotective properties. Although much of the research in marine pharmacology has focused on antitumor, antiviral, and anti-inflammatory effects, several mechanisms relevant to kidney protection can be inferred from the bioactivities of these compounds. Inflammation and oxidative stress are critical factors in the pathogenesis of various kidney diseases, including acute and chronic kidney diseases. Bioactive compounds derived from marine sources exhibit significant anti-inflammatory effects by modulating oxidative stress and immune responses. For instance, anti-inflammatory agents extracted from marine invertebrates, microbes, and algae contribute to the reduction of inflammatory cytokines and oxidative

damage, which are vital for preventing kidney injury and facilitating renal recovery [34]. Compounds derived from Symbiodiniaceae dinoflagellates exhibit anti-inflammatory and vasoconstrictive properties that may enhance renal blood flow and reduce renal inflammation [35]. Terpenoids and Diterpenes: Marine diterpenes, a class of secondary metabolites, have been acknowledged for their diverse biological effects, including anti-inflammatory activities that may protect renal tissues from injury. Current research has focused on elucidating their structures, biosynthesis, and pharmacological potential, indicating their possible roles in mitigating renal inflammation and fibrosis, which are common in kidney diseases [36].

Although marine compounds are not specifically targeted for treating kidney diseases, they have demonstrated the capacity to modulate critical signaling pathways involved in cellular protection and apoptosis. For example, compounds derived from marine cyanobacteria interact with epidermal growth factor receptor (EGFR), vascular endothelial growth factor A (VEGFA), and mitogen-activated protein kinase 3 (MAPK3), which are essential for cell survival, proliferation, and angiogenesis. These pathways are also pivotal in renal recovery post-injury, suggesting that marine compounds may confer protective effects on renal tissues by modulating these molecular targets [37]. Bacteria associated with marine macroalgae, such as Bacillota, produce a range of novel bioactive substances that primarily exhibit antibacterial properties and are being investigated for other therapeutic applications. These microbial products may play a significant role in preserving kidney function indirectly by preventing infections and inflammation, which can exacerbate renal injury [38].

VII. MUSHROOM EXTRACTS

Mushroom extracts exhibit potential for renal protection through various mechanisms, notably their antioxidant, anti-inflammatory, and anti-fibrotic properties, which contribute to maintaining renal health across different pathological conditions. Extracts from *Inonotus obliquus* (Chaga mushroom) have demonstrated significant protective effects against diabetic nephropathy in murine models. These extracts facilitated the regulation of blood

glucose levels, reduced serum creatinine and blood urea nitrogen levels, and improved kidney tissue architecture. These protective effects were linked to decreased expression of transforming growth factor-beta1 (TGF- β 1) and α -smooth muscle actin (α -SMA), markers associated with renal fibrosis and damage. Consequently, *Inonotus obliquus* extract decelerated the progression of diabetes-induced chronic kidney failure by attenuating fibrotic signaling and renal damage [39].

Similarly, extracts from the brown-strain *Flammulina velutipes* (enoki mushroom) were effective in mitigating chronic kidney disease resulting from cisplatin-induced nephrotoxicity in mice. This extract improved renal function indicators, reduced oxidative stress and inflammation, modulated autophagy and apoptosis pathways, and influenced renal transport protein expression. High doses of *Flammulina velutipes* extract enhanced antioxidant levels, decreased inflammatory cytokine levels, and reduced renal fibrosis, suggesting its potential as an adjunctive therapy for preserving renal function during toxic insults [40].

The antioxidant and anti-inflammatory properties of mushrooms are instrumental in enhancing renal health of the host. Medicinal mushrooms, such as *Ganoderma lucidum*, *Hericium erinaceus*, *Pleurotus ostreatus*, and *Agaricus bisporus*, are renowned for their robust capacity to neutralize free radicals and exert anti-aging effects at the cellular level, thereby mitigating oxidative damage that could potentially lead to renal impairment. These mushrooms modulate inflammatory cytokines by reducing pro-inflammatory markers and augmenting protective interleukins, indirectly supporting renal cell health [41]. While certain mushroom species, such as *Amanita proxima*, may cause acute kidney injury due to their toxicity, the medicinal mushrooms under investigation exhibit protective effects attributed to their natural bioactive compounds, which regulate oxidative stress, inflammation, and fibrosis, which are key pathways in renal damage [42].

VIII. ESSENTIAL OILS

Essential oils are concentrated plant extracts containing bioactive compounds, such as terpenoids and phenols, which confer various therapeutic benefits for renal protection. These oils primarily

exert their effects through antioxidant mechanisms that mitigate oxidative stress in renal cells, thereby reducing reactive oxygen species-induced damage. For example, essential oils with high phenolic content, such as those derived from thyme and oregano, function as free radical scavengers associated with renal damage. Essential oils obtained from garlic, turmeric, and basil exhibit anti-inflammatory properties that protect renal tissues by reducing inflammation induced damage.

Empirical studies have demonstrated that essential oils can protect against drug- or toxin-induced renal damage. Specifically, *Citrus sinensis* (orange) essential oil has been shown to improve renal function markers, such as serum urea and creatinine levels, and to enhance kidney tissue integrity in animal models of renal toxicity. The development of nanoformulations incorporating essential oils has further augmented their therapeutic potential by improving their stability, bioavailability, and targeted delivery to renal tissues, thereby enhancing protection against nephrotoxicity. Although these findings are promising, further clinical research is required to ascertain effective dosages, ensure safety, and confirm their integration into therapeutic protocols in humans. Their use should be considered complementary and conducted under professional guidance to optimize renal health outcomes [43], [44].

IX. MECHANISMS OF ACTION:- ANTIOXIDANT PROPERTIES AND ANTI-INFLAMMATORY EFFECTS:

The neutralization of reactive oxygen species (ROS) to prevent oxidative damage to renal cells is exemplified by compounds such as Thymoquinone and Crocetin. Enhancing the activity of endogenous antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase, mitigates ROS. Inhibiting oxidative stress signaling pathways, such as the TLR4/NF- κ B pathway, aims to reduce excessive ROS production and inflammatory mediator levels. Diminishing inflammatory cytokines (e.g., IL-1 β , IL-6, TNF- α) and transcription factors, such as NF- κ B, which contribute to renal inflammation. Modulating immune cell activation, including the shift in macrophage polarization from the pro-inflammatory M1 to the anti-inflammatory

M2 phenotype. Preventing cell death pathways induced by oxidative stress, such as apoptosis, ferroptosis, and PANoptosis, is crucial. Sequestering excess iron to avert ferroptosis, an iron-dependent form of cell death. Utilizing nanoparticle-based delivery systems to enhance the targeted delivery of antioxidants and anti-inflammatory agents to renal tissues. Together, these antioxidative and anti-inflammatory actions work synergistically to protect renal tissues from damage, improve renal function, and support recovery and repair in various kidney injury models [45], [46], [47]

X. REGULATION OF BLOOD PRESSURE

BP regulation protects the kidneys through multiple mechanisms: maintaining renal hemodynamics, reducing glomerular hypertension and proteinuria, preventing inflammatory and fibrotic pathways, and minimizing sympathetic overactivation. Pharmacologic strategies targeting RAAS, mineralocorticoid receptors, and oxidative pathways effectively reduce BP and confer direct renal protection, emphasizing the close interdependence of BP control and kidney health.[48]

XI. MODULATION OF GLUCOSE METABOLISM

Modulating glucose metabolism is instrumental in protecting renal function through several mechanisms, including enhancing mitochondrial energy production and antioxidant defenses, epigenetically regulating genes associated with glucose-induced fibrosis, centrally managing systemic glucose homeostasis, and utilizing natural or synthetic agents to mitigate glucose toxicity and oxidative stress. Collectively, these strategies contribute to the preservation of renal structure and function in conditions such as diabetic kidney disease and acute kidney injury [49], [50].

XII. INHIBITION OF FIBROSIS

Strategies at various levels to inhibit fibrosis and protect renal function include targeting molecular signaling pathways such as relaxin-2, Meis1/Ptprj, and TP53RK; modulating cellular signaling through AOA, cMet, and MCT1; employing

pharmacological agents such as SCO-792 and α -CHCA; and concentrating on epigenetic and neurogenic mechanisms. These approaches offer promising therapeutic avenues for decelerating the progression of chronic kidney disease (CKD) and preserving kidney function.

XIII. REDUCTION OF OXIDATIVE STRESS

Enhancing the body's intrinsic antioxidant mechanisms, such as NRF2, in conjunction with antioxidant supplements like curcumin and selenium, pharmacological agents such as bardoxolone methyl and CEPO, and advancements in renal replacement therapies, is crucial for protecting the kidneys against various renal pathologies. These interventions contribute to the reduction of inflammation, fibrosis, and cellular damage, thereby preserving renal function and improving patient outcomes[51].

XIV. SPECIFIC NATURAL PRODUCTS AND THEIR EFFECTS

Recent investigations into certain natural products have elucidated their various sources, active components, effects on renal function, potential therapeutic applications, and methods of dosage and administration. *Anacyclus pyrethrum*, a species of the Asteraceae family, has been examined for its toxicity and pharmacological properties using its aqueous extract (AEAP). The primary pharmacological effects of AEAP include anxiolytic and antidepressant activities at a dosage of 200 mg/kg in rats, and it is deemed safe, with an LD50 exceeding 5000 mg/kg. Biochemical assessments of renal function during acute toxicity studies indicated no significant adverse effects, suggesting a safe profile for potential therapeutic use, although further research is required to assess long-term effects [52]. Phytochemicals delivered more effectively through phytovesicular nanoconstructs, such as phytosomes, have demonstrated enhanced pharmacological effects on renal function, including anti-inflammatory and renoprotective properties. These bioactive plant compounds, primarily terpenoids, phenolics, and nitrogen-containing metabolites, exhibit antimicrobial, antioxidant, and pharmacological effects that benefit renal health. Phytosome technology enhances the stability, absorption, and

efficacy of drugs, offering promising therapeutic applications for renal disorders, although specific dosing is contingent on the formulation details [53].

Bioactive compounds derived from plants exhibiting diuretic effects are crucial for renal function, as they play a vital role in regulating sodium excretion and blood volume. Flavonoids, such as rutin, acacetin, and naringenin, have demonstrated significant diuretic properties through mechanisms, including the inhibition of the sodium-potassium-chloride co-transporter. These natural diuretics present potential therapeutic advantages for conditions such as edema, hypertension, and renal diseases, with a reduced incidence of adverse effects compared to synthetic drugs. However, clinical trials are necessary to determine standardized dosages and administration methods [54]. Furthermore, advancements in drug delivery systems, including mesoporous silica nanoparticles (MSNs) and amorphous solid dispersion (ASD) systems, have enhanced the bioavailability and pharmacological efficacy of plant extracts. These technologies can decrease the required dosage and toxicity, thereby improving the clinical application of natural nephroprotective agents and other plant constituents [55], [56]. Thymol, a monoterpene phenol derived from aromatic plants, exhibits anti-inflammatory effects by modulating pathways associated with chronic diseases, which may be beneficial in the treatment of renal inflammation. Despite challenges such as low bioavailability and toxicity at elevated doses, innovative nano-encapsulation techniques have enhanced their efficacy. Thymol possesses antimicrobial and antioxidant properties that may contribute to improved renal health [57].

XV. CLINICAL STUDIES AND TRIALS

Recent clinical investigations of natural substances for renal protection have yielded promising results regarding their efficacy and safety in humans. Natural elements, such as selenium, silver, and gold nanoparticles, demonstrate protective effects on the kidneys by reducing oxidative stress and inflammation while promoting the regeneration of renal cells. Traditional Chinese medicine formulations, such as the TangshenQushi Formula (TQF), have shown potential in enhancing renal health in diabetic kidney disease. Other natural

compounds, including resveratrol, epigallocatechingallate, and quercetin, have antioxidant and anti-inflammatory benefits that mitigate renal damage. Safety assessments from randomized controlled trials indicate that many herbal medicines possess acceptable safety profiles without significant adverse effects on the kidneys, although variations in formulations and dosages necessitate careful consideration of their safety. Specialized databases have been developed to facilitate the use of natural health products in patients with chronic kidney disease and those who have undergone transplantation, highlighting the importance of personalized safety evaluations. These promising outcomes underscore the innovative potential of metallic nanoparticles for renal protection and affirm the benefits of certain herbal remedies in slowing disease progression. However, these findings necessitate further high-quality clinical trials to conclusively establish their safety and efficacy, thereby supporting broader clinical applications [47].

XVI. FUTURE DIRECTIONS:

Future research on kidney disease treatment is anticipated to concentrate on innovative drug delivery systems, regenerative therapies, and advanced disease modeling techniques. Nanotechnology-based therapies, such as drug delivery via nanoparticles, offer significant potential by enabling the targeted and controlled delivery of treatments to kidney tissues. This approach enhances localization and effectiveness while minimizing systemic side effects of the treatment. However, challenges such as inconsistent nanoparticle synthesis and the complexity of targeting kidney-specific areas must be addressed through improved synthesis methods, refined targeting strategies, and the use of relevant animal models [58], [59]. Another promising area is mesenchymal stem cell (MSC) therapy, which provides regenerative and immunomodulatory benefits that could improve outcomes in acute kidney injury (AKI) and chronic kidney disease (CKD). Future studies should explore combination therapies, personalized treatments, and technological advancements such as single-cell sequencing and CRISPR/Cas9 gene editing to enhance therapeutic safety and efficacy [60].

The utilization of natural products in drug development also demonstrates a considerable potential. Natural compounds are a valuable source for developing new drugs because of their evolved biological activities, with many anti-cancer drugs already derived from natural sources. Computer-aided drug discovery (CADD) techniques facilitate the identification and optimization of drug candidates based on natural products, thereby expediting the drug development process and reducing the costs. Advances in cheminformatics, genomics, and databases, such as the Endophytic Microorganism Natural Products Database (EMNPD), assist in the efficient mining and understanding of bioactive natural compounds for pharmaceutical development [61], [62], [63].

Integrating natural products into conventional kidney treatments may improve therapeutic outcomes. These natural products may serve as adjuncts or foundations for new drugs that complement existing treatments, including nanotherapeutics and stem cell therapies. Research combining natural product pharmacology with targeted delivery systems for kidney diseases could result in safer and more effective treatments with fewer adverse effects. Furthermore, exploring localized drug delivery and renal-specific targeting can enhance the efficacy of drugs derived from natural products for treating kidney disorders [59], [64], [65].

XVII. CONCLUSION

Natural products offer valuable therapeutic potential for kidney protection owing to their antioxidant, anti-inflammatory, antifibrotic, and metabolic regulatory effects. Evidence from preclinical and emerging clinical studies highlights their ability to improve renal function, reduce oxidative stress, and mitigate the progression of chronic and acute kidney injury. Although promising, the safe and effective integration of these natural compounds into clinical practice requires further research to establish standardized dosing, long-term safety profiles, and mechanisms of action. Overall, natural products serve as powerful complementary tools in renal health management and hold significant potential for future drug development.

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