International Journal of Pharmaceuticals and Health care Research (IJPHR)

ISSN: 2306-6091

IJPHR |Vol.13 | Issue 2 | Apr - Jun -2025

www.ijphr.com

DOI : https://doi.org/10.61096/ijphr.v13.(SPL 1).2025.271-279

Review

Therapeutic Potential Of *Curcuma Longa* In Acute Kidney Injury: Mechanisms And Clinical Prospects

Prakash Pralhad Sarwade[1], Kavita Narayan Gaisamudre[2*], Rajesh S. Gaikwad[3], K. Vijayalakshmi[4], Dr. Radhika[5], Kalpana Sonwani[6]

[1]Associate Professor and Head, Department of Botany, Shikshan Maharshi Guruvarya R. G. Shinde Mahavidyalaya, Paranda Dist. Dharashiv (Osmanabad) 413502, (M.S.), India.
[2]Assistant Professor, Department of Botany, Shriman Bhausaheb Zadbuke Mahavidyalaya, Barshi Tal. Barshi, Dist- Solapur 413401 Maharashtra, India.
[3]Associate Professor, Department of Botany, Swami Vivekanand, Arts, Commerce and Science College, Mantha, Dist. Jalna, (M.S.) India.
[4]Research scholar, PG dept of Zoology, V.O.Chidambaram college, Thoothukudi- 8, Affiliated by Manonmanium sundaranar University, Thirunelveli, Tamil Nadu, India.
[5]HOD & Associate professor, PG &Dept of Zoology, V.o.chidambaram College, Thoothukudi- 8. Affiliated by Manonmanium sundaranar University, Thirunelveli, India.
[6]Associate professor, Department of Pharmacology, Gsrm memorial college of pharmacy, Lucknow, India

*Author for Correspondence: Kavita Narayan Gaisamudre (Sarwade)
Email: sarwadekp@gmail.com

Published on: 06 Jun 2025

Published by:
DrSriram Publications

Abstract

Acute Kidney Injury (AKI) refers to a rapid (onset within 48 h) deteriorated renal function typically induced by ischemia reperfusion injury, nephrotoxicity or sepsis. Currently, there is only very limited pharmacological treatment with direct impact on the pathophysiological mechanisms of AKI and current treatment strategies are mainly supportive. In this regard, the natural compounds with multitargeted biological activity attract ever greater interest. Turmeric (*Curcuma longa*) and curcumin, its main bioactive compound exhibited impressive therapeutic potential in AKI management because of their powerful anti inflammatory, antiapoptotic, antioxidant and antifibrotic properties. Curcumin modulates key molecular pathways important for the progression of AKI such as inhibition of nuclear factor-kappa B (NF-κB) and Toll-like receptor 4 (TLR4) signaling and activation of nuclear factor E2-related factor 2 (Nrf2), inhibiting proinflammatory cytokines and protecting against oxidative damage and cell death. Curcumin has been shown, in preclinical studies in a variety of models of AKI, to significantly improve renal function, reduce histological damage and improve survival. In addition, curcumin has the capability of thwarting the escalation of AKI to the chronic kidney disease (CKD) by damping the fibrotic signaling pathway of the transforming growth factor beta (TGF-β)/Smad. While

promising, clinical translation of curcumin is hindered by its poor oral bioavailability. To date, there have been ongoing research trying to overcome some of these limitations by look into novel delivery systems and combinational therapies. This review summarizes current knowledge of curcumin on the mechanistic basis for nephroprotective effects of curcumin, provides an assessment of experimental and clinical evidence as to its nephroprotective role and discusses foci for future studies on usage of curcumin in the management of AKI. There is great promise that curcumin, a natural and multi-targeted therapeutic candidate, can provide safe and effective treatment for many renal issues in the changing face of renal medicine.

Keywords: Curcuma longa**,** Curcumin, Acute kidney injury, nephroprotection, oxidative stress, inflammation

INTRODUCTION

Acute kidney injury (AKI) is a portentous syndrome with abrupt renal functional impairment, leading to the accumulation of nitrogenous waste products and electrolyte imbalance [1]. The multifactorial syndrome, present in approximately 10-15% of in-hospital and >50% of intensive care unit admissions, is fraught with significant morbidity and mortality risks, with >20-50% mortality rates in severe cases [2]. Multifactorial pathophysiology of AKI involves several interdependent mechanisms, including renal hypoperfusion, tubular injury, oxidative stress, inflammatory cascades, and apoptosis. With the development of more effective renal replacement therapies and supportive care, the absence of specific pharmacotherapies that target the molecular mechanisms of AKI has established an acute imperative for the development of new therapeutic approaches[3].

Traditional herbal medicines have gained widespread popularity in modern nephrology due to their multi-targeting modes of action and superior safety profiles. Among them, *Curcuma longa* (turmeric), a perennial herb from the Zingiberaceae family, has emerged as one of the most promising candidates[4]. The medicinal property of turmeric well established in Ayurvedic and traditional Chinese medicine for centuries was mainly attributed to its active polyphenolic compound, curcumin (diferuloylmethane). Recent scientific studies have further clarified the pleiotropic actions of curcumin, i.e., strong antioxidant, anti-inflammatory, anti-apoptotic, and anti-fibrotic actions, all of which possess high implications for the pathophysiology of AKI[5].

The scientific rationale for the exploration of the therapeutic potential of curcumin in AKI is its ability to modulate various molecular mechanisms of renal injury. Experimental data have shown that curcumin has the ability to scavenge free radicals efficiently, enhance endogenous antioxidant defense, inhibit pro-inflammatory cytokines and transcription factors (e.g., NF-κB and NLRP3 inflammasome), and modulate apoptotic signaling pathways through Bcl-2 family proteins. These multi-oriented activities make curcumin a potential ideal drug for AKI, which is typically the concurrent activation of the pathways of oxidative stress, inflammation, and cell death[6].

Preclinical research in various AKI models, including ischemia-reperfusion injury, cisplatin-induced nephrotoxicity, and sepsis-induced renal injury, have all uniformly shown that curcumin treatment is capable of significantly curtailing renal damage, histological damage, and mortality. Such promising findings have created growing interest in the clinical application of curcumin's therapeutic activity[7]. However, a few challenges must be overcome, particularly its poor oral bioavailability due to low aqueous solubility, extensive metabolism, and systemic elimination. Recent advances in drug delivery systems, e.g., nanoparticle formulations and concomitant therapies with absorption enhancers like piperine, may overcome these pharmacokinetic limitations[8].

While clinical data specifically examining the effects of curcumin in AKI are limited, enhanced studies in other related illnesses such as chronic kidney disease and diabetic nephropathy have reported favorable effects on renal function parameters and inflammatory markers. Curcumin's excellent safety profile with minimal side effects at high doses does have implications for its potential as an intervention therapy in AKI[9]. Nevertheless, well-controlled randomized studies urgently need to provide evidence of curcumin efficacy in human AKI and to identify optimal dosing regimens and formulations. The aim of the present review is to systematically review the published evidence for therapeutic efficacy of *Curcuma longa* and its active compounds in AKI, with specific focus on the molecular mechanisms of its nephroprotection[10]. Preclinical and clinical findings will be discussed, the existing limitations and flaws outlined, and areas for future research and use in the clinic presented. By synthesis of existing knowledge and determination of the most appropriate

gaps in evidence, the review will provide a basis for further research on this potential natural therapy for AKI Fig.1.

Acute Renal Failure (ARF)1 is a notion that has been heavily reevaluated recently. The most severe acute decrease in kidney function, as seen by severe azotaemia and frequently by oliguria or anuria, was traditionally the one that was prioritised. Modern research, however, reveals that even moderate kidney damage or impairment, as shown by subtle shifts in serum creatinine (sCr)and/or urine output (UO), is indicative of major clinical outcomes. The abrupt decline in renal excretory function is the hallmark of acute kidney injury (AKI). Chronic kidney disease (CKD) can develop from acute kidney injury (AKI) or another acute kidney disease (AKD) characterised by a gradual decline in kidney function or ongoing malfunction of the kidneys, accompanied by the permanent loss of kidney cells and nephrons. There is usually more than one aetiology for this illness. The combination of sepsis, ischaemia, and nephrotoxicity frequently coexists in individuals with AKI, making diagnosis and treatment more complicated. In addition, the condition is prevalent even in patients who do not have a life-threatening illness, thus it is crucial that medical personnel, especially those who do not have training in renal illnesses, can quickly identify it when they see it. Chronic kidney disease (CKD), which is characterised by the persistence of renal illness for more than 90 days, is more common among AKI survivors[12]. Furthermore, researchers no longer view AKI and CKD as distinct conditions, but rather as interconnected stages of the same disease. The ongoing pathological processes and unfavourable effects that arise after acute kidney injury (AKI) have lately been recommended to be referred to as acute kidney disease (AKD)[11].

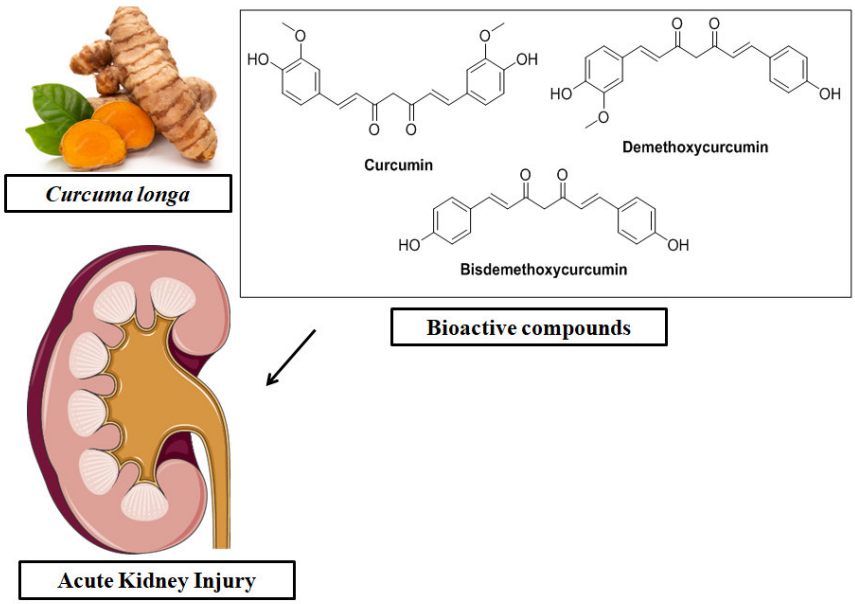

Fig 1: Therapeutic potential of *Curcuma longa* in Acute kidney injury

The prevalence of acute kidney damage (AKI) ranges from 5% to 7.5% among inpatients and can reach 50% to 60% among the critically ill, making it a common diagnosis. Acute kidney injury (AKI) is defined by a sudden decline in renal function and has a complicated pathophysiological mechanism that might have multiple causes[12]. The immediate effects of acute kidney injury (AKI) include longer hospital stays, higher healthcare expenditures, and in-hospital mortality; the longer-term effects include an increased risk of cardiovascular events, the development of chronic kidney disease (CKD), and mortality in the future[13]. The rise in AKI cases over the last several decades may be attributable to better patient care, more accurate diagnosis, and changes in medication usage, such as less nephrotoxic drugs, better dialysis, and less dopamine and diuretics. Although there has been a decrease in mortality rates in critically sick patients with AKI, the rates remain high and tend to rise with the severity of AKI, especially in cases when dialysis is required. Chronic kidney disease (CKD), which is characterised by the persistence of renal illness for more than 90 days, is more common among AKI survivors[14]. Furthermore, researchers no longer view AKI and CKD as distinct conditions, but rather as interconnected stages of the same disease. The ongoing pathological processes and unfavourable effects that arise after acute kidney injury (AKI) have lately been recommended to be referred to as acute kidney disease (AKD). Kidney disease that lasts for 7–90 days after an AKI-initiating event is called acute kidney damage

(AKD). This damage can be acute or subacute, and it also involves a loss of kidney function. The significance of renal recovery is underscored by the fact that a full recovery within 48 hours is usually linked to the quick reversal of AKI. Additionally, the effect of AKD on pre-existing CKD increases the likelihood of kidney disease development[15].

Epidemiology

The real impact of AKI is underestimated due to the lack of a universally accepted definition of the syndrome, which greatly affected both the reported incidence and clinical significance of the condition[16]. The definition, patient population, and study area all have a role in the incidence's variability. The frequency and aetiology of AKI differ significantly between industrialised and poor countries. The prevalence, aetiology, pathophysiology, and public health consequences of acute kidney injury (AKI) in industrialised and developing countries were compared in a recent review. There has been an uptick in the incidence of AKI in industrialised nations. It is estimated to occur in up to 15% of hospital inpatients and up to 60% of critically ill patients, making it the most prevalent[17]. Community AKI, on the other hand, is rare, yet a new study found that it accounts for 4.3% of hospital admissions[18]. The frequency of paediatric AKI is weakly characterised, and major epidemiologic studies involving children are lacking, despite the fact that numerous studies have concentrated on particular populations (the elderly and children). The majority of paediatric epidemiologic studies either concentrated on populations in critical care or children requiring dialysis, or they were conducted in a single centre with a small number of patients. There is an age-dependent correlation between AKI and advanced age, according to several studies, and AKI is on the rise among the elderly (often classified as those 65 and up). This is because the kidneys undergo a number of changes as we get older, both anatomically and physiologically. It's also because many people with chronic kidney disease (CKD), high blood pressure, and cardiovascular disease have other health issues that can necessitate procedures or medications that are harmful to the kidneys. There are both immediate and delayed negative consequences linked to AKI, according to multiple research[19].

Pathophysiology

There are four stages of ATN and the resulting reduction in GFR from a clinical perspective: commencement, extension, maintenance, and recovery. There is a direct correlation between the cellular activities that take place throughout damage and recovery and these clinical phases[17]. When renal blood flow (RBF) becomes low enough, acute cell damage and dysfunction ensue, marking the beginning of acute tuberculosis (ATN). Damage to the cells lining the renal tubules is a hallmark of the first stage. Both the inflammatory reaction and persistent hypoxia after the first ischaemic episode mark the beginning of the extension phase[18]. The corticomedullary junction (CMJ), also known as the outer medullary region, is where both occurrences are most noticeable in the kidney. The renal tubular epithelium remains ischemia-dependent and an inflammatory response is shown in ischaemic ARF, both of which are likely caused by damage to renal vascular endothelial cells during this phase[19]. Damage and cell death persist throughout this stage, with the outer medulla being the site of most necrosis and apoptosis. On the other hand, when blood flow is almost normal again in the outer cortex's proximal tubule cells, they actually undertake cellular repair and show morphological improvement. As part of the maintenance clinical phase, cells try to restore and maintain tubule and cellular integrity by repairing, migrating, apoptosing, and proliferating[20]. The intensity of the initial incident determines the level of stability in the GFR. Slowly but surely, cellular function improves throughout this reorganisation and repair phase, which paves the way for organ function to improve as well. As the flow of blood returns to normal, the balance within and between cells is restored by the epithelial cells. Cellular differentiation, epithelial polarity restoration, and normalisation of cellular and organ function are all aspects of the recovery phase that are being worked on[21].

Bioactive compounds of *Curcuma longa*

In addition to this, acute kidney injury (AKI) which accounts for as many as 2 million deaths worldwide each year, is another source of the human pain and suffering for which *Curcuma longa* (turmeric) might provide assistance since its bioactive compounds are known to also carry therapeutic potential for that disease[22]. Though there are other components, the curcuminoids are the most important of these, at about 2-6% of turmeric and consisting of curcumin (diferuloylmethane), demethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC)[23]. The primary active constituent, curcumin is a very potent antioxidant which scavenges reactive oxygen species (ROS) and increases endogenous antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase. In addition, retention of NF-κB and downstream pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF-α) and interleukins (IL-6, IL-1β) which all contribute to AKI pathogenesis, demonstrates strong anti-inflammatory effects. Curcumin also modulates apoptotic pathways by upregulating antiapoptotic proteins (Bcl2) and downregulation of proapoptotic (Bax), protecting renal tubular cells against injury[24]. The other curcuminoids, DMC and BDMC, are structurally

similar to curcumin, but have enhanced stability as well as complementary effects, notably more powerful anti-fibrotic activity by TGF-β signaling downregulation (which is precisely applicable for preventing AKI progression to chronic kidney disease).

However, in addition to curcuminoids, turmeric is also rich in volatile oils called turmerones (3–7% by mass) that include α-turmerone and β-turmerone and these provide other nephroprotective effects. These compounds also have anti-inflammatory activity which is due to inhibition of microglial activation and they have a protective effect against nephrotoxic agents such as cisplatin, in experimental models[25]. These smaller amounts of other bioactive molecules from the essential oil fraction such as atlantone and zingiberene may provide supplementary antioxidant and anti-fibrotic benefits. In addition, turmeric contains polysaccharide immunomodulatory compounds (Ukonans A–D) and flavonoids (quercetin and kaempferol) that work synergistically together with the main compounds for increasing the overall therapeutic efficacy.

Although this has raised turmeric's bioactive compound prospective application, clinical application has been limited by poor bioavailability[26]. The curcuminoids are poorly soluble in water, metabolized rapidly by the liver (glucuronidation and sulfation) and rapidly eliminated from the systemic circulation[27]. In order to circumvent these deficiencies, a number of formulation strategies have been developed such as nanoparticle delivery systems, mixtures of absorption enhancers e.g. piperine derived from black pepper or phospholipid complexes (e.g., Meriva®) which dramatically enhance the bioavailability and therapeutic role. Being a multi prong system that encompasses antioxidant, anti inflammatory, anti apoptotic and anti fibrotic pathways, turmeric (curcumin) represents a particularly promising candidate for AKI management. Further research is however still needed to optimize delivery methods, determine best dosing regimens and to validate efficacy in clinical trials, especially in human AKI populations[28]. A combination of turmeric, curcuminoids and the mixture of other minor constituents most probably produces synergistic effects which should lead to more therapeutically beneficial outcomes than those of pure curcuminoids. For this reason, it is suspected that whole turmeric extracts or carefully developed formulations based on turmeric are likely to yield the most clinical potential for the prevention and treatment of AKI[29].

Therapeutic effects of *Curcuma longa* in Acute kidney injury

Wang *et al*.,2021 This study aimed to examine the possible therapeutic effects of curcumin on renal function, inflammatory response, and microcirculatory perfusion, as well as its protective effects on S-AKI. The levels of creatinine (Scr), cystatin C (CysC), IL-6, and TNF-α in the blood were noticeably reduced in the CLP+Cur group compared to the CLP group ($P < 0.05$). By measuring the contrast enhanced ultrasound (CEUS) quantitative measures [peak intensity (PI), half of descending time (DT/2), area under curve (AUC); $P < 0.05$], treatment with curcumin increased renal microcirculation at 24 hours. Curcumin therapy mitigated CLP-induced damage in histopathological studies. By lowering inflammatory response and increasing renal microcirculatory perfusion, curcumin can relieve S-AKI in rats. Curcumin has the makings of a new kind of medicine that could help lessen or eliminate S-AKI[30].

Fan *et al*.,2017 The kidneys are extremely vulnerable to ischaemia and reperfusion because of how perfused they are. Ischemia-reperfusion (IR)-induced acute kidney injury (AKI) is a key component of ischaemic acute renal failure (IARF), which occurs often in the perioperative period of clinical practice. As a result, research into the prevention and treatment of IR-induced AKI is essential, since this condition has substantial therapeutic relevance. A polyphenol chemical called curcumin, which comes from the turmeric plant Curcuma longa, has been demonstrated in a prior study to protect the kidneys from ischemia-reperfusion damage (IRI). Nevertheless, our understanding of the exact processes by which curcumin prevents IR-induced AKI remains incomplete. Adiponectin and insulin signal transduction pathways interact with one another, and the protein-coding gene APPL1 is known to play a role in this interaction. Curcumin treatment considerably increased APPL1 expression and inhibited the activation of Akt following IR treatment in the kidney, according to the study's observations of its effects in experimental models of IR-induced AKI, which aimed to investigate the molecular mechanisms of curcumin's effects in kidney ischemia/reperfusion models. We found that hypoxia-reoxygenation (HR) therapy worsened apoptosis of renal tubular epithelial cells in vitro when compared to sham control cells. When administered intravenously, curcumin dramatically reduced the cell death rate of renal tubular epithelial cells. In addition, renal tubular epithelial cells treated with HR had worsened apoptosis after APPL1 knockdown activated Akt. The effects of APPL1 knockdown were directly reversed by inhibiting Akt, on the other hand[31].

Russo *et al*.,2018 The rhizomes of the *Curcuma longa* L. ("turmeric," Zingiberaceae) plant contain the anti-inflammatory polyphenol curcumin, which has a long history of use. In this study, we intended to assess the anti-inflammatory properties of *C. longa* in relation to doxorubicin (DOX, 3.5 mg.kg−1 IV)-induced renal injury. We examined four sets of Wistar rats: two sets with DOX-induced renal damage, one set given regular chow, and one set given standard food combined with *C. longa* (5 mg.g−1). The identical diets were given to two additional control groups that did not suffer from renal damage. Every two weeks, we took measurements of albuminuria, weight, and caloric consumption. When administered to rats with DOX-induced kidney injury for 8

weeks, *C. longa* did not alter albuminuria levels, but it reduced the excretion of urinary inflammatory markers MCP-1 and TGF-β. Additionally, it reduced immunostaining for desmin, vimentin, and ED-1+ cells in the kidney tissues of these rats. Furthermore, glomerular and tubule interstitial damage ratings were considerably lower in the C. longa group compared to the DOX-STD group. Ultimately, by giving rats with DOX-induced kidney injury powdered rhizomes of C. longa for 8 weeks, the researchers were able to decrease albuminuria, urinary inflammatory markers MCP-1 and TGF-β, histopathological alterations, and immunostaining for ED-1+ cells, vimentin, and desmin[32].

Intan *et al*.,2025 Examining the effects on tumour necrosis factor-alpha (TNF-α), KIM-1, and caspase-3 levels, this study sought to assess the renoprotective potential of a combination extract of *Curcuma longa* and Curcuma zedoaria in lowering nephrotoxicity. On days 1–20, twenty-five rats were randomly assigned to one of three groups: the control group (CIS), the combination extract (CUR100), or the combined extract (CUR200) at doses of 100, 200, or 400 mg/kg, respectively. On days 7 and 14 of the 20-day extract therapy, all subjects except the NS group (getting normal saline intraperitoneally) were given intraperitoneal CIS (1 mg/kg). The combined extract group of rats outperformed the CIS group in terms of body weight gain and expression levels of TNF-α, KIM-1, and caspase-3, while the CIS group rats showed no change. Histopathological analysis showed that compared to the CIS group, the extract group had reduced kidney damage. The most noticeable protective effect was produced by the combined extract, which reduced kidney TNF-α, KIM-1, and caspase 3 when given at a dosage of 200 mg/kg. The potential therapeutic agent for lowering nephrotoxicity by suppressing levels of TNF-α, KIM-1, and caspase-3 lies in the combination extract of *C. longa* and *C. zedoaria*. The efficacy of this combo treatment in human subjects needs more investigation[33].

Mechanism of Curcumin in Acute kidney injury

Curcuma longa is the source of curcumin, the principal bioactive compound and it is nowadays emerging as an effective therapeutic strategy for mitigating acute kidney injury (AKI) at multiple cellular and molecular levels. The strong anti inflammatory action is one of the major ways curcumin exerts its renoprotective effects. Furthermore, the upregulation of proinflammatory cytokines (e.g. TNF-α, IL-1β and IL-6) in AKI also further promotes renal tubular damage. Curcumin is actually very good at inhibiting the activation of nuclear factor kappa B (NF-κB), a transcription factor that controls the expression of these cytokines and other inflammatory mediators. It also contains antiinflammatory effects by suppressing Toll like receptor 4 (TLR4) signaling which is an important pathway in inflammation such as during sepsis and ischemia re perfusion induced AKI. Curcumin, not only has anti inflammatory properties but also has strong antioxidant activity. Elevated reactive oxygen species (ROS) and oxidative stress which are associated with AKI, cause lipid peroxidation, DNA damage and mitochondrial dysfunction. In the process of neutralizing the ROS, curcumin upregulates the activity of endogenous antioxidant enzymes, superoxide dismutase (SOD), catalase and glutathione peroxidase. Moreover it also activates the nuclear factor erythroid 2–related factor 2 (Nrf2) pathway which upregulates a suite of nuclear antioxidant response genes which in turn protect renal tissues from oxidative damage.

In addition, curcumin can modulate intrinsic and extrinsic apoptosis pathways in the antiapoptotic manner in renal tubular epithelial cells. It upregulates anti-apoptotic protein (Bcl-2) and downregulates pro-apoptotic factors (Bax and caspase-3) maintaining cellular integrity and function. Curcumin also holds mitochondria to prevent the release of cytochrome c which leads to caspase activation. It is another crucial mechanism for its antifibrotic activity which is of great importance in the late phase of AKI and the progression to chronic kidney disease. Inhibition of the transforming growth factor-beta 1 (TGF-β1)/Smad signaling pathway, the central player in renal fibrosis and epithelial-to-mesenchymal transition (EMT) employment, is another role of curcumin. Curcumin also suppresses interstitial fibrosis and glomerular scarring by suppressing TGF-β1 and associated extracellular matrix proteins. Moreover, curcumin has been found to have protective effect on renal vasculature and improving microcirculation and reducing endothelial dysfunction during ischemic injury. These multifaceted mechanisms give evidence for the nephroprotective potential of curcumin. Although its clinical application is limited by poor bioavailability, novel drug delivery systems, including nanoparticles, liposomes and co-administration with bioenhancers (piperine), can improve bioavailability. Although individually curcumin is not perfect, its anti-inflammatory, antioxidant, anti apoptotic and antifibrotic properties make it a collective potential candidate for prevention and treatment of AKI.

Future prospects

Advances in pharmaceutical technology and an increased knowledge of the molecular mechanisms of curcumin, however, make its future application in the management of acute kidney injury (AKI) seem very promising. Though preclinically curcumin exhibits nephroprotective effects, clinical utility is limited due to poor bioavailability, rapid metabolism and low water solubility. To conquer these drawbacks, future researches need to make the effort for a new formulation like nanoparticles, liposomes, phytosomes and curcumin loaded hydro gels which can increase its absorbance, stability and particularly renal tissue targeting. Furthermore,

curcumin's therapeutic index could be substantially improved by combining curcumin with bioenhancers such as piperine or conjugating it with biopolymers. Future exploration is also required in terms of integrating curcumin into combination therapy with conventional nephroprotective agents or antioxidants so as to obtain synergistic effects and wider clinical outcomes. Standardized dosing regimens, as well as safety and efficacy profiles in diverse AKI populations are urgently needed and can only be established from large scale, well-designed clinical trials. Additionally, the use of systems biology and omics technologies could be leveraged to identify biomarkers to predict responsiveness to curcumin therapy and thus design personalized treatment strategies. It also has clinical importance in evaluating long term benefits of curcumin in preventing progression of AKI to chronic kidney disease (CKD). With strategic research efforts and innovative formulation strategies, curcumin is positioned to be enjoyed as a natural multi-targeted approach in mainstream therapeutic protocols for AKI overall.

CONCLUSION

Finally, *Curcuma longa* and especially its active component curcumin seem to be a very good natural treatment agent for preventing and managing Acute Kidney Injury (AKI). There has been extensive preclinical research showing curcumin's multifaceted protective mechanisms, with potent anti inflammatory, antioxidant, anti apoptotic, antifibrotic effects. Consequently such actions directly strike at these key pathophysiological processes involved in AKI such as oxidative stress, inflammatory cytokines, tubular epithelial cell apoptosis and fibrotic remodeling. Consistent efficacy of curcumin was demonstrated in experimental models of ischemia-reperfusion injury, nephrotoxin induced injury and septic AKI which improved renal function markers, histological architecture and survival. Despite these encouraging findings, its clinical application is limited because of the stability problems and lack of standardization as well as the bioavailability issues. Therefore current and future research must be targeted towards improving its pharmacokinetic profile through advanced drug delivery systems like nanocarriers, liposomes and phytosomal formulation and by usage of absorption enhancers like piperine. To date, the number of clinical trials is few and of small scale; thus large, randomized clinical trials are needed to determine optimal dosing, long-term safety and therapeutic efficacy in humans. In addition, curcumin therapy can be integrated with currently used treatment protocols and with the determination of its use in combination therapy, it may help establish synergism. Curcumin can not only inhibit AKI fibrotic pathways as an acute protection measure but also as an anti – chronic kidney disease agent because of its ability to inhibit fibrotic pathways. Continued research and innovation into curcumin thus make it a potential, natural adjunct or alternative to the clinical management of AKI.

REFERENCES

1. Intan PR, Alegantina S, Fajri H, Ekawasti F, Isnawati A, Lienggonegoro LA, Nikmah UA, Sunarno S, Mariya SS, Sutardi LN, Setiyono A. Combined extracts of Curcuma longa and Curcuma zedoaria ameliorates cisplatin-induced kidney damage in rats. Open Veterinary Journal. 2025 Jan 31;15(1):428.
2. Liu X, Zhou Y, Lu Z, Yang F, Wang Y, Zhang S, Zhang J, Zou H, Lin M. Network Pharmacology and Metabolomics Reveal Anti-Ferroptotic Effects of Curcumin in Acute Kidney Injury. Drug Design, Development and Therapy. 2024 Dec 31:6223-41.
3. Widowati W, Laksmitawati DR, Pratami DK, Rahmat D, Kiran SR, Devi JA, Priyandoko D, Dewi NS, Sutendi AF, Azis R, Hadiprasetyo DS. Protective effects of turmeric extract, curcumin, demethoxycurcumin, bis-demethoxycurcumin, and ar-turmerone from Curcuma longa L. rhizomes on acetaminophen-induced hepatotoxicity in HepG2 cells. Asian Pacific Journal of Tropical Biomedicine. 2025:10-4103.
4. Ghasemzadeh Rahbardar M, Hosseinzadeh H. The ameliorative effect of turmeric (Curcuma longa Linn) extract and its major constituent, curcumin, and its analogs on ethanol toxicity. Phytotherapy Research. 2024 May;38(5):2165-81.
5. Machado IC, Facincani I, Aragon DC, da Silva Coppede J, Pereira AM, Carmona F. Curcuma longa L.(turmeric) as adjuvant therapy in childhood idiopathic nephrotic syndrome: A double-blind, randomized, placebo-controlled clinical trial. Advances in Integrative Medicine. 2025 Mar 1;12(1):87-92.
6. Patel VM, Sadariya KA, Patel DR, Patel RD, Sarvaiya VN, Bhavsar SK. Therapeutic efficacy of Glycyrrhiza glabra and Curcuma longa on adenine induced chronic kidney disease in rats.
7. Al-Worafi YM. Evidence-Based Complementary, Alternative, and Integrated Medicine and Efficacy and Safety: Acute Kidney Injury. Handbook of Complementary, Alternative, and Integrative Medicine.:421-36.

8. Britto I, Couto H, de Paiva BR, Brito JS, Alvarenga L, Cardozo LF, Leite PE, Berretta AA, Ribeiro-Alves M, Delgado VP, Cunha DF. Effects of Curcuma longa L. and Green Propolis Extract-Loaded Microcapsules Supplementation on Inflammation in Hemodialysis Patients: Preliminary Results of a Randomized Clinical Trial. Life. 2025 Jun.
9. Wakil AM, Stephen J, Mohammed A, Ekwem PC, Ngulde SI, Sandabe UK, Mbaya AW, Ojo NA, Sodipo OA. Acute Toxicity and Effects of Ethanolic Extract of Turmeric (Curcuma longa) on Some Serum Biochemical Parameters in Rats. Sahel Journal of Life Sciences FUDMA. 2024 Dec 31;2(4):149-55.
10. Hidayat R, Parlindungan F, Nisa JI, Mahendra AI, Indika MI, Efendi C. Efficacy of Curcuma longa in relieving pain symptoms of knee osteoarthritis patients: a systematic review and meta-analysis of clinical trials. Journal of Rheumatic Diseases. 2025 Jan 1;32(1):17-29.
11. Alvitigala BY, Gooneratne LV, Gnanathasan CA, Wijewickrama ES. Snakebite-associated acute kidney injury in South Asia: narrative review on epidemiology, pathogenesis and management. Transactions of The Royal Society of Tropical Medicine and Hygiene. 2025 Jan 3:trae077.
12. Ostermann M, Lumlertgul N, Jeong R, See E, Joannidis M, James M. Acute kidney injury. The Lancet. 2025 Jan 18;405(10474):241-56.
13. Zaragoza JJ, Chavez-Iñiguez JS, Vazquez-Rangel A. Prevalence of acute kidney injury in Mexico; a systematic review and meta-analysis of pre-pandemic reports. Renal Failure. 2025 Dec 31;47(1):2449573.
14. Patidar KR, Ma AT, Juanola A, Barone A, Incicco S, Kulkarni AV, Hernández JL, Wentworth B, Asrani SK, Alessandria C, Abdelkader NA. Global epidemiology of acute kidney injury in hospitalised patients with decompensated cirrhosis: the International Club of Ascites GLOBAL AKI prospective, multicentre, cohort study. The Lancet Gastroenterology & Hepatology. 2025 May 1;10(5):418-30.
15. Rane RP, Soundranayagam S, Shade DA, Nauer K, DuMont T, Nashar K, Balaan MR. Renal involvement in sepsis: acute kidney injury. Critical Care Nursing Quarterly. 2025 Apr 1;48(2):100-8.
16. Takeuchi T, Rahman AK, Ghazi L, Moe OW, Toto RD, Siew ED, Neyra JA, Gutierrez OM. Epidemiological risk factors for acute kidney injury outcomes in hospitalized adult patients: a multicenter cohort study. Clinical Kidney Journal. 2025 Feb;18(2):sfae426.
17. Soranno DE, Awdishu L, Bagshaw SM, Basile D, Bell S, Bihorac A, Bonventre J, Brendolan A, Claure-Del Granado R, Collister D, Curtis LM. The Role of Sex and Gender in Acute Kidney Injury-Consensus Statements from the 33rd Acute Disease Quality Initiative. Kidney International. 2025 Jan 21.
18. Rao PS, Priyamvada PS, Bammigatti C. Snakebite envenomation-associated acute kidney injury: a South-Asian perspective. Transactions of The Royal Society of Tropical Medicine and Hygiene. 2025 Jan 3:trae114.
19. Steflik HJ, Selewski DT, Corrigan C, Brinton DL. Acute kidney injury associated with increased costs in the neonatal intensive care unit: analysis of Pediatric Health Information System database. Journal of Perinatology. 2025 Jan;45(1):94-100.
20. Gembillo G, Spadaro G, Santoro D. Link between obstructive uropathy and acute kidney injury. World Journal of Nephrology. 2025 Mar 25;14(1).
21. Hachimi A, El-Mansoury B, Merzouki M. Incidence, pathophysiology, risk factors, histopathology, and outcomes of COVID-19-induced acute kidney injury: a narrative review. Microbial Pathogenesis. 2025 Jan 31:107360.
22. Tan X, Li M, Chen J, Liu G, Lu Z. Acute kidney injury and iron metabolism: A narrative review focusing on pathophysiology and therapy. Smart Molecules. 2025:e20240026.
23. Baker ML, Cantley LG. Adding insult to injury: the spectrum of tubulointerstitial responses in acute kidney injury. The Journal of Clinical Investigation. 2025 Mar 17;135(6).
24. Alvitigala BY, Gooneratne LV, Gnanathasan CA, Wijewickrama ES. Snakebite-associated acute kidney injury in South Asia: narrative review on epidemiology, pathogenesis and management. Transactions of The Royal Society of Tropical Medicine and Hygiene. 2025 Jan 3:trae077.
25. Kanbay M, Mizrak B, Alper EN, Copur S, Ortiz A. Acute kidney injury following CAR-T cell therapy: a nephrologist's perspective. Clinical Kidney Journal. 2025 Jan;18(1):sfae359.
26. Rane RP, Soundranayagam S, Shade DA, Nauer K, DuMont T, Nashar K, Balaan MR. Renal involvement in sepsis: acute kidney injury. Critical Care Nursing Quarterly. 2025 Apr 1;48(2):100-8.
27. Selby NM, Francis ST. Assessment of Acute Kidney Injury using MRI. Journal of Magnetic Resonance Imaging. 2025 Jan;61(1):25-41.
28. Zhang C, Xiang Z, Yang P, Zhang L, Deng J, Liao X. Advances in Nano-Immunomodulatory Systems for the Treatment of Acute Kidney Injury. Advanced Science. 2025 May;12(17):2409190.
29. Ostermann M, Lumlertgul N, Jeong R, See E, Joannidis M, James M. Acute kidney injury. The Lancet. 2025 Jan 18;405(10474):241-56.

30. Wang S, Zhao P, Zhang Y, Zhu L, Zhu J, Luo Y, Li Q. The therapeutic effects of curcumin in early septic acute kidney injury: an experimental study. Drug Design, Development and Therapy. 2021 Oct 7:4243-55.
31. Fan Y, Chen H, Peng H, Huang F, Zhong J, Zhou J. Molecular mechanisms of curcumin renoprotection in experimental acute renal injury. Frontiers in pharmacology. 2017 Dec 12;8:912.
32. Russo ER, Facincani I, Nakazato KC, Coimbra TM, Crevelin EJ, Pereira AM, Carmona F. Oral administration of powdered dried rhizomes of Curcuma longa L.(turmeric, Zingiberaceae) is effective in the treatment of doxorubicin-induced kidney injury in rats. Phytotherapy Research. 2018 Dec;32(12):2408-16.
33. Intan PR, Alegantina S, Fajri H, Ekawasti F, Isnawati A, Lienggonegoro LA, Nikmah UA, Sunarno S, Mariya SS, Sutardi LN, Setiyono A. Combined extracts of Curcuma longa and Curcuma zedoaria ameliorates cisplatin-induced kidney damage in rats. Open Veterinary Journal. 2025 Jan 31;15(1):428.