

Role of Curcumin as Anti-Oxidant in Nephrotoxicity

Abstract

Curcumin, a phenolic compound from the rhizome of the *Curcuma longa* linn (turmeric or curcuma) is a plant member of the ginger family (Zingiberaceae), endemic in tropical and subtropical fields of India, China and South East Asia. Ancient texts of Indian medicine explain the use of curcumin in inflammatory diseases, wound healing, and abdominal problems. It has been used as a dietary supplement for centuries and considered pharmacologically safe, recently has been known with anti-cancer and multiple properties, including anti-inflammatory, antioxidant and antiangiogenic. Also there are some evidences about preventive role of curcumin in nephrotoxicity and nephropathy, Antioxidant and anti-oxidative stress properties of curcumin proposed for its useful effect of curcumin in nephropathy. This mini-review has been designed to discuss these aspects of this magic compound.

Keywords: Curcumin; Oxidative stress; Anti-oxidant; Nephrotoxicity; Nephropathy

Review Article

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Mohammad Shterpour¹, Ramin Ataee^{1,2*} and Ali Morad heydari Gorgi³

¹Pharmaceutical Sciences Research Center, Mazandaran University of Medical Sciences, Iran

²EDC center, Mazandaran University of Medical Sciences, Iran

³Thalassemia research center, Mazandaran University of Medical Sciences, Iran

***Corresponding author:** Ramin Ataee, Pharmaceutical Sciences Research Center, Mazandaran University of Medical Sciences, Km 18, Khazar Abad road, Payambar Azam buildings, Mazandaran University of Medical Sciences, Iran, Tel: +98911 323 2804; Email: raminataee1349@gmail.com

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General Description

Curcumin, a phenolic compound from the rhizome of the *Curcuma longa* linn (turmeric or curcuma) is a plant member of the ginger family (Zingiberaceae), endemic in tropical and subtropical fields of India, China and South East Asia [1]. Curcumin or froyl methane is a hydrophobic polyphenol derived and the chief component of the spice turmeric and is derived from the rhizome of the *Curcuma longa*. Its' uses are both orally and as a topical ointment to treat some disorders. It is widely used in traditional Indian medicine to treat hepatic disorders, anorexia, cough, diabetic wounds, rheumatoid arthritis, and sinusitis. Turmeric paste in slaked lime is a popular home remedy for the treatment of inflammation and wounds [1,2]. Ancient texts of Indian medicine explain the use of curcumin in inflammatory diseases, wound healing, and abdominal problems. It has been used as a dietary supplement for centuries and considered pharmacologically safe, recently has been known with anti-cancer and multiple properties, including anti-inflammatory [3], antioxidant [4,5] and antiangiogenic [6,7]. In animal's studies, administration of this compound inhibited polyp formation and increased cell necrosis in colon cancer tissues [8]. Among the potential pathways involved in these anti-cancer or anti-inflammatory properties, inhibition of nitric oxide synthase, activation of receptor tyrosine kinase and protein kinase C (PKC), alteration of the transcriptional factors c-jun/AP-1 and p53 as well as inhibition of arachidonic acid metabolism, lipoxygenase and cyclooxygenase activity have been determined [9,10]. Also there are some studies to combine it with others anti-cancer herbal chemical medicines such as green tea to induce a strong inhibitory effect in oral cancer and non-small cell lung cancer [10].

Turmeric rhizome is including three analog colours

Curcumin, demethoxy curcumin (DMC) and *bis* demethoxy

curcumin (BDMC) which collectively are called curcuminoids. These compounds are the cause of the yellow colour in turmeric and differ in the position of the methoxy groups on the aromatic ring (Figure 1) [2]. Among of the three curcuminoid, curcumin in turmeric is the most abundant 7. Several studies have reported that curcumin turmeric has considerable biological properties including antitumor and anticancer activity, reducing blood and liver cholesterol levels, boosting immune function, cardiovascular disease deterrence, and prevention of damage to biological membranes against oxidation, antiinflammatory and reduce rheumatoid arthritis [2].

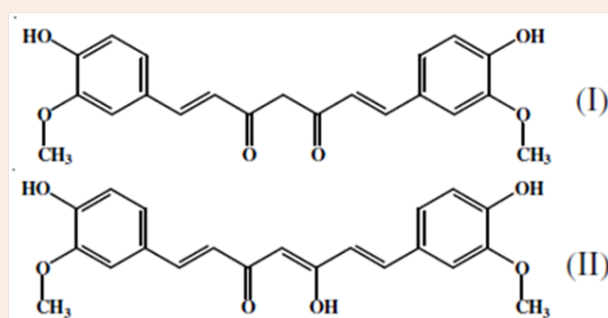


Figure 1: I: Keto form of curcumin; II: Enol form of curcumin.

Anti-oxidant and anti oxidative stress activity of curcumin

Also it has been shown that curcumin is a bifunctional antioxidant [11] because of its properties to react directly with reactive species and up-regulation of many cytoprotective and antioxidant proteins. Also it can scavenge superoxide anion (O₂⁻) [12,13], hydroxyl radicals (OH), H₂O [13,14], singlet oxygen [15], nitric oxide [16,17], peroxyxynitrite [18] and peroxy

radicals (ROO₂) [14]. So these mechanisms can confirm some of the cytoprotective effects of this herbal compound. The phenolic groups in the structure of curcumin can explain its properties to react with reactive oxygen species (ROS) and reactive nitrogen species (RNS) and may probably explain one of the mechanisms through which it protects the epithelial cells of renal tubules from oxidative damage induced by H₂O₂ [19]. The indirect antioxidant activity of curcumin is explained by its ability to induce the expression of cytoprotective proteins such as superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GPx), heme oxygenase 1 (HO-1), glutathione-S-transferase (GST), NAD(P)H: quinone oxidoreductase 1 (NQO1) and γ -glutamylcysteine ligase (γ GCL) [20].

Oxidative stress is an imbalance between free radicals and antioxidant systems to cause chronic diseases such as cancer, diabetic nephropathy or neuropathy, Alzheimer's and Parkinson's diseases [2]. Reactive oxygen species (ROS) and free radicals such as hydroxyl radicals and hydrogen peroxide are produced in the human body during normal metabolic pathways and exposure to exogenous stress such as ionizing radiation and air pollutants which can induce adverse effects on the normal physiological activity of cells. The body's system has antioxidant defense and enzymes which neutralize the ROS. Unfortunately, increasing of ROS levels or decreasing ability for detoxification of the antioxidant defense system can lead to increased oxidative stress and turn cell damage and death [21-23]. Antioxidants have protective effects on the cells so that they can protect it from damages caused by unexpectedly and uncontrollably produced ROS [24,25]. Although a number of synthetic and natural antioxidant compounds have already been identified, the search for effective antioxidant and lesser side effects and toxicity is being continued. Turmeric is one of the plants that contain natural active ingredients and safe [24].

Role of curcumin in nephrotoxicity

According to some studies, preventive role for curcumin in some nephrotoxicities conditions has been known. For example, curcumin treatment in an animal model of diabetic nephropathy diminished proteinuria and improved creatinine clearance [20]. Also, it attenuated oxidative stress by reducing levels of nicotinamide adenine dinucleotide phosphate (NADPH) [20]. Also according to some other studies, it was suggested that, the nephroprotective effect of curcumin was related to the downregulation of the profibrotic cytokines vascular endothelial growth factor (VEGF), TGF- β , CTGF and osteopontin as in extracellular matrix proteins fibronectin and collagen IV [20]. Cellular signalings such as inhibition of nuclear factor kappa-light-chain enhancer of activated B cells (NF- κ B) [26,27] and decrease of macrophage infiltration [27] histone acetyltransferase p300 protein and oxidative stress [26] also these mechanisms may be as those, through which the curcumin protects against diabetic nephropathy. Also, Waseem M et al. [28] at 2013 in a research has shown that curcumin could have protective effect in acute nephrotoxicity model induced with cisplatin in rat and reduced lipid peroxidation and protein carbonyl levels [28]. In Ukei M et al. [29] study at 2013 in mice who received curcumin 10mg/kg

with cisplatin has been shown, The levels of inflammation factors as tumor necrosis factor (TNF)- α and monocyte chemoattractant protein (MCP)-1 have been decreased [29]. Also in a research by Manikandan R et al at 2011, in acute nephrotoxicity model of gentamycin, it was demonstrated that curcumin could reduced iNOS and NF- κ B expression [30] and in a study at 2009 in Turkey by Cekmen M et al. [31] curcumin reduced BUN/Cr and MDA in rats in a model of acetaminophen nephrotoxicity [31]. Also we have a study similar to Cekmen M et al. [31] about protective role of curcumin in acute and chronic nephrotoxicity induced by lithium with similar MDA and histopathological results also by attenuating BUN and creatinine levels in rats by which its' results are under publication.

Conclusion

According to this minireview we can conclude that curcumin because of its' anti-oxidant and anti-oxidative stress properties can have protective effects against many diseases especially nephropathies as in diabetes or other chemical intoxications.

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