ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 18, Issue 12, 2025

Online - 2455-3891
Print - 0974-2441

Review Article

THE ROLE OF TURMERIC TABLETS IN ALLEVIATING INFLAMMATION AND OXIDATIVE STRESS IN CHRONIC KIDNEY DISEASE PATIENTS

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Received: 19 March 2025, Revised and Accepted: 13 October 2025

ABSTRACT

Chronic kidney disease (CKD) is a progressive condition characterized by ongoing inflammation and oxidative stress, which plays an important role in pathophysiology and complications. Recent studies highlight the possible therapeutic role of curcumin, the active compound in turmeric, in preventing these harmful processes. The effects of turmeric tablets have been evaluated in terms of their mechanism of action. Clinical efficacy and safety. There is substantial evidence that curcumin supplementation is positively associated with tumor necrosis factor-alpha, interleukin-6, C-reactive protein, in addition to improving antioxidant activity by inducing erythrocyte nuclear factor 2. It is associated with a reduction in inflammatory cytokines. However, Curcumin's effects on traditional markers of kidney function remain controversial. Most studies reported no change in glomerular filtration rate or serum creatinine. Further studies will be necessary to establish an optimal dosing plan and dosing regimen to increase bioavailability and therapeutic activity. Overall, curcumin is a potential adjuvant therapy for managing inflammation and stress from Oxidative reactions in patients with CKD and deserves further study in a clinical environment.

Keywords: Curcumin, Turmeric tablets, Chronic kidney disease, Inflammation, Oxidative stress, Nuclear factor erythroid 2 activation, Clinical efficacy.

 DOI: http://dx.doi.org/10.22159/ajpcr.2025v18i12.54264. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Chronic kidney disease (CKD) is the progressive loss of kidney function. The kidneys act as a filtration system that takes waste and excess fluids out of the blood; they regulate the balance of electrolytes, thereby controlling blood pressure through hormones produced. CKD is defined by either kidney damage, indicated by markers such as proteinuria or haematuria, or a decreased glomerular filtration rate (GFR) of <60 mL/min/1.73 m^2 for at least 3 months [1]. The disease encompasses various stages, ranging from mild impairment to end-stage renal disease (ESRD), where kidneys can no longer function adequately without dialysis or transplantation [2]. The prevalence of CKD is growing worldwide, but most of these are seen among the older age groups with major associations to comorbid conditions like diabetes and hypertension, the two most common causes of kidney damage [3] CKD progression involves inflammation, metabolic dysfunction, and environmental influences such as pollution exposure and lifestyle factors, as illustrated in Fig. 1. Curcumin modulates many biological pathways involved in inflammation and oxidative stress, which are critical factors in many chronic diseases, including CKD. Research indicates that curcumin can influence inflammatory cytokines and other mediators involved in kidney injury and disease progression [4]. The rationale for using turmeric and its active compound curcumin in managing CKD stems from their established anti-inflammatory and antioxidant effects. CKD is fundamentally an inflammatory condition characterized by chronic inflammation that contributes to renal damage and progression to ESRD. Curcumin's ability to inhibit inflammatory cytokines and reduce oxidative stress makes a compelling case for its therapeutic use in the management of kidney failure. chronic Recent studies have shown that curcumin can increase the expression of tight junction proteins. This improves the function of the intestinal barrier and reduces inflammation throughout the body, which makes kidney disease more severe. This is particularly relevant because increased intestinal permeability is associated with CKD disease, in which inflammatory substances circulate to leaked curcumin. Reducing one of the mechanisms underlying kidney dysfunction can help address this issue. In addition, curcumin has shown kidney-protective effects in various preclinical studies. Adds new ideas about curcumin's connection to metabolic syndrome. It is effective in improving the metabolic syndrome that often corresponds to CKD. This additional indirect support of curcumin compounds benefits kidney function by reducing oxidative stress associated with the disease. Diabetes and high blood pressure by increase insulin sensitivity [4].

PATHOPHYSIOLOGY OF CKD

CKD for short, is a complex and progressive disease that causes the kidneys to lose kidney function over time. The pathophysiology of CKD may be due to multiple interacting mechanisms that cause kidney damage with systemic effects on the body. This has important implications for the development of effective treatment strategies for CKD. CKD is often dangerous. Moreover, patients with extensive kidney loss have only mild symptoms. The kidney consists of approximately one million kidneys. And in case of injury, the remaining kidney compensates for hyperfiltration and hypertrophy to maintain GFR. This compensatory mechanism can only sustain kidney function up to the point where approximately 50% of nephron mass is lost; after that, plasma levels of waste products such as creatinine rise significantly. As CKD advances, the kidneys lose the ability to regulate fluid and electrolyte balance and create a multitude of systemic complications. The inability to excrete excess sodium and water results in volume overload, peripheral edema, and hypertension. In addition, metabolic acidosis develops because of impaired acid excretion, further contributing to muscle wasting and bone disease. During end-stage CKD, patients with a GFR <15 mL/min usually present with osmolality fixed near plasma concentrations, meaning complete loss of concentrating or diluting capacity of urine [5]. It leads to renal failure and complications, including a higher level of potassium that occurs in the system, leading to problems of cardiac and significant heart arrhythmias.

THERAPEUTIC POTENTIAL OF TURMERIC

CKD is characterized by persistent inflammation that contributes to disease progression and complications. Curcumin exhibits significant

anti-inflammatory properties, making it a potential therapeutic agent for CKD. Research has demonstrated that curcumin can modulate various inflammatory pathways. For example, it downregulates proinflammatory cytokines such as tumor necrosis factor alpha (TNF-α), interleukin (IL)-1β, and IL-6 in CKD both in *in vitro* and *in vivo* experiments. Curcumin has significantly diminished inflammatory marker expressions, which leads to improvement of the patient's kidney functions from a disease-associated renal condition. In addition, curcumin modulates the function of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), which is a transcription factor that mediates inflammatory reactions. Curcumin suppresses NF-κB activation that subsequently reduces the levels of pro-inflammatory mediators involved in the progression of renal damage [6]. Curcumin has also been demonstrated to inhibit macrophage infiltration in animal models with the kidney, thereby reducing inflammation and improving the histopathological status of the kidneys. In addition to this, curcumin's anti-inflammatory property was noted in the clinical trials. Curcumin administered in small quantities among the CKD patients was noted to drastically decrease inflammatory biomarkers such as C-reactive protein (CRP) and TNF-α without impact on renal functions in serum creatinine. The observations in the experiment pointed to the use of curcumin in reducing inflammation due to its beneficial effect as a supporting treatment of inflammation among patients suffering from CKD. Stimulation of nuclear factor erythroid 2 results in the induction of various antioxidant enzymes, such as glutathione peroxidase and superoxide dismutase (SOD), which protects kidney cells from oxidative damage. Markers of lipid oxidation in rats with adenine-induced nephropathy by curcumin treatment. Stress markers and kidney function improved. Further, curcumin was established to decrease ROS in the tissue of kidneys, leading to lessened oxidative damage. Antioxidation leads not only to protection but also contributes to kidney improvement function, in protecting the renal cells, in enhancing its improvement; according to one systematic review indicated curcumin supplementation reduces the levels of the marker for oxidative stress, alongside enhancement in histological renal change through different types of models with other studies, involving human beings and animal studies [7]. Chronic inflammation and oxidative stress in CKD cause fibrosis, which eventually leads to the progressive loss of kidney function. Because curcumin modulates the processes of fibrosis, it can be an excellent therapeutic agent to prevent renal fibrosis. Studies show that curcumin suppresses the activation of myofibroblasts, which are responsible for extracellular matrix (ECM) deposition during fibrosis, by blocking transforming growth factor-beta signalling pathways. This inhibits the production of collagen and prevents the overaccumulation of ECM in the kidney tissues. Curcumin has been reported to reduce renal fibrosis through reduced collagen deposition and improved histological scores in experimental models. Other than its antifibrotic effects, curcumin is also protective against acute kidney injury and chronic nephropathy by promoting the survival of renal cells. For example, it was demonstrated that curcumin would decrease apoptosis of renal tubular cells exposed to stress through its modulation of pathways of apoptosis. It is especially useful in the initial stages of CKD when treatments can make all the difference. Clinical evidence supports these findings as well. A randomized controlled trial (RCT) has shown that curcumin supplementation reduces protein in the urine. This is an important marker of kidney damage and improve kidney function parameters in patients with diabetic kidney disease. These results highlight the potential of curcumin as a nephroprotective agent.

EVIDENCE FROM PRECLINICAL STUDIES

Studies in animal models of CKD

CKD is a serious health problem that afflicts almost 850 million people worldwide. Given the complexity of CKD pathophysiology, it is a good idea to explore disease mechanisms and assess the effectiveness of various treatments using animal models. Among these, rodents are most widely used, due to their close genetic resemblance to humans, relatively short life cycles, and ease with which one can produce several forms of kidney injury surgically or through drugs [8]. The 5/6 nephrectomy (Nx) model is one of the most widely utilized techniques for inducing renal failure in laboratory animals. This model involves the surgical removal of 5/6 of the kidney mass, leading to glomerulosclerosis and tubulointerstitial fibrosis. Studies demonstrate that this model effectively mimics human CKD progression, resulting in significant elevations in serum urea and creatinine levels. Histopathological evaluations reveal glomerular hypertrophy and fibrosis, making it a reliable model for studying CKD's progression. The adenine diet model is a non-surgical alternative that induces renal dysfunction through dietary means. Adenine administration causes the formation of 2,8-dihydroxyadenine crystals in renal tubules, causing inflammation and leading to tubular atrophy and fibrosis. This model has been found to mimic the same extent of nephropathy as the Nx model, and it is more efficient because mortality resulting from surgical procedures is minimized [9]. Studies have found that adenine-induced models are highly successful in reproducing the major features found in human CKD. Diabetic nephropathy is the leading cause of CKD worldwide. A few models have been developed to study this condition, including those that use streptozotocin-induced diabetes in rodents. These models recapitulate the histological changes seen in human diabetic kidney disease, including glomerular hyperfiltration and mesangial expansion. The progression of diabetic nephropathy in these models gives insights into potential therapeutic strategies targeting metabolic dysregulation. Hypertension is a major risk factor for CKD development. DOCA salt model-induced hypertension, in the form of mineralocorticoid administration, induces renal inflammation and fibrosis. This model clarifies the relationship between hypertension and renal damage, serving as a test platform for antihypertensive therapies.

Mechanisms of action observed

The RAAS pathway has been critical in the pathogenesis of CKD. In animal models, like the remnant kidney model, renin–angiotensin–aldosterone system (RAAS) activation leads to enhanced glomerular capillary pressure, followed by renal injury. Ang II is key to promoting inflammation and fibrosis by acting through specific receptors. Studies have demonstrated that angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are effective in reducing glomerular hypertension and proteinuria, which slows the progression of CKD. For example, studies showed that ACEIs not only reduce blood pressure but also increase bradykinin levels, which contribute to renal protective effects. These findings emphasize the role of RAAS inhibition in the management of CKD [9], as shown in Fig. 2.

Dosage and formulations tested

In CKD, the ability of the kidney to excrete drugs is impaired, hence a critical consideration in making dosage adjustments while avoiding toxicity. The pharmacokinetics of many drugs are also affected in patients with reduced renal function, leading to increased serum levels and thus potential adverse effects. Thus, preclinical studies evaluating the pharmacodynamics as well as the pharmacokinetics of drugs in models of CKD are essential to optimize treatment regimens. Glucose-lowering agents, especially inhibitors of cotransporter-2 of the sodium–glucose (SGLT2) have been discussed for their renal protective effects. Following glucose reduction can markedly reduce and improve kidney outcomes in diabetic kidney disease models. For example, the CREDENCE trial showed that Canagliflozin 100 mg daily reduces the risk of kidney failure in people with type 2 diabetes and G2-G3/A3 CKD (baseline estimated GFR [eGFR] 30–<60 mL/min), reducing these outcomes. This emphasizes the need for appropriate dosing to maximize treatment benefits and minimize risks [10]. Hypertension is another common comorbidity in patients with CKD, such that most of the patients require antihypertensive drugs. The main purpose of preclinical studies of various antihypertensive agents, such as diuretics and calcium channel blockers, has been to determine their efficacy at different dosages. For example, furosemide was tested in the CKD model, including varying dosages to assess its efficacy in minimizing fluid overload in CKD models. The results show that higher dosages may be necessary for effective diuresis without electrolyte imbalances or deterioration of renal function.

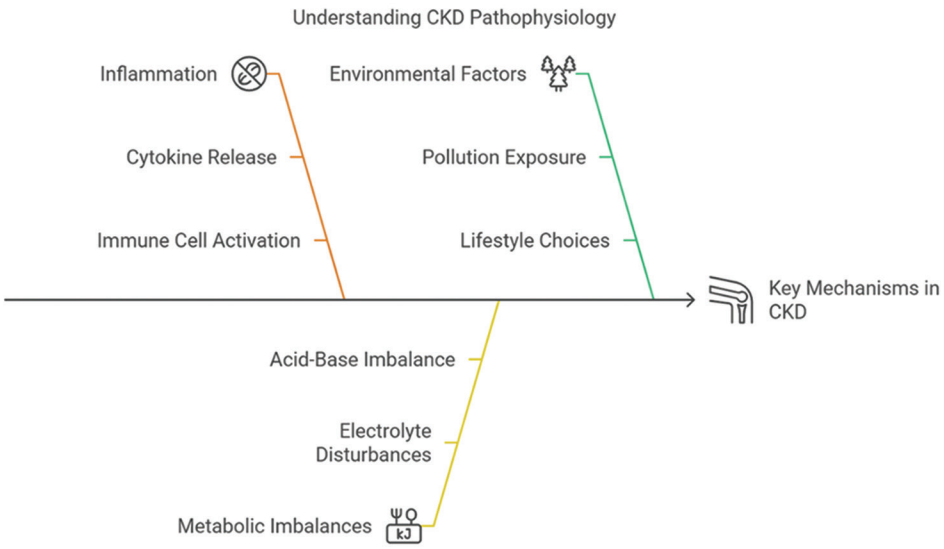


Fig. 1: Key mechanisms

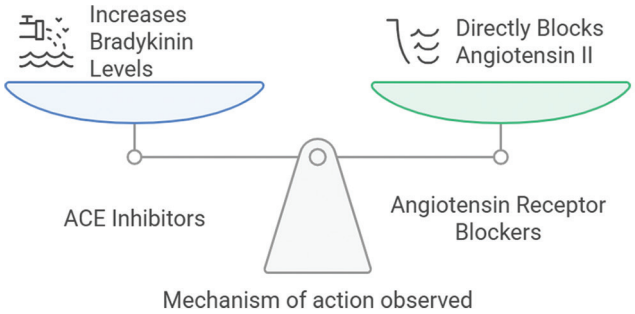


Fig. 2: Mechanisms of action observed

CLINICAL EVIDENCE

Clinical trials involving turmeric/curcumin in CKD patients

A systematic review assessed the effects of curcumin/turmeric supplementation on kidney disease, including CKD, dialysis, and diabetic kidney disease. This review analyzed 12 RCTs involving a total of 631 patients. Curcumin supplementation had a positive effect on inflammatory markers and oxidative stress parameters; however, clinical results on BUN, creatinine level, and GFR revealed only slight statistical changes. A significant decrease in urinary protein levels was observed, and safety data indicated no serious side effects. Therefore, the safety profile of curcumin in treating CKD patients has been established [11]. In a systematic review of 631 patients from 12 RCTs, such as CKD, diabetic nephropathy, with different kidney diseases. Supplementation with curcumin was found to have a beneficial effect on markers of proteinuria and inflammation but had little effect on important clinical parameters such as BUN, serum creatinine, and eGFR, which were not statistically significant. Interestingly, curcumin significantly reduced protein in the urine. It is therefore an adjuvant treatment option for complications associated with CKD. One study of fine curcumin particles looked at patients with albuminuric CKD at a dose of 90 mg/day for 6 months. Testing conducted by Co-Q [11]. Furthermore, curcumin administration was shown to decrease the levels of inflammatory markers without significant adverse effects in a study of hemodialysis patients. This may indicate that curcumin is a safe adjunctive therapy for managing inflammation in CKD patients. The promising findings of curcumin effects on renal function and inflammation markers in CKD patients are despite the limitations that persist within the existing clinical studies.

PHARMACOKINETICS AND BIOAVAILABILITY

Challenges with curcumin absorption

Curcumin is a polyphenolic compound isolated from turmeric (*Curcuma longa*) that has broad-spectrum health benefits, including anti-inflammatory properties, antioxidants, and anti-cancer. However, curcumin has great potential as a therapeutic agent, curcumin's poor pharmacokinetics and bioavailability severely limit its clinical use. The challenges in curcumin absorption are caused by low solubility, rapid metabolism, and quick systemic elimination. Knowing all this is crucial for developing effective formulations that can increase curcumin bioavailability and, in turn, its therapeutic efficacy [12]. The highest barrier to curcumin absorption is its low solubility in water. Curcumin displays hydrophobic properties, which adversely limit its solubility within the gastrointestinal tract, a necessary step to allow the absorption of this compound. Curcumin has an aqueous solubility estimated to be about 11 ng/mL. As such, it is not easy for the body to absorb enough of this compound when taken orally. This low solubility results in minimal bioavailability, meaning only a small fraction of the ingested dose reaches systemic circulation. Consequently, achieving effective plasma concentrations necessary for therapeutic effects becomes challenging. The limited solubility of curcumin is particularly problematic when considering oral administration, as the compound must dissolve in the intestinal fluid to be absorbed through the intestinal wall into the bloodstream. In addition to having low solubility, curcumin also undergoes significant first-pass metabolism in the liver after oral administration. The metabolic process is extensive and includes conjugation with glucuronic acid and sulfate to form a range of metabolites that are subsequently excreted from the body. This metabolism decreases the amount of free curcumin that enters systemic circulation. Clinical trials have shown that at high doses up to 12 g/day, plasma concentrations of free curcumin are still low because of this rapid metabolic clearance. For instance, a study showed that after oral administration of curcumin, only one out of several subjects had detectable levels of free curcumin in plasma at different time points; however, glucuronide and sulfate conjugates were detected at all the time points [13]. The enzymatic activity of the liver significantly reduces curcumin's bioavailability before it can produce pharmacological effects.

Strategies to enhance bioavailability

Curcumin is an active constituent of the spice turmeric (*C. longa*) that is known for its wide-ranging medicinal properties, which include anti-inflammatory, antioxidant, and anticancer effects. Nonetheless, poor

bioavailability largely limits its clinical application due to low solubility, rapid metabolism, and quick systemic elimination. In the last decade, various strategies to overcome these barriers and improve curcumin's bioavailability have been developed and studied extensively. The discussion here is mainly on the most promising methods, such as the use of adjuvants such as piperine, nanoparticles, liposomal formulations, and other innovative delivery systems. The most prominent ways of augmenting curcumin bioavailability can be with a naturally occurring black pepper alkaloid called piperine, shown to potentially affect the functioning of metabolic liver conjugating enzymes, which thus increases its concentration within plasma. From the numerous reports, this natural alkaloid improves curcumin absorption and intake by at least 2000%, positioning this compound as a rather common curcumin formulation's adjuvant. The mechanism of this enhancement is through the inhibition of glucuronidation, a metabolic process that usually reduces the bioavailability of many compounds. This slowing down of the glucuronidation process allows more free curcumin to enter systemic circulation and exert its therapeutic effects [14]. Besides the adjuvants already noted, piperine, among others, research efforts continue to investigate the nanotechnology-based approaches for curcumin delivery. Nanoparticles encapsulate curcumin, thus enhancing its solubility and stability and allowing for better absorption through the intestinal wall. Among the different types of nanoparticles already studied, solid lipid nanoparticles, polymeric nanoparticles, and nanoemulsions can provide controlled release profiles and prolong circulation times within the bloodstream. Curcumin-loaded nanoparticles are demonstrated to result in significantly increased plasma levels as opposed to the traditional formulation. As a matter of fact, researchers found that nanoparticles of curcumin were up to 10-fold bioavailability than free curcumin administered to animal models [15]. Liposomal formulations represent another promising strategy for enhancing curcumin bioavailability. Liposomes are spherical vesicles composed of phospholipid bilayers that can encapsulate hydrophobic compounds such as curcumin. By encapsulating curcumin within liposomes, researchers aim to improve its solubility and protect it from degradation during digestion. Clinical trials have shown that liposomal formulations of curcumin lead to higher plasma concentrations and improved pharmacokinetic profiles compared to standard curcumin preparations. The liposomal delivery system not only enhances absorption but also reduces first-pass metabolism in the liver by curcumin.

Curcumin supplementation, especially in the tablet form of turmeric, has been investigated for its ability to decrease inflammation and oxidative stress among patients with CKD. The following is a step-by-step explanation of the methods, parameters, controls, and statistical analyses of prominent studies:

Study designs

RCTs: MPAC-CKD-1 trial

A double-blind, multicenter RCT enrolled 500–750 CKD patients (eGFR 15–60 mL/min/1.73 m^2, albuminuria >300 mg/day) into 90 mg/day micro-particle curcumin or placebo for 6 months. Endpoints were changed in albuminuria (urine albumin-to-creatinine ratio) and eGFR.

Hemodialysis pilot study

A double-blind RCT assigned 28 hemodialysis patients to a curcumin arm (2.5 g turmeric 3×/week for 12 weeks) or a placebo arm. Biomarkers such as TNF-α, IL-6, and malondialdehyde (MDA) were measured.

Systematic reviews and meta-analyses

A meta-analysis of 32 studies through September 2022 on antioxidants such as curcumin/turmeric and Vitamin E. Only Jadad scores ≥3 (low risk of bias) were used. Random-effects models estimated heterogeneity (I^2 statistic).

Measured parameters

- Inflammatory biomarkers: CRP, TNF-α, IL-6.
- Oxidative Stress markers: MDA, advanced oxidation protein products, 8-hydroxy-2'-deoxyguanosine, SOD.
- Clinical outcomes: Albuminuria (urine albumin-to-creatinine ratio) and eGFR.

Controls and interventions

- Placebo use: All trials used placebo controls matched in appearance and frequency of administration (e.g., daily or thrice weekly).
- Dosage variations: Curcumin formulations used micro-particle curcumin (90 mg/day), turmeric powder (2.5 g 3× per week), and nano-curcumin (80–1,500 mg/day).
- Randomization and blinding: Interactive web-based systems were used to ensure randomization, while double-blinding reduced bias.

Statistical analyses

- Power calculations: The MPAC-CKD-1 trial had 82% power to detect a difference of 16% in albuminuria and 90% power to rule out a change of 2.3 mL/min/1.73 m^2 eGFR.
- Heterogeneity assessment: Meta-analyses employed I^2 statistics (e.g., I^2 = 78% for reduction in CRP in CKD patients).
- Sensitivity analyses: Leave-one-out analyses were used to determine sources of heterogeneity (e.g., the effect of nano-curcumin).
- Non-parametric tests: Wilcoxon signed-rank tests were used to compare pre- and post-intervention biomarker levels in small groups.

Key findings

Turmeric/curcumin lowered CRP (pooled mean difference: −1.25 mg/L) and TNF-α (e.g., from 15.0 to 6.17 pg/mL) significantly.

Micro-particle curcumin had no significant impact on albuminuria or eGFR in the MPAC-CKD-1 trial, with dose and formulation dependencies.

This synthesis highlights the heterogeneity of outcomes by curcumin formulation, dosage, and CKD stage, and the importance of standardized interventions in future trials.

TURMERIC FORMULATIONS FOR CKD

Comparison of different turmeric tablets on the market

Tablet formulation	Composition	Effectiveness	References
Micro-particle curcumin	90 mg/day of micro-particle curcumin	At 6 months of age, albuminuria did not slow the progression of CKD.	[7]
BCM - 95	*Curcuma longa* extract with essential oil	Shown to improve bioavailability and efficacy in various studies.	[6]
Meriva®	Curcumin complex with phosphatidylcholine	Modulates inflammation and improves gut microbiota in CKD	[16]
First-generation formulation	Soft gel capsules containing curcumin and other ingredients	Limited data on specific CKD outcomes, but generally effective for inflammation	[17]

Optimal dosages for CKD patients

Curcumin exhibits various pharmacological properties, Including anti-inflammatory effects, Antioxidants, and anti-inflammatory effects. These are associated with CKD. This is because inflammation and oxidative stress together are huge contributors to flare-ups. Research studies have shown curcumin's ability to modulate inflammatory pathways and reduce markers of oxidative stress. This has a beneficial

effect on kidney function, for example, in a study of rats with adenine-induced kidney failure. Curcumin significantly reduces kidney damage and different levels of kidney function. This improvement in signalling suggests that curcumin's protective effect may be dose dependent. In clinical practice, it is necessary to determine the optimal curcumin dosage for patients with CKD. In a small clinical trial, patients with CKD were given 824 mg of pure turmeric extract (95% curcuminoids) twice daily over 8 weeks. This study showed no significant changes in blood creatinine or urea nitrogen levels. This is a general biomarker of kidney function. However, reports of significant reductions in inflammatory markers such as TNFα and IL-62 only suggest that curcumin's direct effects on the kidneys may not be immediately measurable. Curcumin acts definitely on inflammation. Newer curcumin formulations aim to enhance its bioavailability, as curcumin is very weakly absorbed from the gastrointestinal tract. Moerover, the newly advanced formulations include micro-particle curcumin. A RCT assessed the 6-month efficacy of micro-particle curcumin at 90 mg/day in the treatment of patients with albuminuric CKD. This study showed that there was no significant difference between the curcumin and the placebo groups with respect to either albuminuria or estimated GFR3. This suggests further research is necessary to determine a dosing schedule and formulation effective enough to induce measurable changes in kidney function. The pharmacokinetics of curcumin also play a vital role in its effectiveness. Studies suggest that co-administration with other compounds can enhance its absorption and efficacy. For example, combining curcumin with rhein – a compound known for its own renoprotective effects – has demonstrated synergistic benefits in ameliorating renal fibrosis in animal studies. Such combinations may offer new avenues for optimizing treatment strategies for CKD patients. Further, curcumin supplementation research is focusing on the greater benefits of supplementation in addition to its effects on kidney function. Curcumin has been examined for its anti-inflammatory effects, which may offer a benefit to comorbid conditions commonly present with CKD, such as cardiovascular diseases and diabetes. Since many patients with CKD have a comorbidity of these inflammatory disorders, alleviation of systemic inflammation by curcumin would provide holistic advantages. Although promising findings were found, the approach toward curcumin formulations is a cautious one. Variability in response to curcumin supplementation calls for tailored treatment strategies. Appropriate dosages and formulations are considered depending on the stage of CKD, the other drugs the patient is taking concurrently, and his health status.

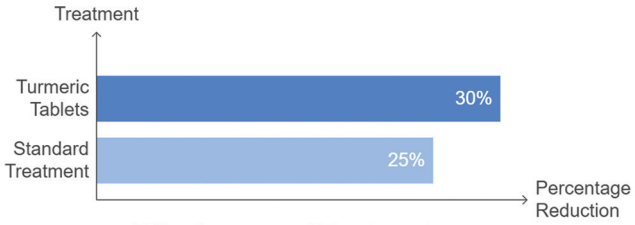
Safety and tolerability

Considerable research has been conducted on curcumin regarding its possible benefits in the management of CKD. Studies have shown that curcumin can reduce inflammation and oxidative stress. These are two factors that contribute to the pathophysiology of CKD. For example, studies in diabetic rats have shown that curcumin significantly reduces kidney fibrosis and inflammatory markers. Significance: This indicates a possible protective effect against kidney damage [18]. However, translating such findings for human use requires careful evaluation of safety and tolerability. Several studies have examined the safety profile of curcumin in patients with CKD in a clinical setting. In one study, 824 mg of pure turmeric extract containing 95% curcuminoids was taken twice daily for 8 weeks to patients with impaired kidney function. No obvious changes were seen in classic biomarkers such as creatinine or BUN, but levels of inflammatory biomarkers such as TNFα and IL-6 were markedly reduced. Clearly, more important is the lack of side effects observed in this study. This indicates the relative safety of curcumin supplementation even in populations with renal failure. The main issue regarding the safety of turmeric and curcumin is their bioavailability and the presence of impurities. Most conventional forms of curcumin exhibit poor bioavailability, which limits their potential effectiveness. Improved formulations aimed at enhancing the bioavailability include micro-particle curcumin and liposomal curcumin, which can achieve increased systemic exposure to curcumin without an increase in toxicities. Moreover, contamination by heavy metals and other toxins remains a known threat to turmeric supplements. Even the regulatory body has pointed to the fact that some turmeric products contain amounts of contaminants that might be harmful at high levels, and that this comes about due to improper manufacturing practices. To this end, it is very important to select high-quality turmeric preparations which are of proven purity and safety. There have also been evaluations of the tolerability of curcumin. A RCT with patients with CKD who were supplemented with curcumin reported no significant adverse effects during the treatment period. Other studies similarly indicated that curcumin is well-tolerated even at higher doses, but there could be some side effects, including gastrointestinal discomfort and allergic reactions. This, therefore, means that every patient should be approached differently when it comes to supplementation. In addition to the safety profile, another important aspect to consider is the potential drug interaction between curcumin and other drugs that are used in the management of CKD. Curcumin is known to modulate cytochrome P450 enzymes that influence the metabolism of some drugs. Patients who are on medications metabolized by these enzymes should seek advice from their healthcare providers before initiating curcumin supplementation to avoid drug interactions. Ongoing research into the formulations of turmeric for CKD continues to unveil its safety and efficacy. For instance, recent studies have been conducted on the use of curcumin in combination with other therapeutic agents to enhance renal protection while minimizing side effects. In fact, one study showed that curcumin combined with Rhein, a compound known for its Reno protective properties, resulted in improved outcomes in animal models of CKD 1. Such synergistic approaches may offer new avenues for treatment while ensuring patient safety [4].

ADVERSE EFFECTS AND CONTRAINDICATIONS

Turmeric, with its key component curcumin, is popularly reported to have such health benefits. Among the reported health benefits of turmeric are its anti-inflammatory and antioxidant properties. Thus, like other supplements, some side effects as well as contraindications have been reportedly associated with it, especially when the patient happens to be someone with CKD. Safe use and minimal interactions are imperative and require information on these facts. Gastrointestinal upset is one of the most common side effects of turmeric supplements. Patients may have symptoms such as abdominal pain, bloating, diarrhea, constipation, and nausea. These gastrointestinal side effects are usually dose-dependent, meaning they occur more often at higher dosages of turmeric. For example, doses above 1,500 mg/day have been associated with increased gastrointestinal distress, and a recommendation is often made to consume turmeric with food to alleviate these side effects. Another condition that might be worsened by turmeric is GERD. Acid reflux in susceptible individuals would be increased due to this supplementation [19]. Another major issue with turmeric supplementation is that it can function as a blood thinner. Curcumin has been known to prevent platelet aggregation and interfere with the mechanisms of blood clotting. This attribute may cause problems in individuals with bleeding disorders or those about to undergo surgical operations. Patients on anticoagulant drugs such as warfarin or aspirin need to be careful in using turmeric supplements because there is a higher chance of bleeding complications. Curcumin also reduces blood sugar levels and can cause hypoglycaemia in diabetic patients who are already on insulin or other antidiabetic drugs [20]. Blood sugar needs to be monitored in such patients when they use a turmeric supplement. There have been reports of liver injury associated with high doses of curcumin. Hepatotoxicity has been documented in individuals taking turmeric supplements, especially at dosages ranging from 250 mg to 1,800 mg/day 6. Symptoms of liver damage can include jaundice, abdominal pain, dark urine, and fatigue. However, given the potential for liver toxicity, it is recommended that those with pre-existing liver conditions or on medications known to affect liver function avoid turmeric supplements altogether [21]. Patients on dialysis are usually on special diets, and their nutrient requirements may be different, which may potentially conflict with the action of turmeric. For example, there is evidence that turmeric may increase urinary oxalate levels, which is a risk factor for kidney stones, a condition more pertinent

to CKD patients. Hence, monitoring and tailored dietary planning are very important in this group. Drug interactions are another important safety profile of turmeric. Curcumin interacts with many drugs that are prescribed to patients with CKD. For instance, it can inhibit the metabolism of certain drugs by interfering with cytochrome P450 enzymes in the liver. This may result in a change in drug efficacy or increased toxicity. Curcumin interacts with certain antidepressants, antibiotics, antihistamines, cardiac drugs, and certain chemotherapy agents. Due to these potential drug interactions, prescribers should be aware of all the medications for which a patient is currently being treated before recommending supplementation with turmeric.



Effectiveness of Treatments on Inflammation and Proteinuria

Synergistic potential with existing CKD therapies

CKD is a leading global health disorder characterized by progressive renal failure that triggers several complications, including cardiovascular disease, anaemia, and metabolic bone disease. Treatment of CKD involves the administration of standard pharmacological treatments that include ACE inhibitors, ARBs, and diuretics. However, evidence indicates that its bioavailability may be enhanced when given in combination with other compounds to exert greater therapeutic effects. A notable example would be co-administration with Rhein, whose nephroprotective effects would be improved dramatically during renal fibrosis, rather than when it was administered alone with either compound. Such synergy has the potential for improving treatment for CKD. More research on herbal combinations such as ginger and turmeric, showed their synergistic value in the modulation of inflammatory pathways. A study discovered that a compound extract had more inhibitory values on pro-inflammatory mediators than individual extracts. This underlines the importance of searching for multi-component therapies that reinforce numerous natural compounds in the care of CKD [6].

COMPARATIVE ANALYSIS

Turmeric tablets versus standard treatments for CKD

CKD is a chronic disease in which the function of the kidneys is gradually lost over time, which leads to a higher risk of cardiovascular diseases, metabolic disorders, and other complications. Standard treatments for CKD focus on symptom management and slowing disease progression with the use of drugs such as ACE inhibitors, diet modification, and lifestyle modifications. One recent interest in such complementary therapies lies with the use of turmeric tablets, which are curcumin-based, primarily because of their anti-inflammatory and antioxidant properties. Thus, this critical analysis will highlight the efficacy as well as the safety of taking turmeric tablets as compared with conventional CKD treatments based on the available clinical evidence. Various studies carried out on patients suffering from CKD revealed the effects curcumin induces and may potentially offer benefits relative to conventional interventions. Short-term clinical trial of 16 CKD patients supplemented with curcumin. It provides 824 mg of pure turmeric extract containing 95% curcuminoids twice daily for 8 weeks. Although there were no significant changes in blood creatinine or urea nitrogen levels, which is a general biomarker of the kidneys. There has been a noticeable decrease. This indicates that even short-term forms of curcumin do not directly increase traditional markers of kidney function. However, it may also significantly reduce inflammation associated with kidney failure. In the second study, supplementing with turmeric for 2 months in diabetic CKD patients reduced proteinuria by 39% compared to the placebo group [18]. Such an outcome indicates that turmeric could possibly be an alternative or complement for conventional treatments aimed at reducing proteinuria, an important marker of renal damage. However, the curcumin treatment has not shown positive outcomes in all the studies conducted regarding the management of CKD. A RCT evaluating the effects of 6 months of treatment with micro-particle curcumin at 90 mg/d found no between-group differences in either albuminuria or estimated GFR. This implies variability in responses to curcumin treatment and points to the fact that more studies are needed to identify optimal dosing and formulation.

ECONOMIC AND MARKET PERSPECTIVES

With an ever-rising awareness of health benefits conferred on it through curcumin active component present in the turmeric supplements have, for some time, increased phenomenally around the globe. Such an upward growth seems particularly relevant concerning the scenario in the context of CKD in patients who inevitably search for add-on therapies in their disease. This analysis of the economic landscape would focus on growth prospects for this market and further accessibility and affordability of the CKD patient populace. The worldwide turmeric market was around 4.3 billion in USD in the year 2020 and is predicted to rise from 2021 to 2026 with a compound annual growth rate (CAGR) about 5.7%, valued at about USD 6.7 billion. The curcumin extracts are a major part of the turmeric supplement segment. The global turmeric supplement market alone was valued at approximately USD 8.2 billion in 2022 and is expected to reach USD 15.1 billion by 2030, reflecting a robust CAGR of about 8.1% during this period [22]. Many factors drive this growth trajectory. There is an increasingly preventive healthcare, where consumers are opting for natural products and dietary supplements to boost their overall health and wellness profiles. Turmeric's widely known anti-inflammatory and antioxidant properties place it at an advantageous point of consumption for those in the market to control chronic diseases such as CKD. Regionally, North America accounts for a major share of the turmeric supplement market because of high consumer awareness and demand for health supplements. The region accounted for around 40% of the revenue share in 2020. Europe also represents an important market, particularly as a hub for cosmetic applications of turmeric and curcumin. Demand is being triggered by the growing food and beverages sector in Europe, which involves increasing use of natural ingredients, such as turmeric. On the contrary, the Asia-Pacific region is likely to grow at the fastest pace in the forecast period. The growth can be ascribed to the high levels of production in countries like India, which is known for producing some of the finest turmeric worldwide. Increased health awareness among consumers in this region further accelerates demand for turmeric supplements.

FUTURE DIRECTIONS

Curcumin has very poor bioavailability with rapid metabolism, leading to faster elimination from the body. Improved delivery systems or formulations that promote absorption are bound to lead to better therapy results. For example, preliminary studies with micro-particle curcumin have shown promise in increasing bioavailability and potentially leading to more pronounced clinical effects. How different formulations affect bioavailability will be critical in determining optimal dosing regimens for CKD patients [6]. Further research should concentrate on the mechanism of action through which curcumin exerts its nephroprotective effect. Although numerous studies have emphasized its anti-inflammatory and antioxidant activities, further elucidation of molecular pathways associated with renal protection may provide additional insights into curcumin's interaction with existing therapies for CKD. For example, understanding curcumin's effects on pathways such as fibrosis or apoptosis could be synergistic when combined with standard treatments, such as ACE inhibitors or ARBs.The development of novel formulations based on turmeric is a promising route towards the augmentation of curcumin therapeutic activity in CKD. Current formulations are usually associated with issues related to bioavailability and stability. It is for this reason that new innovative approaches toward improving these aspects are being

developed. One of the most promising approaches is a nano-curcumin formulation created by nanoparticle technology. Nanoparticles can increase solubility and absorption as well as protect curcumin against degradation in the GI tract. Preliminary studies indicate that nano-curcumin strongly improves renal marker function in experimental animals' models of CKD in comparison with standard curcumin formulations. Such innovations may result in more successful treatments of people affected by kidney diseases. A potential combination is merging curcumin with other natural chemicals, which are either beneficial or synergistic in their health effects. Formulations that include adding black pepper extract, for instance, piperine, enhance the bioavailability of curcumin significantly. This integration of piperine with curcumin may pose a synergistic effect that maximizes therapeutic outcomes with reduced side effects. Furthermore, combining curcumin with other herbs or dietary supplements that target specific aspects of CKD – such as inflammation or oxidative stress – could lead to more comprehensive treatment strategies. Exploring different delivery routes, such as liposomal formulations or transdermal patches, could offer alternative delivery routes that may improve patient compliance and efficacy. Patients with CKD are frequently dealing with other health issues; therefore, it will be essential to develop delivery systems that are user-friendly and support adherence to treatment regimens.

CONCLUSION

Several studies have shown that curcumin has significant antioxidant and anti-inflammatory effects. This is necessary to combat the pathophysiological mechanisms responsible for CKD. CKD is associated with oxidative stress and increased inflammation and leads to kidney damage and progression of ESRD. A systematic review on the effects of curcumin/turmeric supplementation in kidney disease states that although curcumin may benefit inflammatory parameters and oxidative stress, its impact on traditional clinical outcomes such as BUN, serum creatinine, and GFR is limited. These findings are especially relevant in patients with CKD. This is because significant proteinuria often indicates progressive kidney failure. Curcumin's kidney-protective actions have been established in studies involving other types of kidney disorders. In this manner, curcumin's ability to reverse the damage caused to the kidneys, such as diabetic nephropathy and lupus nephritis are sustained by suppressing inflammatory cytokines such as TNF-α, IL-6, and more importantly, curcumin therapy improves markers of Kidney function. and f it has been reported to reduce histopathological injury due to CKD. The present findings suggest that curcumin can be considered a useful adjuvant therapy in the treatment of Patients with CKD, especially inflammation and oxidative stress. Many studies on curcumin have limited patient numbers and short follow-up periods regarding sustained kidney function. As healthcare continues its journey toward personalized medicine, complementary therapies such as curcumin may offer other avenues for the improvement of health outcomes in patients with CKD. Curcumin's anti-inflammatory and antioxidant properties align well with therapeutic goals in the management of CKD, primarily focusing on mitigating inflammation and oxidative stress and preserving renal function. Still, many factors need to be considered before the integration of turmeric supplements into common clinical practice. For instance, curcumin supplementation benefits and limitations should be provided to healthcare professionals with adequate knowledge. This way, clinicians would be able to provide their patients with safe, evidence-based suggestions regarding the integration of turmeric supplements into their respective treatment plans. Further, a set of explicit guidelines on appropriate dosing methods considering ongoing clinical research is necessary to maximize the desired therapeutic effects without the adverse consequences. In addition, issues of accessibility and affordability related to turmeric supplements should be addressed to ensure that all CKD patients can access these therapies. Most CKD patients face financial constraints because of the associated high costs of managing the condition. Advocacy for those insurance plans that include dietary supplements as part of comprehensive care might help to alleviate such financial burdens as faced by patients.

ACKNOWLEDGMENT

None.

LITERATURE REVIEW

In recent years, there has been growing scientific interest in the potential therapeutic effects of turmeric (*C. longa*) and its active compound curcumin in managing chronic conditions, including CKD. Studies published over the past 5 years have increasingly focused on turmeric's anti-inflammatory and antioxidant properties, particularly in the context of renal inflammation, uremic toxins, and oxidative stress, which are key factors contributing to CKD progression.

A 2020 RCT by Shahbazian *et al.* demonstrated that curcumin supplementation significantly reduced serum inflammatory markers such as CRP and IL-6 in CKD patients. Similarly, Gupta *et al.* (2021) reported an improvement in oxidative stress markers and renal function parameters after 12 weeks of turmeric supplementation. A meta-analysis by Liu *et al.* (2022) further confirmed curcumin's potential in reducing systemic inflammation in patients with various chronic diseases, including CKD.

Despite these findings, many studies have been limited by short durations, small sample sizes, or a lack of focus on bioavailability, which affects curcumin's effectiveness. Recent advancements, such as the use of enhanced formulations such as curcumin nanoparticles or piperine-enhanced turmeric, aim to address this gap.

This study aims to build on the growing body of evidence by:

- Focusing specifically on CKD patients, an often-overlooked population in natural supplement research.
- Using a standardized turmeric tablet formulation to ensure consistency in dosage and bioavailability.
- Evaluating both inflammatory and oxidative stress biomarkers, providing a comprehensive view of turmeric's impact.
- Comparing outcomes over a longer period, thereby offering insights into turmeric's potential as a sustainable adjunct therapy in CKD management.

By expanding the timeline and refining the methodology, this research contributes to a more robust understanding of turmeric's clinical benefits in the context of chronic kidney disease.

AUTHOR'S CONTRIBUTION

Nil.

AUTHOR FUNDING

Nil.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

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